The Nature and Significance of Temperament Differences for Social-Emotional Functioning in the Context of Autism in Early-Life

Lacey Carmen Chetcuti

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College of Science, Health and Engineering
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List of Abbreviations

ADOS-T	Autism Diagnostic Observation Schedule, Toddler Module
AOSI	Autism Observation Scale for Infants
ASD	Autism Spectrum Disorder
DASS-21	Depression, Anxiety, and Stress Scales
DSM-5	Diagnostic and Statistical Manual of Mental Disorders, 5th edition
ECBQ	Early Childhood Behavior Questionnaire
ELC	Early Learning Composite
IBQ-R	Infant Behavior Questionnaire-Revised
ITSEA	Infant-Toddler Social and Emotional Assessment
LPA	Latent Profile Analysis
MSEL	Mullen Scales of Early Learning
SACS-R	Social Attention and Communication Surveillance-Revised

Thesis Abstract

While an extensive literature has documented differences in temperament associated with Autism Spectrum Disorder (hereafter, *autism*), little is known about how children with autism traits differ from one another in early-life. Nonetheless, individual differences in temperament might help to explain the observed heterogeneity. This research sought to clarify the nature and role of individual temperament differences in the context of emerging autism, including as predictive of social-emotional functioning (specifically, internalizing and externalizing symptoms). The existing literature on temperament in autism was summarized through a systematic review/meta-analysis, with knowledge gaps outlined in a companion editorial. Four empirical studies drew on data collected prospectively from a community-referred cohort of 103 infants (68% male) recruited due to showing early autism traits at around age 12-months. Caregivers completed questionnaire measures of child temperament and social-emotional functioning at mean child ages of 12- (Time 1 [T1]), 18- (Time 2 [T2]), and 24 months (Time 3 [T3]). At T1, infants with autism traits were classified into three subgroups with distinct temperament trait constellations. Follow-up analyses revealed continuity in the qualitative features of these temperament subgroups, and in children's classifications among these at T2 and T3. A similar pattern of subgroup differences in concurrent social-emotional functioning was also apparent at each timepoint. This research also explored potential indirect pathways to early childhood social-emotional difficulties, involving interplay among infant temperament and caregiver self-reported psychological distress. Cross-sectional and prospective longitudinal analyses revealed a pathway from caregiver psychological distress through infant temperament to early childhood social-emotional difficulties in this sample of children with autism traits. These results were maintained when controlling for children's level of autism traits and correspond to previously-reported findings for children with typical development, providing empirical support for the theorized transdiagnostic relevance of temperament.

Publications Reproduced in the Thesis

Chetcuti, L., Uljarević, M., Ellis-Davies, K., Hardan, A. Y., Whitehouse, A. J., Hedley, D., ... & Prior, M. R. (2021). Temperament in individuals with Autism Spectrum Disorder: A systematic review. *Clinical Psychology Review*, *85*, 101984. https://doi.org/10.1016/j.cpr.2021.101984

Chetcuti, L., Uljarević, M., & Hudry, K. (2019). Editorial Perspective: Furthering research on temperament in autism spectrum disorder. *Journal of Child Psychology and Psychiatry*, *60*(2), 225-228. https://doi.org/10.1111/jcpp.12957

Chetcuti, L., Uljarević, M., Varcin, K. J., Boutrus, M., Wan, M. W., Green, J., ... the AICES Team. (2020). Subgroups of temperament associated with social–emotional difficulties in infants with early signs of autism. *Autism Research, 13*(12), 2094-2101. https://doi.org/10.1002/aur.2381

Chetcuti, L., Uljarević, M., Varcin, K. J., Boutrus, M., Dimov, S., Pillar., S., ... the AICES Team (2020). *Continuity of temperament subgroup classifications from infancy to toddlerhood in the context of emerging autism.* Manuscript in preparation (planned submission early 2021 to the *Journal of Clinical Child and Adolescent Psychology*).

Chetcuti, L., Uljarević, M., Varcin, K. J., Boutrus, M., Wan, M. W., Slonims, V., ... the AICES Team (2020). The role of negative affectivity in concurrent relations between caregiver psychological distress and social-emotional difficulties in infants with early signs of autism. *Autism Research*, *13*(8), 1349-1357. https://doi.org/10.1002/aur.2296

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Chetcuti, L. Uljarević, M., Varcin, K., Boutrus, M., Pillar, S., Dimov, S., … Hudry, K., & the AICES Team (2020, July). *Subgrouping infants with early autism signs on the basis of temperament: Classification continuity and predictive utility.* Oral presentation at the Australasian Society for Autism Research (ASfAR) Conference, Wellington, New Zealand.

Chetcuti, L. Uljarević, M., Varcin, K., Boutrus, M., Pillar, S., Dimov, S., … Hudry, K., & the AICES Team (2020, July). *Subgrouping infants with early autism signs on the basis of temperament: Classification continuity and predictive utility.* Poster session presented at the International Congress on Infant Studies (ICIS) Virtual Congress.

Chetcuti, L., Uljarević, M., Varcin, K., Boutrus, M., Pillar, S., Dimov, S., … Hudry, K., & the AICES Team (2020, July). *Child temperament and caregiver psychological distress predict internalizing and externalizing symptoms in children with autism features.* Poster session presented at the International Congress on Infant Studies (ICIS) Virtual Congress.

Chetcuti, L., Uljarević, M., Varcin, K., Whitehouse, A. J. O., Hudry, K., & the AICES Team. (2019, May). *Utility of temperament for predicting psychopathology in infants with early signs of autism spectrum disorder (ASD).* Poster session presented at the International Society for Autism Research (INSAR) Annual Meeting, Montreal, Canada.

Chetcuti, L., Uljarević, M., Varcin, K., Whitehouse, A. J. O., Hudry, K., & the AICES Team. (2019, May). *Negative affectivity mediates the link between caregiver psychological distress and psychopathology in infants with early signs of autism*. Poster session presented at the International Society for Autism Research (INSAR) Annual Meeting, Montreal, Canada.

Chetcuti, L., Uljarević, M., Varcin, K., Whitehouse, A. J. O., Hudry, K., & the AICES Team. (2018, December). *Utility of temperament for predicting psychopathology in infants with early signs of autism spectrum disorder (ASD).* Poster session presented at the Australasian Society for Autism Research (ASfAR) Conference, Gold Coast, Australia.

Chetcuti, L. Hudry, K., Ellis-Davies, K., Putnam, S., Whitehouse, A. J., Prior, M. R., & Uljarević, M. (2017, November). *Temperament in individuals with Autism Spectrum Disorder (ASD): A systematic review.* Poster session presented at the Australasian Society for Autism Research (ASfAR) State-Based Conference, Melbourne, Australia.

Chetcuti, L. Hudry, K., Ellis-Davies, K., Putnam, S., Whitehouse, A. J., Prior, M. R., & Uljarević, M. (2017, May). *Temperament in individuals with autism spectrum disorder (ASD): A systematic review.* Poster session presented at the International Society for Autism Research (INSAR) Annual Meeting, Rotterdam, Netherlands.

Other Publications Related to the Thesis

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Hudry, K., **Chetcuti, L.**, Boutrus, M., Pillar, S., Baker, E. K., Dimov, S., ... & the AICES Team. (2020). Performance of the Autism Observation Scale for Infants with community-ascertained infants showing early signs of autism. *Autism*. Advance online publication. https://doi.org/10.1177/1362361320965397

Statement of Authorship

This thesis includes work by the student (LC) that has been submitted or accepted for publication (see page xiii). For the systematic review and meta-analysis (Chapter 1), LC and MU contributed equally to the literature search, data extraction, analysis, and interpretation, and drafting of the manuscript. Other co-authors contributed to conception, design, and manuscript revision (KE, AYH, DH, SP, KH, MRP). For the editorial perspective (Chapter 2), LC conceptualized the topic and drafted the manuscript with supervision, input, and revision by KH and MU. For all empirical publications (Chapters 5-8), LC collected data, searched the literature, conceptualized and analysed the studies, drafted the manuscripts and incorporated revisions. Other co-authors contributed to supervision (KH, MU), data collection (MB, SD, SP, KV), and/or acquisition of funding for the larger trial and manuscript revision (JB, CD, JG, TI, LS, VS, MWW, AJOW). Members of 'the AICES Team' were involved in aspects of the larger trial beyond the focus of the current program of research.

All research procedures reported in this thesis were approved by the Child and Adolescent Health Service Ethics Committee (2016008EP, June 8 2016).

Except where reference is made in the text of the thesis, this thesis contains no material published elsewhere or extracted in whole or in part from a thesis accepted for the award of any other degree or diploma. No other person's work has been used without due acknowledgment in the main text of the thesis. This thesis has not been submitted for the award of any degree or diploma in any other tertiary institution.

Lacey Carmen Chetcuti

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General Introduction

Children differ from one another, from as early as the first few months of life, in their characteristic ways of thinking, feeling, and behaving. Whereas one child might approach unfamiliar people and novel situations with eagerness and interest, another may perceive the same situation as distressing or threatening and react negatively. These affective tendencies, as well as the systems that regulate them, constitute a child's temperament and play a crucial role in organizing thought and behaviour (Goldsmith et al., 1987; Shiner et al., 2012). For example, temperament can influence how children situate themselves in the world and shape the behaviour and expectations of others (Shiner & Caspi, 2003). Consequently, childhood temperament is an important contributor to adaptation and wellbeing in school and later work environments and is thought to form the affective 'core' around which more complex personality traits develop over time.

Whereas an expansive literature recognizes the contribution of temperament to developmental differences in the general population, there is a lack of comprehensive understanding of such effects in the context of autism spectrum disorder (ASD). ASD is diagnosed when social-communication and restricted/repetitive behavioural differences impact everyday functioning (American Psychiatric Association [APA], 2013)[1]. However, autistic traits present in a variety of ways and may be accompanied by other functional challenges, and also in the general (non-ASD-diagnosed) population (Wing, 1997). It is considered here that temperamental individuality might help to explain some of the heterogeneity evident among children with autism traits in early childhood – before an ASD diagnosis can be given – and contribute to long-term outcomes.

One area of concern for children on the autism spectrum is the development social-emotional skills; that is, the capacity to recognize, and adaptively express emotions, comply with social norms for behaviour, and develop positive relationships with others. Difficulties in social-emotional functioning emerge early in life in the form of (a) internalizing symptoms – reflecting the tendency to experience distress *inwards*, for example, through withdrawal and sadness, as characteristic of depression and anxiety disorders – and/or (b) externalizing symptoms – reflecting distress directed *outwards* towards others, for example, through aggression and impulsivity as characteristic of oppositional defiant- (ODD), conduct- (CD), and attention-deficit/hyperactivity disorders (ADHD; Achenbach, 1966; APA, 2013).

[1] It is recognized that there is no single term that is preferred by all people on the autism spectrum. This thesis uses identity-first language (i.e., 'autistic person' or 'person on the autism spectrum'), rather than person-first language (i.e., 'person with ASD') as this is the preference of the autistic community. The term 'autism spectrum disorder' ('ASD') is used in reference to the diagnostic criteria, and when suited to the publishing journal.

The presence of internalizing and/or externalizing symptoms adds complexity to the presentation and experience of autism, can complicate clinical decisions regarding diagnosis and care, and negatively impact long-term outcomes. There is thus a strong impetus to determine factors associated with social-emotional difficulties, as this could enable earlier and more proactive supports for children with autism traits and their families. To this end, the current program of research was conducted with the aim of understanding the nature of individual temperament differences and role of these in predicting social-emotional functioning outcomes in the context of emerging autism.

Children's temperament differences, though determined in part by genetic factors, continue to develop with age and through environmental experiences (Shiner et al., 2012). Therefore, a more considered investigation of temperament and developmental differences necessarily involves consideration of the context within which a child develops. Caregivers are of central importance in children's lives – particularly early on – and their actions and attributes can play a role in shaping developmental pathways. In particular, the challenges encountered by caregivers raising a child with autism can contribute to greater feelings of psychological distress (i.e., anxiety, depression, and/or stress symptoms), which in turn may serve to elaborate children's temperament differences over time. Accordingly, this research also considered whether these relations – between the temperament of children with autism traits and psychological distress of their caregivers – might translate into a pathway for the development of internalizing and externalizing symptoms.

Research Procedure

This program of research was embedded within a larger intervention trial conducted at two sites in Australia (Melbourne and Perth), detailed by Whitehouse et al. (2019). The participants were infants showing early signs of autism, and their caregivers. Infants were identified by community healthcare professionals on the basis of showing key early signs of autism on an established screening instrument. Nonetheless, autism traits presented with a high degree of variability (see Hudry et al., 2020), which was conducive of the objective of this project to examine individual differences in the context of emerging autism. This research drew on data collected at three timepoints, when children were of mean age 12-, 18-, and 24-months. Direct behavioural assessments were employed at each timepoint to characterize the sample (i.e., in terms of autism traits and developmental level) and caregiver-report questionnaires were used to measure the primary variables of interest (i.e., child temperament, child social-emotional functioning, and caregiver psychological distress). Two studies in this thesis are based on these data, cross-sectionally, collected at the first assessment point (Chapters 1 and 3), while two others utilize the longitudinal dataset (Chapters 2 and 4). The candidate (LC) conceptualized these studies and oversaw all data collection at her local (Melbourne) site, and was responsible for all analysis, interpretation, chapter/article preparation and journal submission (see page x for a statement of co-author contributions) for the work presented here.

Thesis Format and Structure

This thesis contains six articles (of which four are empirical) that are thematically linked and describe a cohesive research program. Full publication details are provided in each relevant chapter, summarized briefly below.

Chapter 1: This chapter provides an overview and integration of different temperament concepts and clarifies the current understanding of temperament in ASD by way of systematic review and meta-analysis. This article has been submitted to *Clinical Psychology Review* (Chetcuti, Uljarević, Ellis-Davies, et al., 2020 [under review]).

Chapter 2: This chapter revisits conclusions from the former chapter by way of identifying unanswered empirical questions and highlighting future directions for the field. This editorial piece is published in the *Journal of Child Psychology and Psychiatry* (Chetcuti, Uljarević, & Hudry, 2019).

Chapter 3: This chapter provides a description and discussion of internalizing and externalizing symptoms in relation to autism, and outlines the specific aims and hypotheses of each empirical study.

Chapter 4: This chapter describes common methodological features of this research program.

Chapter 5: This chapter presents a cross-sectional empirical study of temperament differences in the sample of infants with autism traits and the relation of these to concurrent social-emotional difficulties. This article is published in *Autism Research* (Chetcuti, Uljarević, Varcin, Boutrus, Wan, Green, et al., 2020).

Chapter 6: The empirical study presented in this chapter extends upon the previous analysis by exploring continuity in the nature of temperament differences in the sample – including of prospective associations with social-emotional functioning variables – from the infants' first to last assessment points. This article has been formatted for planned submission to the *Journal of Clinical Child and Adolescent Psychology* (Chetcuti, Uljarević, Varcin, Boutrus, Dimov, et al., 2020 [in preparation]).

Chapter 7: This chapter presents a preliminary and cross-sectional investigation of the effects of caregiver psychological distress on infant temperament associated, in turn, with infants' social-emotional difficulties. This article is published in *Autism Research* (Chetcuti, Uljarević, Varcin, Boutrus, Wan, Slonims, et al., 2020).

Chapter 8: Extending upon the analysis reported in the previous chapter, this chapter presents an empirical study of reciprocal longitudinal interplay between child temperament and caregiver psychological distress in the development of social-emotional difficulties. This article has been submitted to *Development and Psychopathology* (Chetcuti, Uljarević, Varcin, Boutrus, Pillar, et al., 2020 [under review]).

Chapter 9: This chapter presents a general discussion and interpretation of findings, with consideration given to the strengths and limitations of the studies included. Directions for clinical practice and future empirical research are also offered.

This thesis has been formatted in accordance with the American Psychological Association (APA, 2010) publication guidelines. Articles have been consistently formatted in this style independent of the style requirements of the peer-reviewed journal to which manuscripts were submitted/accepted. Figures and tables for each study are presented in the body of the manuscript, rather than appended at the end, for ease of reading. Appendices relating to a specific article are presented within the relevant chapter, while appendices relating more broadly to the research program are presented at the end of the thesis.

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CHAPTER 1

Systematic Literature Review and Meta-Analysis

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Chetcuti, L., Uljarević, M., Ellis-Davies, K., Hardan, A. Y., Whitehouse, A. J., Hedley, D., ... & Prior, M. R. (2021). Temperament in individuals with Autism Spectrum Disorder: A systematic review. *Clinical Psychology Review*, *85*, 101984. https://doi.org/10.1016/j.cpr.2021.101984

Temperament in Individuals with Autism Spectrum Disorder: A Systematic Review

Lacey Chetcuti[1,†], Mirko Uljarević[2,3,†], Katherine Ellis-Davies[4], Antonio Y Hardan[3], Andrew J O Whitehouse[5], Darren Hedley[1], Samuel Putnam[6], Kristelle Hudry[1], Margot R Prior[2]

[†]Authors contributed equally to the production of this manuscript

[1]School of Psychology and Public Health, La Trobe University, Melbourne, Australia; [2]Melbourne School of Psychological Sciences, University of Melbourne, Melbourne, Australia; [3]Stanford Autism Center, Department of Psychiatry and Behavioral Sciences, Child and Adolescent Psychiatry, School of Medicine, Stanford University, USA; [4]Department of Psychology, Swansea University, Wales, United Kingdom; [5]Telethon Kids Institute, University of Western Australia; [6]Department of Psychology, Bowdoin College, United States

1.1. Abstract

The study of temperament in Autism Spectrum Disorder (ASD) has the potential to provide insight regarding variability in the onset, nature, and course of both core and co-morbid symptoms. The aim of this systematic review was to integrate existing findings concerning temperament in the context of ASD. Searches of Medline, PsychInfo and Scopus databases identified 64 relevant studies. As a group, children and adolescents with ASD appear to be temperamentally different from both typically developing and other clinical non-ASD groups, characterized by higher negative affectivity, lower surgency, and lower effortful control at a higher-order level. Consistent with research on typically developing children, correlational findings and emerging longitudinal evidence suggests that lower effortful control and higher negative affect are associated with increased internalizing and externalizing problems in ASD samples. Longitudinal studies suggest there may be temperamental differences between high familial risk infants who do and do not develop ASD from as early as 6-months of age. Limitations of existing research are highlighted, and possible directions for future research to capitalize on the potential afforded through the study of temperament in relation to ASD are discussed.

1.2. Introduction

Autism Spectrum Disorder (ASD) is characterized by social-communication impairments – such as deficits in social-emotional reciprocity and in developing, maintaining, and understanding relationships – alongside restricted/repetitive patterns of behavior/interest and/or atypical responses to sensory input. The model of ASD symptom expression proposed within the 5th edition of the Diagnostic and Statistical Manual of Mental Disorders (DSM-5; American Psychiatric Association, 2013) goes some way in terms of alignment with the current dimensional conceptualization of this cluster of neurodevelopmental conditions than was true for the categorical model adopted within the previous edition (see Vivanti et al., 2013). However, neither the former nor the current classification system successfully capture the heterogeneity observed among individuals with ASD, nor adequately explains the sources of individual difference in presentation and outcome.

Alongside the varying manifestations of the core symptom profile, significant heterogeneity is apparent across every facet of ASD, including the timing of onset and course of symptom emergence, developmental outcomes in terms of cognitive/language impairment, and the presence of comorbidities including behavioral problems and mental health difficulties (Bryson et al., 2007; Prior et al., 1998). Such variation in phenotypic expression and associated outcomes beckons a need to provide support and treatment that is appropriately tailored to the individual needs of each person. Nevertheless, an inadequate understanding of the underlying processes and mechanisms that give rise to heterogeneity in ASD is a major impediment to this objective; precluding the refinement of intervention protocols and targets and making it difficult to predict longer-term outcomes on the basis of early presentation.

Although symptom severity and level of associated cognitive/language impairments are important prognostic indicators – such that individuals with milder symptom severity, greater functional abilities, and better verbal skills during childhood appear more likely to have optimal adult outcomes (Magiati, Tay, & Howlin, 2014) – heterogeneity in ASD is not fully attributable to disorder-specific characteristics. Rather, it has been suggested (Insel, Landis, & Collins, 2013; Mundy, Henderson, Inge, & Coman, 2007) that factors that are not specific to particular categorical diagnoses, but rather vary among all individuals regardless of diagnostic label, may provide important prognostic value over and above core symptom severity and level of cognitive functioning. Temperament is one such factor of potential importance for explaining the heterogeneity of ASD (Chetcuti, Uljeravic, & Hudry, 2019).

Temperament is the term used to characterize biologically-based, individual differences in affectivity, reactivity, and regulation, particularly within the childhood years (McAdams, 1995; Revelle, 1995). A 40-year research base supports the conceptualization of temperament as a central organizer of development (Marshall, Fox, & Henderson, 2000); demonstrating the importance of temperament in understanding childhood developmental differences and later life outcomes. In this regard, research on temperament in the context of ASD could hold significant potential for furthering our understanding of the variability inherent to this cluster of conditions.

Therefore, the current review was conducted with the aim of providing a snapshot of existing literature on the topic of temperament and ASD. A brief overview of temperament concepts is provided, so as to identify the common tenets and reconcile a taxonomy of higher-order dimensions. This unified taxonomy is adopted to systematically integrate findings obtained via different measures representing distinct theoretical traditions. Next, we consider the influence of temperament on developmental outcomes and manifestations of psychopathology in typically developing/non-ASD populations, to provide a premise for comparison to individuals with ASD. We conclude this review by offering future directions and suggestions for how research in this area may be strengthened.

1.2.1. Overview of Conceptualizations of Temperament

In a seminal roundtable discussion and publication, Goldsmith and colleagues (1987) brought together researchers representing prominent temperament theories galvanizing the field. These models are described below.

A pioneering influence on the study of temperament came from the work of Thomas and Chess and colleagues (1968) who delineated the following nine temperament dimensions: *activity*, *approach-withdrawal* (to/from new stimuli), *rhythmicity* (regularity of biological functions), *mood* (positive or negative), *distractibility* (ease of soothing), *threshold* (to respond), *intensity* (of response), *persistence*, and *adaptability* (to new experiences). Thomas et al. conceptualized temperament as the *style* rather than the content of behavior and emphasized the transactional relations between children's temperamental characteristics environmental influences, such as family dynamics. Hence, they stressed the influence of "goodness of fit" or the compatibility between a child's temperament and his/her environment. In addition to the nine dimensions, Thomas et al. also introduced a typology of child temperaments – *easy*, *difficult*, and *slow-to-warm-up* temperament types – each with clear clinical implications (McClowry, Rodrigues, & Koslowitz, 2008). From within the Thomas and Chess model, Kyrios and Prior (1990) identified a higher-order temperament factor among pre-schoolers – that of self-regulation – which was derived from a cluster of dimensions including distractibility, persistence and rhythmicity related behaviors.

Buss and Plomin (1975, 1984) proposed that the dimensions of *emotionality*, *activity*, and *sociability* were stable over time and showed considerable generality across different temperament theories. An impulsivity dimension, originally included in Buss and Plomin's model of temperament, was later removed because it was considered not to have genetic/biological influence. However, more recent work has suggested that impulsivity (or components thereof are) is heritable and relevant in the clinical domain (Gagne & Saudino, 2010).

Goldsmith (1982, 1987) conceptualized temperament as individual differences in the tendency to experience and express emotional behavior, with a focus on dimensions such as *positive affectivity, fear, anger,* and *psychobiological reactivity*. Emotion and emotion regulation were also central to the conceptualization of temperament proposed by Rothbart (in Goldsmith et al., 1987) who placed increased emphasis on underlying psychobiological processes. Within what can be considered a neurobiological approach, Rothbart proposed numerous temperament domains which were later integrated into the following higher-order factors: *surgency* (including activity level, sociability, and pleasure expressed in anticipation of reward or during high-intensity activities); *negative affectivity* (including anger, sadness, fear, physical discomfort, and recovery from distress); and a factor labelled *regulatory capacity* in infants and *effortful control* in older individuals (including the ability to focus attention, demonstrate satisfaction during low-intensity activities and, among older children, the capacity to exercise inhibitory control). These factors were subsequently integrated into more comprehensive biological and environmental themes relevant to personality models for adults (Putnam, Ellis, & Rothbart, 2001; Rothbart, Ahadi, & Hershey, 1994).

A neurobiological approach also underlies a conception of temperament proposed by Cloninger (1986) who originally argued for *novelty seeking*, *harm avoidance* and *reward dependence* as basic dimensions and proposed these to be associated with the monoaminergic activity (Cloninger, 1987). *Persistence* was later introduced as a fourth basic temperament dimension (Cloninger, Przybeck, Svrakic, & Wetzel, 1994). Cloninger's conceptualization differs from the aforementioned theories in that it was originally developed as a theory of adult personality, and later expanded to describe temperament in childhood. However, psychometric limitations have been noted in several versions of inventories based on Cloninger's model, calling into question his hypothesized structure of temperament traits (Farmer & Goldberg, 2008).

As can be seen, individual variability is the norm across all facets of temperament theory. While different theoretical approaches have offered various definitions of temperament, common to most is the understanding that individual differences in temperament are identifiable from early in life, persist over time, and show cross-contextual stability. Most conceptualizations also consider temperament to be heritable, although the extent to which this is a definitional criterion is debated (see Shiner et al., 2012).

1.2.2. Reconciling a Higher-Order Framework for Temperament Traits

Although consensus on the dimensional structure of temperament has not been reached, several narrative reviews (Shiner et al., 2012; Zentner & Bates, 2008) and structural analyses of temperament measures (Mervielde & De Pauw, 2012) suggest that different conceptual models may converge on a set of overarching traits; potentially identified as affectivity/emotionality, sociability, and self-regulation. The unified taxonomy of overarching temperament traits (described below) is useful, as it facilitates the systematic integration of findings obtained via different measures representing different theoretical traditions.

An *affectivity/emotionality* trait describes an individual's tendency to experience negative emotions. This trait is clearly captured within each theoretical model; emerging from the mood and adaptability dimensions of Thomas and Chess, Buss and Plomin's emotionality, Rothbart's negative affectivity, and Cloninger's harm avoidance factors. A *sociability* trait refers to the tendency to actively engage with others, which is represented by sociability and shyness in Buss and Plomin's model, captured by Rothbart's surgency dimension, and Cloninger's reward dependence. Although Thomas and Chess's model lacks a clear sociability component, persistence, intensity, and approach-withdrawal are empirically related to sociability/shyness and surgency at certain ages (Mervielde & De Pauw, 2012). While sometimes viewed as a basic or independent dimension of temperament, activity level is viewed as an expression of behavioural activation and thus subsumed in this taxonomy within the dimension of sociability. This is consistent with Rothbart's model wherein the activity is subsumed within surgency, and with adult personality taxonomies where energy/activity level is conceived as a facet of extraversion. Finally, a factor that can be broadly termed *self-regulation* refers to the capacity to regulate emotions and action, which captures Thomas and Chess's and Cloninger's persistence dimensions, and Rothbart's effortful control.

1.2.3. Temperament as a Predictor of Developmental Outcomes

A major research focus of temperament research has concerned the ways in which temperament affects health, emotional adjustment, and social outcomes, both directly and indirectly through reciprocal interaction with parenting practices (Belsky & Pleuss, 2009; Sanson, Hemphill, & Smart, 2004). For instance, persistence and effortful control have been shown to have a positive influence on social competence, self-esteem, and educational outcomes (Keogh, 2003; Spinrad et al., 2007). Child temperament is also known to have a reciprocal influence on parenting behaviors as well as on relationships with siblings and peers. For example, within the domain of social development, temperamental traits have been associated with mother-infant interaction elicitation of particular types of parental response (McClowry et al., 2008). Furthermore, Kim and Kochanska (2012) found that infants' negative affectivity at 7 months moderated the impact of parent-child mutuality on later child self-regulation at 15 months. More specifically, infants high in negative emotionality showed lower levels of self-regulation when in a less responsive parent-child relationship but better self-regulation when in a responsive relationship.

Importantly, different domains of temperament interact with one another when predicting behavioral outcomes. The interactions between reactivity and regulatory dimensions of temperament are particularly relevant; such that regulatory capacities buffer against the potential adverse impact of negative emotionality (Kim & Kochanska, 2012).

1.2.4. Temperament in Relation to Psychopathological Symptoms and Disorders

In addition to developmental outcomes, extensive research has explored whether individual temperament characteristics relate to differences in psychopathology. While some studies have focused exclusively on the prediction of discrete clinical symptoms and disorders (e.g., ADHD), many have investigated links between temperament and common psychopathological symptoms hierarchically organized into broad-band internalizing and externalizing dimensions (Achenbach, 1966). Temperamental inhibition/social withdrawal has been shown to be a risk factor for the development of anxiety and other internalizing problems (Kagan & Snidman, 2004; Prior, Sanson, Smart, & Oberklaid, 1999; Putnam & Stifter, 2005) while positive emotionality/sociability has been found to contribute to externalizing problems (Kochanska & Kim, 2012). Similarly, irritability/negative emotionality and low self-regulation have been associated with both internalizing and externalizing (Eisenberg et al., 2001).

In recent years, researchers have moved towards exploring the nature of relations among temperament traits and psychopathological symptoms. Four explanatory models have been explicated (Watson, Clark, & Harkness, 1994); the *predisposition/vulnerability* model states that certain temperamental characteristics increase the probability of developing psychopathology, while the *continuity/spectrum* model posits that temperament and psychopathology share etiological underpinnings and represent opposite ends of the same underlying continuum. Other models suggest there may be an etiological distinction between temperament and psychopathology and posit that temperament may exacerbate (*pathoplasty/exacerbation* model) or be exacerbated by psychopathology (*complication/scar* model) after onset.

These explanatory models are not mutually exclusive, and all have received at least some empirical support. Nevertheless, studies that have tested competing models simultaneously through statistical modelling provide strong support for a continuity/spectrum association, as opposed to predisposition/vulnerability (De Bolle, Beyers, De Clercq, & De Fruyt, 2012; De Bolle, De Clercq, Caluwé, & Verbeke, 2016; Martel, Gremillion, Roberts, Zastrow, & Tackett, 2014). Likewise, twin studies show that a substantial proportion of the genetic influences underlying temperament are shared with psychopathology (Gjone & Stevenson, 1997).

In summary, a large body of research in non-ASD populations has demonstrated that particular dimensions of temperament can have both direct and indirect positive and negative influences on development across the lifespan and across a broad range of domains including social-emotional, behavioral, and psychopathology outcomes. In view of this evidence, we propose that research on temperament in the context of ASD could hold significant potential for furthering our understanding of the variability inherent in the developmental trajectories and outcomes for individuals with this cluster of conditions (for a discussion, see Chetcuti et al., 2019). Indeed, researchers have been exploring temperament in the context of ASD for around 30 years, and this is a timely opportunity to systematically integrate the findings across existing work to ascertain how temperament has been conceptualized and measured in this particular clinical field, to identify consistencies in the evidence base and gaps that still require attention and importantly, to propose a roadmap for future research in this area.

1.3. Methods

1.3.1. Databases and Search Terms

Medline, PsychInfo and Scopus databases were searched for published articles available through March 11th, 2020. Combinations (including truncated versions) terms related to ASD and temperament were searched across all available fields: autism, asperger(s), pervasive developmental disorder, ASD, temperament, behavioural inhibition, negative affect, positive affect, surgency, extraversion, effortful control, reactivity, regulation, self-regulation, behavioural style, approach, avoidance, persistence, activity, rhythmicity. Terms within each subset were entered with the Boolean operation ‘OR’, and then aggregated using the operator ‘AND’. Database searches were supplemented by a review of the reference sections of identified empirical and review papers involving temperament studies.

Both the first and second author independently screened articles for inclusion and articles were included based on consensus decision. Several inclusion and exclusion criteria were set for the retention of papers. First, papers were included if the target population comprised individuals diagnosed with an ASD (inclusive of autism, ASD, Autistic Disorder, Asperger's Disorder, Asperger Syndrome, atypical autism, or PDD-NOS). Studies that explored the association between temperament and *ASD traits* – either in the general population or among samples of individuals with other conditions (e.g., Anorexia Nervosa, ADHD etc.) – were excluded from this review. Within retained publications, no restrictions were imposed in terms of whether exploration of temperament was the primary study goal or whether temperament was included as one among a number of constructs of interest. Where temperament was not the primary focus, however, only the study section relevant to temperament was summarized for this review. Studies that did not use questionnaire or observational measures that specifically captured temperament in a quantitative manner were not eligible for inclusion, for instance, studies that only explored neurobiological systems linked to temperament (e.g., right/left lateralization), studies on executive functioning, studies looking at qualitative temperament behaviour. No restrictions were imposed regarding the ages of individuals with ASD, nor regarding sample size, though single case studies and case series were not included. Non-empirical papers and unpublished studies were not included, nor were those published in languages other than English. These eligibility criteria were applied to database searches where possible through use of limits and filters, and during article screening.

1.3.2. Search Results and Coding Procedures

The search process is depicted in Figure 1. After removing duplicates and obviously non-relevant papers, initial searches yielded 789 studies, 629 of which were excluded following the reading of the abstract, resulting in 160 studies potentially retained for analysis. Following a full review, a further 101 studies were excluded due to (i) being irrelevant or (ii) not meeting the aforementioned criteria. Review of reference lists yielded another 5 studies, for a total of 64 studies included in this analysis.

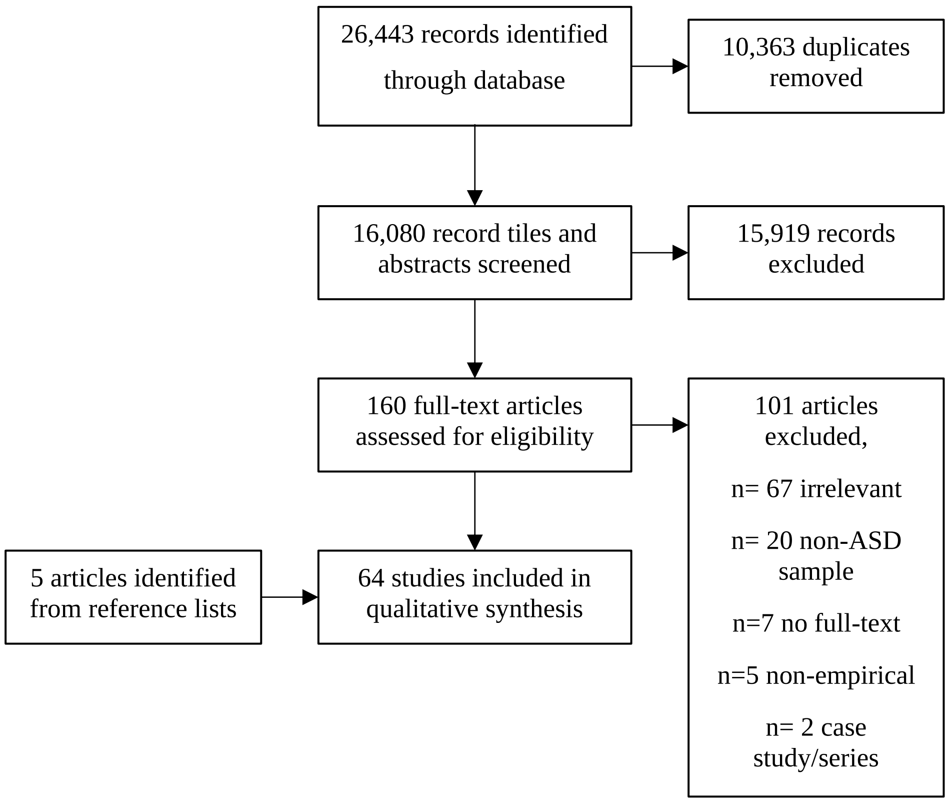

Figure 1. PRISMA flow diagram.

Retained studies were coded for: (a) full description of the ASD group in terms of chronological age (CA) and sex composition and other control group/s; (b) design (cross-sectional vs. longitudinal); (d) features of temperament measures adopted, including name, type (i.e., questionnaire/interview/observational study), informant (i.e., parent- or self-report). Background information is summarized in Table 1. Studies were then coded in terms of the results obtained, summarised across Table 2 (cross-sectional and longitudinal studies) and Table 3 (prospective studies of ASD).

1.3.3. Statistical Analysis

A meta-analysis was performed to consolidate studies (i) comparing level of specific temperament dimensions between ASD and non-ASD (normative and/or clinical) groups and (ii) exploring association between temperament dimensions and other factors. Where measures were comparable but not identical, the reported statistics were standardised to facilitate combination and comparing of the effect estimates. The mean correlations between temperament dimensions and other factors were aggregated using a random-effects model.

1.4. Results

1.4.1. Overview of Studies

Among the 64 studies retained for review, 45 were cross-sectional, one was a long-term follow-up study, 18 were prospective longitudinal. The majority of studies focused on very young children and younger adolescents. Twenty-nine studies provided a comparison of ASD to TD individuals only, and 18 studies provided a comparison to individuals with some other clinical condition – most frequently, individuals with ADHD (6 studies) or with developmental delay/Down syndrome (10 studies) – alongside a TD group, in most cases.

Table 1

Overview of the Studies

	Subject Characteristics						Temperament Measure			
	ASD			Other						
Study	***n***	**Age[a]**	**% Male**	**Type**	***n***	**Design**	**Name**	**Type**	**Format[b]**	**Alignment**
Adamek et al. (2011)	111	M= 4.2 yrs (SD= 1.5)	82	Reference TD	517	CS	CBQ-Short Form	Q	PR (87% Mo)	Ro
Anckarsäter et al. (2006)	66	Mdn= 31 yrs (Range= 19-60)[c]	55[c]	1) ADHD 2) ADHD + ASD	1) 100 2) 47	CS	TCI	Q	SR	Cl
Baker et al. (2019)	46	M= 81.51 mths (SD= 24.18)	80	-	-	CS	Dysregulation Coding System	O	-	-
Bailey et al. (2000)	31	M= 64.1 mths (Range= 36-84)[c]	100	1) FXS 2) Reference TD	1) 31 2) 350	CS	BSQ	Q	SR	T&C
Barger et al. (2019)	649	M= 4.9 yrs (SD= 0.6)	82	TD	866	CS	BSQ	Q	PR (Mo)	T&C
Berkovits et al. (2017)	108	M= 5.7 yrs (SD= 1.1)	82.4	-	-	L	ERC	Q	PR (Mo)	-
Biebrich & Morgan (2004)	14	M= 8.37 yrs (SD= 2.46)	86	DS	15	L	MN-PARS	O	-	-

Biebrich & Morgan (1998)	18	M= 8.23 yrs (SD= 2.53)	78	DS	18	CS	MN-PARS	O	-	-
Bolte et al. (2008)	49	M= 10.3 yrs (SD= 3.8)	72[c]	-	-	CS	JTCI	Q	PR (Mo)	Cl
Bolton et al. (2012)	86	6 mths	NR	-	-	L	CTQ	Q	PR (Mo)	T&C
Bos et al. (2018)	66	M= 11.65 yrs (SD= 1.27)	100	TD	89	L	Mood Questionnaire	Q	SR	-
Bostrom et al. (2010)	12	M= 37.42 (SD= 24.15)[c]	61.8[c]	1) DS 2) ID/DD 3) CP/MI 4) Other diagnoses 5) TD	1) 9 2) 14 3) 5 4) 15 5) 178	CS	EASI Temperament Survey	Q	PR (Mo & Fa)	B&P
Brock et al. (2012)	54	M= 56.17 mths (SD= 13.67)	83	1) DD 2) Reference TD	1) 33 2) 350	CS	BSQ	Q	PR (NR)	T&C
Bryson et al. (2018)	16	6 mths	44	1) HR-No ASD 2) LR	1) 67 2) 53	L	IBQ	Q	PR (NR)	Ro
Burrows et al. (2016)	104	M= 13.31 yrs (SD= 2.06)	87	TD	94	CS	EATQ-R	Q	SR	Ro

Chuang et al. (2012)	67	M= 64.21 mths (SD= 9.01)	85	TD	44	CS	BSQ Chinese version	Q	PR (NR)	T&C
Chuang et al. (2014)	106	M= 54.4 mths (SD= 9.6)	85	-	-	CS	BSQ Chinese version	Q	PR (NR)	T&C
Clifford et al. (2013)	17	M= 7.2 mths (SD= 1.1)[c]	65	1) LR 2) HR-TD 3) HR-Atypical	1) 48 2) 24 3) 12	L	IBQ-R, ECBQ	Q	PR (NR)	Ro
De Pauw et al. (2011)	175	M= 10.28 yrs (SD= 2.4)	85	TD	500	CS	CBQ Dutch very short form, EATQ-R	Q	PR (50% Mo)	Ro
Del Rosario et al. (2014)	10-16	M= 6.5 mths (SD= 0.9)	86	HR-TD	7-27	L	CTS	Q	PR (NR)	T&C
Faja & Dawson (2015)	21	M= 82.0 mths (SD= 7.1)	71	TD	21	CS	CBQ	Q	PR (NR)	Ro
Fenning et al. (2018)	46	M= 6.39 years (SD= 1.95)	80	-	-	CS	Dysregulation Coding System	O	-	-
Garon et al. (2009)	34	6-12 mths	65	1) LR 2) HR-No ASD	1) 73 2) 104	L	TBAQ-R	Q	PR (NR)	Ro
Garon et al. (2016)	98	6-12 mths	NR	1) LR	1) 162	L	IBQ, TBAQ-R	Q	PR (NR)	Ro

				2) HR-No ASD	2) 285					
Glaser & Shaw (2011)	19	M= 9.48 yrs (SD= 3.81)	63	22q13 DS	18	CS	TABS	Q	PR (NR)	-
Gomez & Baird (2005)	65	M= 8.3 yrs	89	Reference TD	120	CS	TABS	Q	PR (94% Mo)	-
Gottlieb & Bortner (1984)	12	M= 5.2 yrs (SD= 7.2 mths)	NR	1) DD/ID 2) Reference TD	1) 12 2) 350	CS	BSQ	Q	PR (NR)	T&C
Helles et al. (2016)	40	M= 11.5 yrs (SD= 4.8)	100	Reference TD	NR	L	TCI	Q	SR	Cl
Hendry et al. (2018)	16	M= 8.80 mths (SD= 0.83)	89	1) LR 2) HR-No ASD	1) 23 2) 75	L	CBQ-Short Form	Q	PR (NR)	Ro
Hepburn & Stone (2006)	110	M= 57.3 mths (SD= 15.4)	86	Reference TD	350	CS	BSQ	Q	PR (Mo)	T&C
Hirschler-Guttenberg et al. (2015)	40	M= 63.38 mths (SD= 12.35)	87	TD	40	CS	Modified Lab-TAB	O	-	Ro
Hirschler-Guttenberg et al. (2015)	39	M= 63.38 mths (SD= 12.35)	87	TD	40	CS	Modified Lab-TAB	O	-	Ro

Hoijer & Sizoo (2020)	74	Mdn= 28.5 yrs (IQR 23-42.3)	61	-	-	CS	TCI Dutch abbreviated version	Q	SR	Cl
Jahromi et al. (2012)	20	M= 58.95 mths (SD= 11.50)	NR	TD	20	CS	Lab-TAB, Unsolvable puzzles task	O	-	Ro, -
Kasari & Sigman (1997)	28	M= 42.39 mths (SD= 11.61)	93	1) DD/DS 2) TD	1) 26 2) 28	CS	BSQ	Q	PR (NR)	T&C
Kerekes et al. (2013)	1886	9 and 12 yrs	55	-	-	CS	JTCI	Q	PR (89% Mo)	Cl
Konstantareas & Stewart (2006)	19	M= 6.16 yrs	63	TD	23	CS	CBQ	Q	PR (Mo)	Ro
Konstantareas & Papageorgeu (2006)	43	M= 122.6 mths (SD= 71.8)	84	-	-	CS	DOTS-R-Child	Q	PR (Mo)	T&C
Korbut et al. (2020)	26	M= 3.30 yrs (SD= 0.68)	73	-	-	L	ECBQ	Q	PR (NR)	Ro
Macari et al. (2017)	165	M= 26.46 mths (SD= 5.77)	82	1) DD 2) TD	1) 58 2) 92	L	TBAQ-S	Q	PR (74.5% Mo)	Ro
Macari et al. (2018)	43	M= 21.9 mths (SD= 3.0)	88	1) DD 2) TD	1) 16 2) 40	CS	Modified Lab-TAB, ECBQ	Q, O	PR (NR)	Ro
Millea et al. (2013)	28	M= 12.34 yrs (SD= 1.93)	89	-	-	CS	EATQ-R Short Form	Q	SR	Ro
Myles et al. (2007)	156	M= 14.97 yrs	79	Reference TD	NR	CS	EATQ-R	Q	PR (NR)	Ro

Nazim & Khalid (2019)	92	M= 8.62 yrs (± 1.87)	66	-	-	CS	CBQ Urdu version, TMCQ Urdu version	Q	PR (NR)	Ro
Ostfeld-Etzion et al. (2016)	40	M= 63.38 mths (SD= 12.35)	88	TD	40	CS	CBQ	Q	PR (Mo)	Ro
Ozyurt et al. (2018)	31	Mdn= 44 mths (IQR= 12)	61[c]	1) DLD 2) TD	1) 45 2) 52	CS	ERC	Q	PR (Mo)	-
Paterson et al. (2019)	61	M= 6.45 mths (SD= 0.59)	79	1) HR-No ASD 2) LR	1) 221 2) 114	L	IBQ-R	Q	PR (NR)	Ro
Pijl et al. (2020)	75	M= 8.3 mths (SD= 1.4)	75	1) HR-Atypical 2) HR-Typical 3) LR	1) 34 2) 75 3) 66	L	IBQ-R, ECBQ	Q	PR (NR)	Ro
Ratekin (1993)	30	M= 42.53 mths (SD= 11.28)	90	1) DD 2) TD	1) 30 2) 30	CS	PTQ, NR	Q, O	-	-
Reyes et al. (2019)	37	M= 34.11 mths	78	1) DD 2) TD	1) 29 2) 27	L	CTS	Q	PR (NR)	T&C
Rivers & Stoneman (2018)	50	M= 7.6 yrs	84	TD Siblings	50	CS	TAB-R, SATI	Q	PR (98% Mo)	T&C

Samyn et al. (2011)	27	M= 12.73 yrs (SD= 1.46)	100	1) ADHD 2) TD	1) 27 2) 27	CS	ECS, ACS, EATQ-R	Q	PR (NR), SR	Ro
Samyn et al. (2015)	31	M= 12.83 yrs (SD= 1.41)	100	1) ADHD 2) TD	1) 30 2) 148	CS	ECS, ACS, EATQ-R	Q	PR (NR), SR	Ro
Samyn et al. (2017)	25	M= 12.94 yrs (SD= 1.45)	100	1) ADHD 2) TD	1) 25 2) 25	CS	ECS, ACS, EATQ-R	Q	SR	Ro
Schwartz et al. (2009)	44	M= 155.34 mths (SD= 28.08)	84	TD	38	CS	EATQ-R	Q	SR	Ro
Shephard et al. (2018)	15	M= 7.31 mths (SD= 1.19)[c]	48[c]	1) HR-No ASD 2) LR	1) 27 2) 37	L	IBQ-R, ECBQ	Q	PR (NR)	Ro
Sizoo et al. (2009)	75	M= 33.6-36.9 yrs (SD= 10.6-13.8)	80	1) ADHD 2) Reference TD	1) 53 2) NR	CS	VTCI	Q	SR	Cl
Sizoo et al. (2014)	75	M= 34.3 yrs (SD= 11.87)	81	ADHD	53	CS	VTCI	Q	SR	Cl
Soderstorm et al. (2002)	31	Mdn= 23 yrs (Range= 17-55)	90	Reference TD	NR	CS	TCI	Q	SR	Cl
Uljarević et al., (2017)	71	M= 18.71 yrs (SD= 2.51)	69	-	-	CS	ATQ	Q	SR	Ro
Vuijk et al. (2018)	66	M= 38 yrs (SD= 12.5)	100	Reference TD	66	CS	TCI	Q	SR	Cl

Yirmiya et al. (2006)	21-30	M= 20.23 wks (SD= 3.24)	37-62	HR-TD	21-31	L	ICQ	Q	PR (Mo)	-
Zantinge et al. (2019)	21	M= 60 mths (SD= 9.33)	95	TD	45	CS	Lab-TAB	O	-	Ro
Zwaigenbaum et al. (2005)	12-19	M= 6.44 mths (SD= 12.50)[c]	NR	1) HR-No ASD 2) LR	1) 32 2) 15-23	L	IBQ, TBAQ	Q	PR (Mo)	Ro

Note. [a] Age is chronological, at the first timepoint for longitudinal studies. [b] Parent respondent(% mother or father) is in parentheses. [c] Characteristics not reported separately for ASD. PR= parent report; SR= self-report; NR = not reported. ASD= Autism Spectrum Disorder; TD= Typically Development; ADHD= Attention Deficit Hyperactivity Disorder; FXS= Fragile X Syndrome; DLD= Developmental Language Delay; DS= Down Syndrome; ID= Intellectual Disability; CP/MI= Cerebral Palsy/Motor Impairment; DD= Developmental Delay; LR= Low Risk; 22q13 DS= 22q13 Deletion Syndrome; HR= High Risk; L= Longitudinal; CS= Cross-sectional; CBQ= Children's Behavior Questionnaire; TCI= Temperament and Character Inventory; BSQ= Behavioral Style Questionnaire; ERC= Emotion Regulation Checklist; MN-PARS= Minnesota Preschool Affect Rating Scales; JTCI= Junior Temperament and Character Inventory; CTQ= Carey Temperament Questionnaires; EASI= Emotionality Activity Sociability and Impulsivity; EATQ-R= Early Adolescent Temperament Questionnaire-Revised; IBQ= Infant Behavior Questionnaire-Revised; ECBQ= Early Childhood Behavior Questionnaire; SIB-R= Scales of Independent Behavior-Revised; TBAQ= Toddler Behavior Assessment Questionnaire; TABS= Temperament and Atypical Behavior Scale; DOTS-R-Child= Dimensions of Temperament Scale–Revised; TBAQ-R= Toddler Behavior Assessment Questionnaire-Revised; Lab-TAB= Laboratory Temperament Assessment Battery; PTQ= Preschool Temperament Questionnaire; TAB-R= Temperament Assessment Battery-Revised; SATI= School-Aged Temperament Inventory; ECS= Effortful Control Scale; ACS= Attentional Control Scale; VTCI= Dutch Temperament and Character Inventory; ATQ= Adult Temperament Questionnaire; ICQ= Infant Characteristics Questionnaire; Ro= Rothbart; Cl= Cloninger; T&C= Thomas and Chess; B&P= Buss and Plomin.

Most studies matched individuals in groups on at least one variable – most commonly chronological age (CA) – either exclusively (7 studies) or in combination with other parameters (12 studies). In three studies, ASD and comparison groups differed in terms of mental age/IQ (Glaser & Shaw, 2011; Gotleib & Bortner, 1984; Ratekin, 1993). Thus, there was substantial variability across studies in the sampling of target and comparison groups as well as in methods of group matching.

1.4.2. Measuring Temperament

Fifty four studies used questionnaire measures of temperament, while eight reported on observational measurement and two combined both of these methods (i.e., Macari et al., 2018; Ratekin, 1993). The most frequently used questionnaire measures were based on the work of Rothbart and colleagues, with 27 studies using age-appropriate versions of their measures. Thirteen studies used measures based on the conceptualizations proposed by Thomas and Chess (1968). Nine studies used a questionnaire measure based on Cloninger's model (1986, 1987) while only one study used the measure based on Buss and Plomin's model (1975, 1984). Six remaining studies used questionnaire measures not clearly aligned with any of the dominant models of temperament (see Table 1).

In terms of informants, 13 studies relied on self-report, while two included both self- and other-report measures, and 39 relied on other-report alone. The choice of informant seemed dependent on participants' age and developmental stage; such that research with younger children predominantly relied on parent-report, and self-report measures were more frequently utilized in later childhood/adolescence. Only one study had both mothers and fathers provide independent reports on the temperament of each child participant (i.e., Bostrom, Broberg, & Hwang, 2010).

Among the 54 questionnaire-based studies, only ten examined the psychometric properties of the temperament measure adopted with the ASD participant sample in question. Five studies explored the psychometric properties of measures derived from the conceptual approach of Thomas and Chess. Konstantareas and Papageorgeu (2006) computed Cronbach's α on the overall Dimensions of Temperament Scale–Revised (DOTS–R–Child: Windle, & Lerner, 1986), finding α=.62, but did not report data for individual DOTS-R subscales. Internal consistency >.70 was also reported by Rivers and Stoneman (2008) for activity level, persistence, behaviour inhibition, and negative emotionality scales of the Temperament Assessment Battery-Revised (TAB-R). Del Rosario, Gillespie-Lynch, Johnson, Signman, and Hutman (2014) found that among 6-month-old infants with later diagnosed ASD, only one of the nine scales of the Revised Infant Temperament Questionnaire (RITQ) – the activity scale – had adequate internal consistency (Cronbach's α=.74), though this situation improved such that by 36 months of participant age, only three of the Behavior Style Questionnaire (BSQ) scales (i.e., persistence, sensory reactivity and rhythmicity) had internal consistency coefficients < .70.

Hepburn and Stone (2006) reported test-retest reliability scores (mean=26 days between assessments) >.68 for all of the BSQ subscales, and internal consistency >.70 for all apart from rhythmicity (α=.48), mood (α=.51) and threshold (α=.40). Similarly, Barger et al. (2019) reported internal consistency estimates >.70 for all subscales apart from mood (α=.67), persistence (α=.60), rhythmicity (α=.59), and threshold (α=.52). Of note, the CTS also do not tend to have strong internal consistency in non-ASD populations (Windle & Lerner, 1986).

Five studies explored the psychometric properties of measures derived from the conceptual approach of Rothbart. Konstantareas and Stewart (2006) found that, with the exception of the smiling and laughter scale ($\alpha\leq$.53), internal consistency values for the Children's Behavior Questionnaire (CBQ) fine-grained scales were >.63, with most being above .75. Internal consistency estimates >.60 were reported for all fine-grained scales of the Toddler Behavior Assessment Questionnaire-Revised (TBAQ-R) (Garon et al., 2009), but only four (of 12) scales comprised in the Early Adolescent Temperament Questionnaire-Revised (EATQ-R) (Burrows, Usher, Schartz, Mundy, & Henderson, 2016). Nonetheless, Burrows et al. (2016) reported acceptable internal consistency for the EATQ-R dimensions (surgency [α=.72], negative affect [α=.76], effortful control [α=.74], and affiliation [α=.64]), as did Uljarević, Richdale, Evans, Cai, and Leekam (2017) for the effortful control dimension of the Adolescent/Adult Temperament Questionnaire (ATQ; α=.84) and Korbut et al. (2020) for Early Childhood Behavior Questionnaire (ECBQ) dimensions apart from surgency-extraversion (α=.84).

Two studies examined the factor structure of temperament questionnaires in the context of ASD. Barger et al. (2019) derived factors corresponding to the original BSQ maladaptability, activity, and rhythmicity scales were in children with ASD and a population comparison group. However, several novel factors emerged across both groups blending BSQ items from different scales – labelled environmental sensitivity, quiet persistence, food openness, social inattention, social approach, and crying – and the ASD group showed evidence of a unique negative social interactions factor. Further, Garon et al. (2016) found the same higher-order factors and factor loadings could be specified for the Infant Behavior Questionnaire (IBQ) and Toddler Behavior Assessment Questionnaire-Revised (TBAQ-R) among high and low familial ASD risk infants. However, differences in factor intercepts indicated non-invariance of IBQ and TBAQ-R across groups.

In summary, the majority of studies of temperament in ASD have used only one method of assessing temperament, most frequently questionnaire-based methods. From the psychometric evidence reported, it seems reasonable to utilize measures of temperament developed for use with TD populations among ASD samples. Measures based on the temperament models put forward by Chess and Thomas and Rothbart have garnered the most psychometric support in samples with ASD; however, two studies (i.e., Barger et al., 2019; Garon et al., 2016) suggest there may be differences in instrument factor structure. Furthermore, very few studies have used both self- and informant-reports of temperament and only one study has used both maternal and paternal reports (Bostrom et al., 2010).

Finally, although several studies have explored the relationship between temperament and both the core and associated/co-morbid problems experienced by people with ASD, only one study adopted the conservative method of removing items from temperament measures in an attempt to avoid overlap with other related constructs. Specifically, Adamek et al. (2011) removed two and reworded three CBQ items from the anger/frustration subscale in order to avoid overlap between temperamental negative affectivity and problem behaviors, as measured by the Aberrant Behavior Checklist. We return to consider this point further, below.

1.4.3. Summary of Empirical Results

A detailed summary of results from each study is presented in Tables 2-4. Here, we first consider the findings of studies that have compared temperament trait levels between samples of individuals with ASD and TD individuals, before turning to those that have compared individuals with ASD to those with other clinical conditions. To facilitate interpretation we synthesize the findings using the higher-order framework presented above and focus our narrative on those studies that have used assessments based on the dominant models of temperament (i.e., those of Rothbart, Thomas and Chess, Buss and Plomin, and Cloninger) in examining between-group similarities and differences. Nevertheless, Table 2. presents results for all studies, including those that have adopted questionnaire measures not clearly aligned with any of the dominant frameworks. Finally, we consider findings regarding associations among measures of temperament and other factors examined within studies (Table 3), before summarising the findings of prospective longitudinal investigations of temperament and ASD diagnosis (Table 4). Due to wide variability across studies in terms of temperament assessments and characteristics of ASD and comparison groups, data was not appropriate for the meta-analysis. Therefore, findings regarding temperamental differences between ASD and both TD and other clinical groups were summarized qualitatively. Although similar measurement and design issues were present with regards to studies exploring association among temperament dimensions and other factors, it was possible to synthesize some of this evidence using the meta-analytic approach. These findings are reported after qualitative description of these studies and summarized in Table 5.

Table 2

Summary of Between-Group Differences

	Affectivity/Emotionality		**Sociability**		**Self-regulation**	
Study	**ASD vs TD**	**ASD vs**	**ASD vs TD**	**ASD vs**	**ASD vs TD**	**ASD vs**
Adamek et al. (2011)	>anger/frustration <discomfort ≈soothability ≈sadness		>high intensity pleasure ≈activity level ≈impulsivity ≈shyness		<inhibitory control <attentional focusing >low intensity pleasure	
Anckarsäter et al. (2006)	>harm avoidance	ADHD: ≈harm avoidance	<reward dependence	ADHD: <reward dependence	<novelty seeking ≈persistence	ADHD: <novelty seeking ≈persistence
Bailey et al. (2000)	<adaptability ≈mood	FXS: >mood ≈adaptability	<intensity <approach ≈activity	FXS: <activity <intensity ≈approach	<persistence <distractibility <threshold >rhythmicity	FXS: <distractibility <threshold ≈rhythmicity ≈persistence
Barger et al. (2019)	>maladaptability >crying		<social approach >social inattention ≈activity		<rhythmicity <quiet persistence <food openness	

			<environmental sensitivity	
Biebrich & Morgan (2004)	DS: ≈negative affect (irritability, hostility, compliance; T1/2)	DS: <positive affect (affective sharing; T1/2)		DS: <self-regulation (attention, object orienting, persistence; T1/2)
Biebrich & Morgan (1998)	DS: >negative affect	DS: <positive affect ≈activity level		DS: <self-regulation
Bostrom et al. (2010)	DS: >emotionality CP/MI: >emotionality ID: ≈emotionality OD: ≈emotionality	DS: <sociability >shyness ≈impulsivity ≈activity CP/MI: <sociability ≈impulsivity ≈shyness ≈activity ID: <sociability		

				>impulsivity ≈shyness ≈activity OD: <sociability ≈impulsivity ≈shyness ≈activity		
Brock et al. (2012)	<adaptability ≈mood	DD: ≈adaptability ≈mood	>activity <approach <intensity	DD: <approach ≈activity ≈intensity	<rhythmicity <persistence <distractibility <threshold	DD: <distractibility ≈rhythmicity ≈persistence ≈threshold
Burrows et al. (2016)	>negative affect (aggression, depressive mood) ≈frustration		<surgency (high intensity pleasure, fear, shyness) ≈affiliation (affiliation, pleasure sensitivity,		<attention ≈effortful control (activation control, inhibitory control)	

		perceptual sensitivity)		
Chuang et al. (2012)	<adaptability >mood	>activity <approach ≈intensity	<persistence <distractibility <threshold ≈rhythmicity	
De Pauw et al. (2011)	>negative affect	<surgency	<effortful control	
Faja & Dawson (2013)		≈approach ≈impulsivity	<effortful control (attention focusing, inhibitory control, low intensity pleasure) ≈perceptual sensitivity	
Glaser & Shaw (2011)				22q13 DS: >self-regulatory difficulties (detached) ≈hypersensitive ≈underreactive ≈dysregulated

Gomez & Baird (2005)					>self-regulatory difficulties (detached, hypersensitive, underreactive, dysregulated)	
Helles et al. (2016)		No longer ASD: ≈harm avoidance ASD with comorbidity: <hard avoidance		No longer ASD: >reward dependence ASD with comorbidity: ≈reward dependence		No longer ASD: <novelty seeking ASD with comorbidity: ≈novelty seeking
Hendry et al. (2018)					<effortful control	HR-No ASD: <effortful control
Hepburn & Stone (2006)	<adaptability ≈mood		≈activity ≈approach ≈intensity		<threshold of responsiveness <persistence ≈distractibility ≈rhythmicity	

Hirschler-Guttenberg et al. (2015)					≈emotion regulation	
Hirschler-Guttenberg et al. (2015)	>negative emotionality with father (but ≈ with mother)		<positive emotionality		>self-regulatory behaviour	
Hoijer & Sizoo (2020)		ASD with suicidal ideation: <harm avoidance ASD with suicidal attempt(s): ≈harm avoidance		ASD with suicidal ideation: ≈reward dependence ASD with suicidal attempt(s): ≈reward dependence		ASD with suicidal ideation: >novelty seeking ≈persistence ASD with suicidal attempt(s): ≈novelty seeking ≈persistence
Jahromi et al. (2012)					<persistence	
Kasari & Sigman (1997)	>difficult temperament	DD/DS: >difficult temperament				
Konstantarea & Stewart (2006)	<soothability ≈discomfort		≈shyness		<attention focusing <attention shifting	

			≈smiling and laughter		<inhibitory control ≈perceptual sensitivity	
Macari et al. (2017)	>negative emotionality (soothability) ≈anger ≈discomfort ≈sadness ≈social fear	DD: ≈negative emotionality ≈soothability ≈anger ≈discomfort ≈sadness ≈social fear	<surgency (positive anticipation) ≈activity ≈high intensity pleasure	DD: <surgency (positive anticipation) ≈activity ≈high intensity pleasure	<effortful control (attention shifting, inhibitory control, low intensity pleasure, perceptual sensitivity) ≈attention focusing	DD: <effortful control (attention shifting, inhibitory control, low intensity pleasure, perceptual sensitivity) ≈attention focusing
Macari et al. (2018)	<fear intensity ≈anger intensity ≈ incongruent negative emotions	DD: <fear intensity >anger intensity ≈incongruent negative emotions	≈joy intensity	DD: ≈joy intensity		
Myles et al. (2007)	>fear >frustration >aggression		>affiliation >shyness		<activation control	

	>depressed mood		≈surgency/high intensity pleasure			
Ostfeld-Etzion et al. (2016)	≈anger frustration ≈discomfort ≈soothability ≈fear ≈sadness		≈activity level ≈approach ≈high intensity pleasure ≈impulsivity ≈shyness ≈smiling and laughter		<attention focusing <inhibitory control <perceptual sensitivity ≈attention shifting ≈low intensity pleasure	
Ozyurt et al. (2018)		DLD: >emotional lability				DLD: <emotion regulation
Ratekin (1993)	>sensitivity <mood <adaptability	DD: >sensitivity <mood <adaptability	<approach >intensity	DD: <approach >intensity	>distractibility <task orientation <personal social flexibility	DD: >distractibility <task orientation <personal social flexibility
Reyes et al. (2019)	>mood (T1/2) <adaptability (T2)	DD: >mood (T1/2) <adaptability (T1/2)	<approach (T1/2) >intensity (T1) ≈activity	DD: >activity (T2) <approach (T1/2) ≈intensity	<distractibility (T1/2) <rhythmicity (T2) <persistence (T2)	DD: <distractibility (T1/2) <rhythmicity (T2)

	≈threshold	<persistence (T2) ≈threshold
Samyn et al. (2011)	<inhibitory control (PR/SR) <activation control (PR) <attention control (PR/SR) <attention focusing <attention shifting ≈persistence/low distractibility ≈impulsivity	ADHD: >activation control (SR) >persistence/low distractibility >impulsivity ≈attention focusing ≈attention shifting ≈inhibitory control ≈attention control
Samyn et al. (2015)	<attention control (PR) <activation control (PR) <inhibitory control (PR) <persistence/low distractibility <attention focusing	ADHD: >attention control (PR/SR) >activation control (SR) >impulsivity (SR) >persistence/low distractibility

					<attention shifting ≈impulsivity	≈attention focusing ≈attention shifting ≈inhibitory control
Schwartz et al. (2009)	>negative affectivity		<surgency ≈affiliativeness		≈effortful control	
Sizoo et al. (2009)	>hard avoidance		<reward dependence		≈novelty seeking ≈persistence	
Sizoo et al. (2014)	>harm avoidance	ADHD: >harm avoidance	≈reward dependence	ADHD: ≈reward dependence	≈novelty seeking ≈persistence	ADHD: <novelty seeking ≈persistence
Soderstrom et al. (2002)	>harm avoidance		<reward dependence		<novelty seeking ≈persistence	
Vuijk et al. (2018)	>harm avoidance		<reward dependence		<novelty seeking ≈persistence	
Zantinge et al. (2019)	≈fear expression					

Note. “<” and “>” are signs used to denote that one group shows either higher or lower level of behaviours/traits/problems in question. ASD= Autism Spectrum Disorder; TD= Typically Development; ADHD= Attention Deficit Hyperactivity Disorder; FXS= Fragile X Syndrome; DLD= Developmental Language Delay; DS= Down Syndrome; ID= Intellectual Disability; CP/MI= Cerebral Palsy/Motor Impairment; DD= Developmental Delay; 22q13 DS= 22q13 Deletion Syndrome; T= timepoint; PR= parent report; SR= self-report.

1.4.4. Temperamental Differences between ASD and TD Samples

Studies using questionnaire measures based on Rothbart's conceptualization of temperament have shown that, when compared to TD children/adolescents, those with ASD tend to show a characteristic pattern of scores across the broad factors/constructs assessed; lower effortful control, lower surgency and affiliativeness, and higher negative affect (Adamek et al., 2011; De Pauw, Mervielde, Van Leeuwen, & De Clerq, 2011; Glaser & Shaw, 2011; Garon et al., 2009; Uljarević et al., 2017; Macari, Koller, Campbell, & Chawarska, 2017; Myles et al., 2007; Ostfeld-Etzion, Feldman, Hirschler-Guttenberg, Laor, & Golan, 2016; Samyn, Roeyers, & Bijttebier, 2011; Samyn, Roeyers, Bijttebier, Rosseel, & Wiersema, 2015; Schwartz et al., 2009).

This profile appears to hold irrespective of the specific age of participant samples (although see Schwartz et al., 2009, for an exception). However, findings from a recent study (i.e., Macari et al., 2018) suggest that the *specific* profile of temperament differences between individuals with and without ASD might depend on the context of temperament assessment. Macari et al. (2018) assessed the peak intensity of emotion expressed in response to a modified set of induction probes derived from the Laboratory Temperament Assessment Battery (Lab-TAB; Goldsmith & Rothbart, 1999). Unlike questionnaire-based studies, they found that toddlers with ASD expressed similar intensity, joy and anger but less intense fear than age-matched TD controls. This result has yet to be replicated, though it is interesting to note that Zatinge et al. (2019) found a positive correlation between rate arousal and fearful expression among TD controls but no such correlation among children with ASD.

Studies using measures based on Thomas and Chess's model of temperament tend to report consistent findings in terms of lower adaptability, distractibility and persistence among individuals with ASD compared to TD controls (Hepburn & Stone, 2006; Bailey, Hatton, Mesibov, Ament, & Skinner, 2000; Brock et al., 2012; Chuang, Tseng, Lu, Shieh, & Cermak, 2014), consistent with higher negative affectivity and lower effortful control reported in studies using measures based on Rothbart's model of temperament. Several studies report lower intensity among individuals with ASD (Bailey et al., 2000; Brock et al., 2012) though others report no such significant between-group differences (Chuang et al., 2014), and one study (Reyes et al., 2019) reported higher intensity among children with ASD in the toddler years but non-significant differences at a subsequent timepoint. Two studies have classified children into difficult and easy temperament subtypes, with Kasari and Sigman (1997) reporting that children with ASD had more difficult temperament compared to TD peers, and Chuang et al. (2014) finding that 34.3% of children with ASD were classified as having difficult temperament (compared to 10% in TD samples; Thomas, 1968) and only 34.5% having easy temperament characteristics. Since difficult temperament primarily comprises lower adaptability and negative mood, these findings are consistent with higher negative affectivity reported in studies using Rothbart's scales.

Studies using the Temperament and Character Inventory (Cloninger et al., 1994) have almost consistently reported increased harm avoidance (consistent with higher negative affectivity in Rothbart's scales) and reduced reward dependence in ASD compared to TD samples (Anckarsäter et al., 2006; Sizoo et al., 2009; Vuijk et al., 2018; Soderstrom, Rastam, & Gillberg, 2002; although see Sizoo et al., 2014), whereas reduced novelty seeking was reported in some studies (Anckarsäter et al., 2006; Soderstrom et al. 2002; Vuijk et al., 2018) but not all (Sizoo et al., 2009, 2014). A study by Helles, Gillberg, Gillberg, Billstedt, and Wallinius (2016) compared temperament profiles among the following 3 subgroups of adults who had been diagnosed with ASD in childhood: a) those who no longer met ASD criteria, b) those with ASD plus psychiatric comorbidity, and c) those with ASD only (without comorbidity). When compared to a reference sample, both the ASD plus comorbidity and ASD only groups had higher harm avoidance, while the ASD only group had lower novelty seeking and the ASD plus comorbidity group had lower self-directedness and cooperativeness. Individuals who no longer met ASD criteria had higher reward dependence.

In summary, while methodological differences make it difficult to conclusively identify patterns of lower-order temperament traits in relation to ASD, there does appear to be some convergence of findings at a higher-order level. Higher negative affect, adaptability, and harm avoidance, and higher rates of broadly difficult temperament appear to converge to suggest that children and adolescents with ASD can be distinguished from TD controls by a profile of higher affectivity/emotionality. Similarly, lower sociability, affiliativeness, persistence, reward dependence, and effortful control indicate a profile of lower surgency and self-regulation in ASD. Findings of lower distractibility might also be related to difficulties with self-regulation, such that individuals with ASD tend to show abnormal disengagement of visual attention and perseverative interests (Landry & Bryson, 2004). While yet to be replicated, evidence of an attenuated fear response in ASD a laboratory setting (e.g., Macari et al., 2018) raises the question of whether context plays a role in the pattern of findings of across studies.

1.4.5. Temperamental Differences between ASD and Other Clinical Samples

Studies that have compared temperamental trait levels between individuals with ASD and ADHD have found higher activation control and persistence (Samyn et al., 2011, 2015) and harm avoidance (Sizoo, van der Gaag, & van den Brink, 2015), but lower impulsivity (Samyn et al., 2011, 2015) and sensory seeking (Sizoo et al., 2014) among individuals with ASD. Anckarsäter et al. (2006) found that individuals with dual diagnoses of ASD and ADHD have higher novelty seeking than those diagnosed with ASD alone.

Studies comparing temperament between samples of individuals with ASD and those without ASD but with developmental delay found that ASD group had lower self-regulation, positive affect, and surgency (Macari et al., 2017), lower approach and distractibility (Brock et al., 2012; Reyes et al., 2019) (but Ratekin, 1993, identified higher distractibility), as well as more difficult temperament (Kasari & Sigman, 1997). Interestingly studies by Bostrom et al. (2010) and Macari and colleagues (2017) reported no differences between ASD and developmentally delayed groups in terms of negative affect, and Macari and colleagues (2018) observed less intense fear in toddlers with ASD compared to developmentally delayed controls.

Two studies have compared temperament between groups of individuals with ASD and individuals with known genetic syndromes, finding higher threshold for change, lower activity and intensity, and more negative mood and greater distractibility in ASD when compared to individuals with Fragile X syndrome (Bailey et al., 2000), and lower intensity when compared to individuals with 22q13 Deletion Syndrome (Glaser & Shaw, 2011).

In summary, similar to studies comparing samples of individuals with ASD to TD controls, studies that have drawn a comparison to individuals with other clinical/developmental conditions suggest the possibility of certain group-level temperamental differences. Again, the variety of temperament instruments, along with the variety in comparison groups, used in these studies precludes the systematic integration of findings concerning lower-order temperament dimensions. Nonetheless, individuals with ASD can be distinguished from other clinical samples by higher affectivity/emotionality (higher harm avoidance, more negative mood), low sociability (lower impulsivity, activity, approach, intensity, positive affect), and low self-regulation (greater distractibility), just as when compared to TD individuals.

1.4.6. Longitudinal Investigations into Temperament and ASD

Compared to the relatively large number of cross-sectional studies, synthesized above, longitudinal studies on temperament and ASD have emerged only recently in the literature. Table 3 summarises findings from 19 studies, three of which used assessments based on Thomas and Chess's model of temperament, another 11 drawing upon Rothbart's assessments and one following Cloninger's model. The remaining four used measures not clearly aligned with a dominant theoretical model.

One study reviewed above (Helles et al., 2016) compared current temperament profiles of adults diagnosed with ASD in childhood who had participated in a long-term follow-up study. Eight studies examined the longitudinal stability of child temperament in ASD and reported significant cross-time correlations (Berkovits, Eisenhower, & Blacher; 2017; Biebrich & Morgan, 2004; Garon et al., 2016; Macari et al., 2017; Reyes et al., 2019) and a trajectory of decreasing activity level, adaptability, and self-regulation (Del Rosario et al., 2014; Pijl et al., 2020; Reyes et al., 2019) and increasing surgency (Paterson et al., 2019) in early-life. Two studies (i.e., Berkovits, et al., 2017; Bos, Diamantopoulou, Stockmann, Begeer, & Rieffe, 2018) explored the longitudinal relation between temperament and aspects of child functioning and found that emotion dysregulation was predictive of increased behavioural difficulties in school-aged children with ASD. Finally, Macari et al. (2017) explored how changes in particular aspects of temperament across a 12-month period predicted outcomes in various aspects of the ASD clinical phenotype. Lower change scores suggesting less improvement or decline in perceptual sensitivity predicted more severe later ASD symptoms, while improvements in inhibitory control and low-intensity pleasure predicted gains in level of adaptive social skills over the same time period.

Ten studies have taken the approach of tracking the early development of infants with an older sibling with ASD, thereby considered to be at higher-than-usual risk for also being diagnosed with the condition (see Zwaigenbaum et al., 2005, for a review) and able to be followed prospectively from early infancy until late toddlerhood/early childhood when diagnostic outcome status could be determined. These are summarized in Table 4.

Table 3

Summary of Correlational Findings

Study	**Construct(s) of Interest (Measure)**	**Correlational Results**
Adamek et al. (2011)	Irritability (ABC).	Irritability + correlated with negative affectivity (and sadness, anger/frustration, discomfort, and soothability [−] subscales) and surgency (and activity level and high intensity pleasure subscales), and – correlated with effortful control (and inhibitory control subscale).
Baker et al. (2019)	Chronological age.	Older age associated with a stronger + association between child independent and dyadic dysregulation, and stronger − association between parental scaffolding and child independent dysregulation.
Barger et al. (2019)	Chronological age; Gender; Cognitive level (MSEL); ASD symptoms (SCQ); Maternal race; Maternal education.	Chronological age + correlated with negative social, only; Gender NS correlated with any temperament factor; Cognitive level + correlated with quiet persistence, activity rhythmicity, and negative social; ASD severity + correlated with maladaptivity, social inattention, and crying, and − correlated with environmental sensitivity, quiet persistence, social approach, rhythmicity, food openness, and negative social; Maternal race differences found for maladaptivity, social inattention, crying, and food openness;

		Maternal education differences found for quiet perseverance and crying.
Berkovits et al. (2017)	Time; Cognitive level (WPPSI-III); Language (CASL-2); Problem behaviour (CBCL); Social skills (SSIS); ASD symptoms (SRS, ADOS-2).	Emotion regulation and lability/negativity stable from T1 to T2; Cognitive level NS correlated with emotion regulation or lability/negativity; Language NS correlated with emotion regulation or lability/negativity; Problem behaviour – correlated with emotion regulation and + correlated with lability/negativity; Change (at T2) in externalizing predicted by emotion regulation; Change (at T2) in internalizing predicted by lability/negativity; Social skills + correlated with emotion regulation and – correlated with lability/negativity; ASD symptoms (per SRS) – correlated with emotion regulation and + correlated with lability/negativity (but NS correlated per ADOS-2).
Biebrich & Morgan (2004)	Time.	T1 self-regulation + correlated with T2 self-regulation; Positive affect and negative affect NS correlated at T1 and T2.

Bolte et al. (2008)	ASD symptoms (SRS).	ASD symptoms + correlated with novelty seeking and harm avoidance, – correlated with reward dependence, self-directedness, and cooperativeness.
Bos et al. (2018)	Disruptive behaviour (CSI); Anxiety symptoms (CSI); Depression symptoms (CDI); Somatic complaints (SCL).	Disruptive behaviour (at T3) + predicted by worry/rumination (at T1); Anxiety symptoms + predicted by negative emotionality; Depression symptoms + predicted by worry/rumination; Somatic complaints + predicted by worry/rumination and negative emotionality.
Bostrom et al. (2010)	Informant (mother vs father).	Mother report of child temperament + correlated with father report of child temperament across all scales (activity, shyness, sociability, emotionality, and impulsivity).
Brock et al. (2012)	Sensory features (SP, SEQ, TDDT-R, SPA).	Sensory features + associated with withdrawal and negative mood; Sensory hyporesponsiveness – associated with adaptability, threshold, and distractibility.
Bryson et al. (2018)	Visual attention (gap-overlap task).	Left-directed disengage latencies associated with activity, soothability, fear, and + associated with distress to limitations at 12 mths (NS correlated with temperament at 6 mths); Right-directed disengage latencies – associated with fear and + associated with distress to limitations at 12 mths (NS correlated with temperament at 6 mths).

Burrows et al. (2016)	Problem behaviour (BASC-2).	Internalizing + associated with negative affect and – associated with surgency and effortful control; Externalizing + associated with negative affect and – associated with effortful control.
Chuang et al. (2012)	Sensory features (SP-C).	Sensory seeking – associated with activity level and adaptability, and + associated with distractibility; Sensory avoidance – associated with adaptability and + associated with persistence; Sensory hypersensitivity –associated with intensity; Sensory hyposensitivity – associated with mood and persistence.
Chuang et al. (2014)	Health-related quality of life (TAPQOL-C).	Social functioning – associated with intensity and + associated with threshold; Cognitive functioning – associated with distractibility; Emotional functioning – associated with intensity and distractibility and + associated with rhythmicity.
De Pauw et al. (2011)	Problem behaviour (CBCL).	Internalizing – associated with surgency and effortful control, and + associated with negative affect;

		Externalizing – associated with effortful control and + associated with surgency and negative affect.
Del Rosario et al. (2014)	Time.	T1 to T5 decreases in activity level and adaptability.
Faja & Dawson (2013)	Chronological age; Cognitive level (DAS-2); Attention problems (BASC-2); Hyperactivity (BASC-2); Social skills (SSRS, VABS-2); ASD symptoms (ADOS-SA).	Age, cognitive level, attention problems, hyperactivity, and social skills NS associated with effortful control; ASD symptoms – correlated with effortful control.
Garon et al. (2009)	ASD symptoms (ADOS-SA).	ASD symptoms – associated with behavioural approach (after cognitive level controlled)
Garon et al. (2016)	Time. ASD symptoms (ADOS, ADI-R).	T1 positive/negative affect + associated with T2 positive/negative affect. T3 ASD symptoms – associated with T2 effortful control.
Helles et al. (2016)	General functioning (GAF); Cognitive level (WAIS-III); ADHD symptoms (ASRS);	General functioning – correlated with harm avoidance, and + correlated with reward dependence and persistence;

	Depression symptoms (BDI); ASD symptoms (ASDI).	Cognitive level and ADHD symptoms NS correlated with temperament; Depression symptoms + correlated with harm avoidance; ASD symptoms – correlated with novelty seeking.
Hendry et al. (2018)	Visual attention (eye-tracking)	Change in look duration to faces (from 9 to 15 mths) – associated with effortful control; Change in look duration to non-social scrambled face stimuli NS associated with effortful control.
Hirschler-Guttenberg et al. (2015)	Maternal regulation facilitation (observed); Maternal temperament (ATQ); Maternal parenting style (PSDQ).	Maternal regulation facilitation – associated with child self-regulation of anger, and + associated with child co-regulation of anger and fear; Maternal temperament NS associated with child temperament; Authoritarian parenting + associated with child self-regulation of anger, and – associated with child co-regulation of anger; Authoritative parenting + associated with child self-regulation of fear.
Hirschler-Guttenberg et al. (2015)	Dyadic reciprocity (observed); Cognitive level (SB).	Mother-child and father-child reciprocity – correlated with child self-regulation;

		Mother-child reciprocity – correlated with child negative emotionality; Cognitive level + correlated with self-regulation (interaction with father, only).
Kasari & Sigman (1997)	Parent stress (PSI); Social engagement and responsiveness (observed): Cognitive level (Cattell, SB); Language (RDLS); ASD symptoms (ABC).	Parent stress (related to child characteristics) + correlated with difficult temperament; Time engaged with parent (but not examiner) – correlated with difficult temperament; Responsiveness to examiner (but not parent) – correlated with difficult temperament; Cognitive level – correlated with difficult temperament; Expressive and receptive language – correlated with difficult temperament; ASD symptoms + correlated with difficult temperament.
Konstantarea & Papageorgeu (2006)	Maternal stress (QRS).	Maternal stress + correlated with activity level (general), task orientation and rhythmicity (daily habits, and – correlated with flexibility/rigidity, mood, and rhythmicity (sleep).
Konstantarea & Stewart (2006)	Chronological age;	Chronological age NS associated with temperament;

	Cognitive level (DPII); ASD symptoms (CARS).	Cognitive level + associated with negative affectivity; ASD symptoms – associated with effortful control.
Korbut et al. (2020)	Challenging behaviour (HSQ-PDD).	Challenging behaviour frequency/severity (T2) + correlated with (T1) negative affectivity, and – correlated with (T1) effortful control (but NS after cognitive level controlled); Challenging behaviour severity (T2) – correlated with (T1) surgency (but NS after cognitive level controlled).
Macari et al. (2017)	Time; Cognitive level (MSEL); ASD symptoms (ADOS-G).	T1 effortful control, surgency, and negative emotionality + correlated, respectively, with T2 effortful control, surgency, and negative emotionality; Non-verbal cognitive level + correlated with surgency (positive anticipation scale), verbal cognitive level NS correlated with temperament; ASD symptoms NS correlated with temperament; ASD symptoms at T2 associated with minimal improvement in perceptual sensitivity from T1 to T2.
Macari et al. (2018)	Informant (observed vs parent-report); ASD symptoms (ADOS-2).	Observed fear intensity + correlated with parent-reported fear, and observed joy intensity + correlated with parent-reported positive anticipation;

		ASD symptoms (social affect domain) – correlated with intensity of joy;
Millea et al. (2013)	Social anxiety (SASC-R).	Social anxiety + associated with negative affectivity; Social anxiety-socialization association moderated by negative affectivity,
Nazim & Khalid (2019)	Cognitive level (NR); Problem behaviour (NR); ASD symptoms (CARS).	Cognitive level + correlated with effortful control and – correlated with negative affectivity; Problem behaviour + correlated with negative affectivity and – correlated with surgency and effortful control; ASD symptoms + correlated with negative affectivity and – correlated with effortful control.
Ostfeld-Etzion et al. (2016)	Self-regulated compliance (observed).	Self-regulated compliance + associated with attention focusing.
Ozyurt et al. (2018)	Language (TELD-3); Maternal depression (BDI); Cognitive level (DDST).	Receptive language + correlated with emotion regulation and – correlated with emotional lability; Expressive language + correlated with emotion regulation; Maternal depression + correlated with emotional lability; Cognitive level + correlated with emotion regulation.

Paterson et al. (2019)	Cognitive level (MSEL); ASD symptoms (AOSI).	Verbal and non-verbal cognitive level NS correlated with temperament (after correction); ASD symptoms NS associated with temperament.
Pijl et al. (2019)	Time.	T1 to T2 decreases in surgency and effortful control.
Reyes et al. (2019)	Time.	T1 activity and approach + correlated, respectively, with T2 activity and approach; T1 to T2 decreases in rhythmicity, persistence, and threshold of responsiveness.
Rivers & Stoneman (2018)	Sibling relationship (SIB, SSRS)	Sibling relationship NS correlated with temperament of child with ASD; Positive sibling relationship – associated with persistence of both siblings (TD and ASD).
Samyn et al. (2011)	ADHD symptoms (DBD); ASD symptoms (SRS).	PR inattention and hyperactivity/impulsivity – correlated with inhibitory control (PR/SR), activation control (PR/SR), attention control (PR/SR), persistence/low distractibility (SR), impulsivity (SR), attention focusing (SR), and attention shifting (SR); TR inattention – correlated with inhibitory control (PR/SR), activation control (PR/SR), attention control (PR/SR), persistence/low

		distractibility (SR), impulsivity (SR), attention focusing (SR), and attention shifting (SR); TR hyperactivity/impulsivity – correlated with inhibitory control (PR/SR), activation control (PR/SR), attention control (PR/SR), persistence/low distractibility (SR), impulsivity (SR), and attention focusing (SR); ASD symptoms – correlated with inhibitory control (PR/SR), activation control (PR), attention control (PR/SR), attention focusing (SR), and attention shifting (SR).
Samyn et al. (2017)	Executive attention (ANT).	Executive attention NS correlated with effortful control.
Schwartz et al. (2009)	Problem behaviour (BASC-2); ASD symptoms (ASSQ, SCQ).	Internalizing + correlated with negative affectivity and – correlated with surgency; Externalizing, social skills, atypicality, and withdrawal NS correlated with temperament; ASD symptoms NS correlated with temperament.
Shephard et al. (2019)	ADHD symptoms (Conners 3); Anxiety symptoms (SCAS); ASD symptoms (SRS-2).	Mid-childhood ADHD symptoms + associated with toddlerhood activity level, inhibitory control, and fear (after ASD symptoms controlled); Mid-childhood anxiety and ASD symptoms + associated with toddlerhood shyness and fear;

Sizoo et al. (2014)	ASD symptoms (AQ).	ASD symptoms + correlated with harm avoidance and – correlated with reward dependence; Social interaction + correlated with arm avoidance and – correlated with reward dependence; Attention to details NS correlated with temperament.
Zantinge et al. (2019)	Physiological arousal (heart rate).	Physiological arousal NS correlated with expression of fear.

Note. "+" and "–" denote positive and negative correlations/associations. NS= non-significant; ASD= Autism Spectrum Disorder; ADHD= Attention Deficit Hyperactivity Disorder; T= time; PR= parent-report; SR= self-report; TR= teacher-report; ABC= Aberrant Behavior Checklist; MSEL= Mullen Scales of Early Learning; SCQ= Social Communication Questionnaire; WPPSI-III= Wechsler Preschool and Primary Scale of Intelligence–Third *Edition;* CASL-2= Comprehensive Assessment of Spoken Language–Second Edition; SSIS-SS= Social Skills Improvement System; SRS= Social Responsiveness Scale; ADOS-2= Autism Diagnostic Observation Schedule–Second Edition; CSI= Child Symptom Inventory; CDI= Children's Depression Inventory; SCL= Somatic Complaints List; SP= Sensory Profile; SEQ= Sensory Experiences Questionnaire; TDDT-R= Tactile Defensiveness and Discrimination Test; SPA= Sensory Processing Assessment for Young Children; BASC-2= Behavior Assessment System for Children–Second Edition; SP-C= Sensory Profile, Chinese; TAPQOL-C= Preschool Children Quality of Life, Chinese; CBCL= Child Behavior Checklist; DAS-2= Differential Ability Scales–Second Edition; SSRS= Social Skills Rating System; ADI-R= Autism Diagnostic Interview-Revised; ADOS-SA= Autism Diagnostic Observation Schedule, Social Affect; VABS-2= Vineland Adaptive Behavior Scales–Second Edition; GAF= Global Assessment of Functioning; WAIS-III=Wechsler Adult Intelligence Scale–Third Edition; ASRS= Adult ADHD Self-Report Scale; BDI= Beck Depression Inventory; ASDI= Asperger Syndrome Diagnostic Interview; ATQ= Adult Temperament Questionnaire; PSDQ= Parenting Styles and Dimensions Questionnaire; SB= Stanford-Binet Intelligence Scale; PSI= Parenting Stress Index; RDLS= Reynell Developmental Language Scales; ABC= Autism Behavior Checklist; QRS= Questionnaire on Resources and Stress; DPII= Developmental Profile–Second Edition; HSQ-PDD= Home Situations Questionnaire–Pervasive Developmental Delays; ADOS-G= Autism Diagnostic Observation Schedule–Generic; SACS-R= Social Anxiety Scale for Children–Revised; CARS= Childhood Autism Rating Scale; TELD-3= Test of Early Language Development–Third Edition; DDST= Denver II Developmental Screening Test; AOSI= Autism Observation Scale for Infants; SIB= Sibling Inventory of Behavior; SSRS=

Satisfaction with the Sibling Relationship Scale; DBD= Disruptive Behavior Disorder Rating Scale; ANT= Attention Network Test; ASSQ= Autism Spectrum Screening Questionnaire; SCAS= Spence Children's Anxiety Scale; AQ= Autism Quotient.

Table 4

Summary of Prospective Studies of ASD Diagnostic Outcome

Study	**6 Months**	**12 Months**	**18 Months**	**24 Months**	**36 months**
Bolton et al. (2012)	**ASD vs No ASD:** ≈activity, rhythmicity, approach, adaptability, intensity, mood, persistence, distractibility, and threshold (after gender and full-scale IQ controlled).	NA	NA	**ASD vs No ASD:** <adaptability, persistence, and threshold; ≈activity, rhythmicity, approach, intensity, mood, and distractibility (after gender and full-scale IQ controlled).	NA
Clifford et al. (2013)	(7 mths) **HR vs LR:** <surgency (high intensity pleasure and approach subscales); ≈negative affect and effortful control. **HR-ASD vs LR**:	(14 mths) **HR vs LR:** <surgency (approach subscale) and effortful control (cuddliness subscale); ≈negative affect. **HR-ASD vs LR:** <smiling and laughter;	NA	**HR vs LR:** <effortful control (cuddliness and inhibitory control subscales); ≈surgency and negative affect. **HR-ASD vs LR:**	NA

	≈surgency, negative affect and effortful control. **HR-Atypical vs LR:** <approach; ≈surgency, negative affect and effortful control. **HR-TD vs LR:** <surgency (approach subscale); ≈negative affect and effortful control. **HR-ASD vs HR-TD:** >surgency (perceptual sensitivity subscale); ≈negative affect and effortful control. **HR-ASD vs HR-Atypical:**	<effortful control (cuddliness subscale); ≈surgency and negative affect **HR-Atypical vs LR:** ≈surgency, negative affect, and effortful control. **HR-TD vs LR:** <surgency; ≈negative affect and effortful control. **HR-ASD vs HR-Atypical:** <effortful control (cuddliness subscale); ≈surgency and negative affect. **HR-ASD vs HR-TD:** ≈surgency, negative affect, and effortful control.		>negative affect (sadness, shyness, and soothability subscales); <effortful control (low intensity pleasure and cuddliness subscales); ≈surgency. **HR-Atypical vs LR:** ≈surgency, negative affect, and effortful control. **HR-TD vs LR:** ≈surgency, negative affect, and effortful control. **HR-ASD vs HR-Atypical & HR-TD:** ≈surgency, negative affect, and effortful control.

	≈surgency, negative affect and effortful control.				
Del Rosario et al. (2013)	**HR-ASD vs HR-TD** <adaptability and approach; ≈activity, mood, intensity, distractibility, persistence, sensory reactivity, rhythmicity.	**HR-ASD vs HR-TD** <adaptability; ≈activity, approach, mood, intensity, distractibility, persistence, sensory reactivity, rhythmicity.	**HR-ASD vs HR-TD** ≈activity, adaptability approach, mood, intensity, distractibility, persistence, sensory reactivity, rhythmicity.	**HR-ASD vs HR-TD** >adaptability and approach; ≈activity, mood, intensity, distractibility, persistence, sensory reactivity, rhythmicity.	**HR-ASD vs HR-TD** >adaptability and approach; ≈activity, mood, intensity, distractibility, persistence, sensory reactivity, rhythmicity.
Garon et al. (2009)	NA	NA	NA	**HR-ASD vs LR:** <behavioural approach and effortful emotion regulation. **HR-ASD vs HR-No ASD:** <behavioural approach; ≈effortful emotion regulation. **HR-No ASD vs LR:** >behavioural approach;	NA

				<effortful emotion regulation.	
Garon et al. (2016)	NA	**HR vs LR:** <distress to limitations; >fear; ≈smiling and laughter, activity level, soothability, and duration of orienting **HR-ASD vs HR-No ASD:** <positive affect; ≈negative affect.	NA	**HR vs LR:** >anger, sadness, and fear; <inhibitory control, soothability, attention focus, high pleasure, and low pleasure; ≈attention shifting, activity level, and positive anticipation. **HR-ASD vs HR-No ASD:** <effortful control and positive affect; ≈negative affect.	NA
Paterson et al. (2019)	**HR-ASD vs LR & HR-No ASD:** <surgency (smiling and laughter subscale) and regulatory capacity (low	**HR-ASD vs LR:** <surgency (approach, vocal reactivity, and smiling	NA	**HR-ASD vs LR:** <surgency (positive anticipation, sociability) and effortful control;	NA

	intensity pleasure subscale); ≈negative affect.	and laughter subscales) and regulatory capacity; >negative affect (sadness and falling reactivity subscales). **HR-ASD vs HR-No ASD:** <surgency (approach, vocal reactivity, and smiling and laughter subscales) and regulatory capacity; ≈negative affect.		>negative affect (discomfort, frustration, sadness). **HR-ASD vs HR-No ASD:** <surgency (positive anticipation and sociability subscales) and effortful control; ≈negative affect.	
Pijl et al. (2019)	(8 months) **HR-ASD>HR-Atypical> HR-TD> LR:** Negative affect.	(14 months) **LR> HR-TD> HR-Atypical> HR-ASD:** Surgency. **HR-ASD>HR-Atypical> HR-TD> LR:** Negative affect; Effortful control.	NA	**HR-ASD>HR-Atypical> HR-TD> LR:** Negative affect; Effortful control.	NA

Yirmiya et al. (2006)	(4 months) **HR-ASD vs HR-TD:** ≈unpredictable, fussy-difficult, inadaptable, and dull.	(14 months) **HR-ASD vs HR-TD:** ≈unpredictable, fussy-difficult, inadaptable, and dull.	NA	NA	NA
Zwaigenbaum et al. (2005)	**HR-ASD vs HR-No ASD & LR:** <activity level; ≈smiling and laughter, fear, distress to limitations, soothability, and duration of orienting	**HR-ASD vs HR-No ASD & LR:** >distress to limitations and duration of orienting; ≈activity level, smiling and laughter, fear, and soothability.	NA	**HR-ASD vs HR-No ASD & LR:** <attention shifting, inhibitory control, positive anticipation and affective responses.	NA

Note. “<” and “>” are signs used to denote that one group shows either higher or lower level of behaviours/traits/problems in question. ASD= Autism Spectrum Disorder; HR-ASD= high-risk siblings diagnosed with ASD; HR-TD= high-risk siblings with typical development; HR-No ASD= high-risk siblings without ASD (without specification of ‘TD’ or ‘Atypical’); HR-Atypical= high-risk siblings without ASD, but with atypical development; LR= low-risk infants/toddlers/siblings.

Del Rosario et al. (2014) found that infants who developed ASD showed higher activity and lower approach and adaptability across infancy, and as early as 6 months, compared to TD infants. Unlike Del Rosario et al., Zwaigenbaum et al. (2005) found *decreased* activity at 6 months among high-risk siblings later diagnosed with ASD, relative to non-ASD-diagnosed and low-risk comparison infants. Although a comparative pattern of extreme distress reactions, longer durations of orienting to objects, and decreased expression of positive affect was evident by 12 months in siblings later diagnosed with ASD. Four studies (Garon et al., 2009, 2016; Clifford et al., 2013; Paterson et al., 2013) using Rothbart's temperament measures found that higher negative affect and lower effortful control (and lower positive affect/surgency, only for Garon et al., 2016 and Paterson et al., 2019) distinguished 24-month-olds who later received an ASD diagnosis from those who had a more typical developmental outcome. Furthermore, Garon et al. (2016) found that lower effortful control at 24 months was associated with more severe ASD symptoms at 36 months. Finally, one study examined temperament as an early predictor of ASD outcome in a general population sample. Bolton, Golding, Emond, and Steer (2012) reported that no temperament dimension at 6-months found to be predictors of ASD traits (after controlling for gender and IQ) among those infants who *did not* develop ASD. However, by 24 months of age, adaptability, persistence and threshold were all significant predictors of later ASD diagnosis.

Two recent prospective studies examined the *specific* predictive value of temperament for later ASD diagnosis. Through use of a novel machine-learning algorithm method, Pijl et al. (2020) found that temperament trait combinations at 24 months had low positive predictive value and specificity for ASD diagnostic outcome at 36 months among infants at higher familial likelihood. Nevertheless, effortful control and its combination with surgency and negative affect had a high negative predictive value for ruling out ASD diagnosis. Shephard et al. (2019) investigated the specificity of associations between infant temperament traits and childhood symptoms of ADHD and anxiety, as compared to ASD. Higher activity and low inhibitory control were specifically associated with ADHD and not ASD or anxiety, whereas higher fearfulness and shyness predicted both anxiety and ASD symptoms.

Notwithstanding significant methodological heterogeneity within this small number of studies – in terms of assessment time-points, measures used, and statistical approach – it seems possible that temperament differences between individuals with and without ASD may be observed from as early as 6-months of age. This type of research, while still in its early days, presents promising potential for the field.

1.4.7. Concurrent Associations among Temperament and Other Factors

As can be seen in Table 3, studies have also explored associations between temperament and a wide range of other core and co-morbid symptoms among individuals with ASD. In general – and as reported for non-ASD populations – lower levels of temperamental effortful control and/or higher levels of negative affect have been associated with more behavioral problems (Adamek et al., 2011; Berkovits et al., 2017), internalizing and externalizing symptoms (De Pauw, 2011; Burrows et al., 2016; Korbut et al., 2020; Nazim & Khalid, 2019; Schwartz et al., 2009), anxiety (Uljarević et al., 2017), and social anxiety (Millea, Shea, & Diehl, 2013) among individuals with ASD. By contrast, studies looking at the association between temperament and core ASD symptoms (e.g., Bölte, Poustka, & Constantino, 2008; Fenning, Baker, & Moffitt, 2018; Kerekes et al., 2013), cognitive level (e.g., Faja & Dawson, 2015; Kasari & Sigman, 1997), language (e.g., Berkovits et al., 2017; Ozyurt et al., 2018), and sensory features (e.g., Brock et al., 2012; Chuang et al., 2014) have all yielded inconsistent results (please refer to Table 2 for more detail).Finally, recent studies using more experimental approaches reported associations between childhood temperament traits and eye-tracking measures of visual-spatial attention (Bryson et al., 2018) and social attention (Hendry et al., 2018) in ASD, but non-significant relations between temperament and heart rate (Zantinge et al., 2019) or performance on a neuropsychological task assessing executive attention (Samyn et al., 2017).

Other studies have explored associations between temperament and familial characteristics, including parental stress levels and sibling relationship quality. For example, Konstantareas and Papageorgiou (2006) found that increased level of stress in mothers was associated with lower infant flexibility, mood, and regular sleep, and higher levels of activity and general rhythmicity. There are also findings suggesting heightened negative emotionality and self-regulatory difficulties in children with ASD may be associated with parenting that is less synchronous and responsive (Kasari & Sigman, 1997; Hirschler-Guttenberg, Golan, Ostfeld-Etzion, & Feldman, 2015).

Effect sizes and heterogeneity statistics for the association of temperamental dimensions of negative affectivity, effortful control and surgency with other factors are shown in Table 5. It was only possible to synthesize evidence for IQ (3 studies; Korbut et al., 2020; Nazim & Khalid, 2019; Macari et al., 2017), behavioural problems (5 studies; Adamek et al., 2011; De Pauw et al., 2011; Korbut et al., 2020; Nazim & Khalid, 2019; Schwartz et al., 2009) and ASD social and communication symptoms (3 studies; Faja & Dawson, 2015; Macari et al., 2017; Schwartz et al., 2009). For association with IQ, mean effect size *r* was significant for sociability (r= .14, p= .004, 95% CI= .046, .234) but not for negative affectivity (r= -.15, p= .10, 95% CI= -.321, .029) and self-regulation (r= .15, p= .07, 95% CI= -.013, .313). For association with problem behaviours, mean effect size *r* was significant for negative affectivity (r= .45, p< .001, 95% CI= .313, .597), self-regulation (r= -.25, p< .001, 95% CI= -.339, -.16) but not for sociability (r= -.16, p= .21, 95% CI= -.414, .093). For association with social and communication impairments, mean effect size *r* was significant for negative affectivity (r= -.13, p= .044, 95% CI= -.255, -.004), but not for self-regulation (r= -.12, p= .13, 95% CI= -.288, .038) nor sociability (r= .11, p= .10, 95% CI= -.02, .231). As can be seen from Table 5, with the exception of self-regulation-problem behaviours, negative affectivity and sociability-social communication impairments associations, all other mean effect were highly heterogeneous (I^2 range 45.14%-84%).

Table 5

Meta-Analysis of Studies Exploring the Relationship Between Temperament and Other Factors

	Mean ES	***se***	**95% CI**	***p***	**Q**	***I^2***	***p***
IQ							
Negative Affectivity	-.15	.089	[-.321, .029]	.10	8.21	65.97%	.04
Self-regulation	.15	.083	[-.013, .313]	.07	7.10	60.83%	.069
Sociability	.14	.048	[.046, .234]	.004	4.39	.84%	.22
Problem Behaviors							
Negative Affectivity	.45	.072	[.313, .597]	< .001	14.48	57.36%	.025
Self-regulation	-.25	.045	[-.339, -.16]	< .001	7.02	.01%	.319
Sociability	-.16	.129	[-.414, .093]	.215	43.76	86.86%	< .001
Social Communication							
Negative Affectivity	-.13	.064	[-.255, -.004]	.044	.17	0%	.92
Self-regulation	-.12	.08	[-.288, .038]	.13	9.47	45.14%	.092
Sociability	.11	.06	[-.02, .231]	.10	1.42	0%	.49

Note. IQ= Intelligence Quotient

1.5. Discussion

In order to better understand sources of variability in the core and co-morbid symptom presentation and outcomes among individuals with ASD, we advocate the need to step away from models that concentrate purely on describing group differences and move toward adopting individual differences frameworks that seek to *understand* the variability that presents between people. Gaining insights into the sources of noted heterogeneity is crucial in informing the development of adequate support for individuals with ASD and those who care for them.

In the broader literature, temperament has been shown to have both positive and negative developmental influences, from infancy/toddlerhood through early childhood and into the school years and beyond. For this reason, we suggest temperament may provide a helpful framework for understanding individual differences among individuals with ASD.

In this systematic review, we have attempted to integrate findings from existing studies concerning temperament in the context of ASD, toward a better understanding of the role of temperament across a broad set of positive and negative developmental outcomes. Our aim in conducting a systematic review was to provide a snapshot of the current state of the field of research, rather than to statistically address a specific question/hypothesis. Despite a 30-year history, there is still a great deal more to be understood, with many methodological issues to be considered and research gaps to be filled.

1.5.1. Limitations of Extant Research

The large majority of studies identified in this review of temperament and ASD (nearly 90%) used questionnaire or interview measures of temperament. As discussed in more detail elsewhere (Shiner et al., 2012; Zentner & Bates, 2008), questionnaire measures of temperament have numerous advantages over observational and experimental measures, such as the ease of use and the ability to sample behaviors over time and across different contexts to generate rich data that lend themselves easily to group comparisons, factor analyses and person-centered statistical approaches (e.g., cluster analysis). However, research in non-ASD populations has clearly demonstrated that parental characteristics such as stress, anxiety, and depression can substantially bias the reporting of child temperament (Forman et al., 2003), which may be particularly important in the context of ASD, due to elevated levels of affective symptoms in parents of children with ASD and subthreshold ASD-like traits (referred to as the Broader Autism Phenotype; Piven et al., 1994). Hence, we cannot rule out the possible amplification of parent-reported differences in the temperament of individuals with and without ASD as a result of informant bias. Another potential consideration related to parental report – especially in the context of high-risk infant sibling designs – is the potential for parents to either exaggerate (i.e., contrasting effect) or under-estimate (i.e., assimilation effect) differences between their own children, by evaluating them relative to one another (Majdandžić, van den Boom, & Heesbeen, 2008).

Although structured and semi-structured observational protocols for assessing temperament do not suffer from such issues, they also have their own limitations such as potential lack of ecological validity, temporal and contextual restrictedness, and influence of “noise” variables (e.g., the child’s transient mood or somatic health issues). The optimal way to assess temperament then may be to combine both observational and questionnaire-based measures, and preferably both maternal and paternal reports (Rothbart & Bates, 1998). Yet, only two among the 64 studies included in this review has adopted this latter method (i.e., Macari et al., 2018; Ratekin, 1993).

Furthermore, the issue of measurement confounding in temperament research is well established in this field (Lemery, Essex, & Smider, 2002; Sanson, Prior, & Kyrios, 1990). Nevertheless, only one study among those reviewed here in the context of ASD (i.e., that of Adamek et al., 2011) addressed potential item overlap between measures of temperament and other constructs of interest. For example, perceptual sensitivity is a subscale within questionnaires based on the Rothbart’s model of temperament, and other questionnaire measures contain a number of items related to the reactivity to sensory input (e.g., within the Distractibility and Threshold of Response scales of the Behavioural Style Questionnaire and Carey Infant Temperament Questionnaire). With atypical reactions to sensory input included in the DSM-5 as core diagnostic criteria for ASD, it is clear that there is a significant room for item measurement overlap. This represents a significant limitation of the existing research. In order to understand the nature of the relationship between constructs, it is essential to ensure that measures provide unique rather than overlapping information, lest the strength of the relationship be artificially inflated. Furthermore, this issue speaks to the broader question about the nature of the relationship between temperament and ASD, to which we will return.

Notwithstanding the challenges introduced via different conceptualizations/models of temperament and different measures employed, existing research on temperament and ASD can also be criticized for remaining largely descriptive in nature. The majority of existing studies have focused on identifying how temperament characteristics differ between individuals with ASD and other populations, where relatively fewer studies have explored the relationship between temperament and either ASD traits or co-morbid symptoms. However, associations here are likely to be complex. Indeed, influential alternative models have been developed to explain the potential role of temperament in development, including through indirect (i.e., moderating and mediating) effects, and interactional and transactional models (Belsky & Pleuss, 2009; Rothbart & Bates, 1998). All of these emphasize the need to explore interactions between temperament, other intrinsic child characteristics, aspects of the environment (e.g., characteristics of parents and the family) and the wider socio-cultural context, in order to fully characterize developmental pathways.

There is evidence from a prospective study of infant siblings of children with ASD that the quality of parent-infant interaction – which is influenced by both infant temperament and parent responsiveness – is associated with a later diagnosis of ASD (Wan et al. 2013). While this finding requires replication in independent samples, the possibility that infant temperament may be associated with developmental outcomes – including a developmental trajectory toward later ASD diagnosis – provides a potential opportunity for very early intervention in ASD (Green et al., 2015). Future research will also need to go beyond reporting correlational data and simple group comparisons to instead employ refined statistical techniques, such as structural equation modelling, in order to explore the complex developmental relationships and effects likely at play. A good guide for this approach is in work aiming to identify profiles or clusters of temperamental traits that might predict positive and negative aspects of development (Putnam & Stifter, 2005).

1.5.2. Current State of the Field and Future Directions

Most existing studies have examined the presence or absence of differences on certain dimensions of temperament among groups of children with and without ASD, and these seem to show that, at a higher-order level, individuals with ASD may be temperamentally different from those without ASD – whether TD individuals or those presenting other conditions.

Some studies have started to look at the extent to which temperamental variation corresponds to variation in both core symptoms (Bölte et al., 2008; Fenning et al., 2018; Kerekes et al., 2013) and co-morbid features (Adamek et al., 2011; De Pauw et al., 2011; Schwartz et al., 2009; Millea et al., 2013) and other characteristics such as cognitive level (Faja & Dawson, 2015; Kasari & Sigman, 1997) among groups of children with ASD, however, findings have been inconsistent. Furthermore, due to methodological limitations and inconsistent and incomplete reporting of the relevant statistics, we were able to analyse five or fewer studies for each of the specific summary effects in our meta-analysis. Therefore, significant methodological improvements are needed before studies of this type can begin to provide insights into the extent to which temperament can explain variability in development and learning. In addition, in order to fully understand the potential value of temperament as a predictive variable, longitudinal investigation is required from infancy through the toddlerhood and preschool years.

Some researchers have begun to investigate temperament within prospective longitudinal designs, exploring the potential value of early individual differences as indicators of later diagnostic outcome status, suggesting that temperamental differences may be observed in individuals with ASD from as early as 6-months of age. Longitudinal studies hold the exciting potential to establish the extent to which variability in early temperament might correspond to individual differences characteristics and skills and may inform our understanding of predictors of treatment outcome in ASD. As shown in other neuropsychiatric disorders (Joyce, Mulder, & Cloninger, 1994; Karalunas et al., 2014), this approach might thus be critical for increasing our understanding of the impact of temperament on clinical characteristics and long-term outcomes in ASD. Indeed, two recent studies (Bos et al., 2018; Berkovits et al., 2017) showed that emotion regulation abilities contribute to the development and maintenance of internalizing and externalizing symptoms in children with ASD.

Including existing models linking temperament dimensions with specific brain regions and networks (see Whittle, Allen, Lubman, & Yücel, 2006) within future research could be especially powerful when incorporated into longitudinal designs. A very good illustration of the value of this approach has been recently offered by Karalunas et al. (2014) who first employed a community detection clustering method, identifying three subgroups of children with ADHD based on their temperament profiles (mild, surgent and irritable subtype). This group then validated their identified subgroups in terms of their distinctive neurobiological profiles, incorporating cardiac physiological indices and resting-state functional brain connectivity, and predicting clinical outcomes one year later. Of note, the identified subtypes were independent of DSM-5 clinical demarcations.

Despite diversity among theories of temperament and a wide variety of nominated traits, as we have shown in the taxonomy proposed in the introduction, there is a good degree of coherence in the way we conceive of this construct and can observe its effects on development. As we have suggested above, *affectivity/emotionality, sociability* (including concepts related to activity level), and what can be broadly termed *self-regulation* present as almost universal dimensions among different theories of temperament. These have been shown to be associated with particular brain areas/networks (Whittle et al., 2006) and to have at least some distinct genetic underpinnings (Saudino, 2005). Furthermore, these constructs are largely covered by measures based on the four temperament models proposed by Rothbart (Rothbart & Goldsmith, 1985), Chess and Thomas (1968), Buss and Plomin (1975, 1984), and Cloninger (1986, 1987). They align closely with the domains shown by Karalunas et al. (2014) to be useful in parsing heterogeneity in ADHD, and map well onto the key domains of function identified by the National Institute of Mental Health (NIMH) Research Domain Criteria (RDoC) initiative (Insel et al., 2013; for a discussion, see Chetcuti et al., 2019), which is increasingly being adopted as a framework for describing clinical phenomenology. Hence, we suggest that researchers exploring temperament in ASD should adopt these dimensions in their work to enable generalization of findings across studies and future meta-analysis.

The systematic integration of existing work within a unified higher-order taxonomy has brought to light a rather consistent pattern of relations between temperament and ASD across studies. The evidence indicates that individuals with ASD may be distinguished from other groups by high affectivity/emotionality, low sociability, and low self-regulation. The question of precisely *how* ASD and temperament are related is thus an important question for the field. As mentioned above, there are four explanatory models for the link between temperament and psychopathology: the *predisposition/vulnerability* model, the *continuity/spectrum* model, the *pathoplasty/exacerbation* model, and the *complication/scar* model (see Watson et al., 1994).

Evidence linking early temperament characteristics to the later severity of ASD symptoms (Garon et al., 2016; Macari et al., 2017) suggests that a predisposition/vulnerability model represents a viable explanation for the relation between temperament and ASD. Nevertheless, it is difficult to tease apart competing explanations from behavioural quantifications alone; such that the same temporal relationship may not be apparent when measurement is taken at the level of underlying neurobiology. Indeed, ASD-driven perturbations in brain architecture and functional connectivity appear to unfold before behavioural disorder symptoms (Hazlett et al., 2011, 2017; O'Reilly, Lewis, & Elsabbagh, 2017).

1.5.3. Conclusion

Despite nearly three decades of research, challenges remain for the drawing of strong conclusions on the topic of temperament in individuals with ASD. Nevertheless, work in this area holds promise to further our knowledge of the early developmental pathway/s toward ASD diagnosis, and predictors of outcomes beyond this point. Our review has identified limitations in the existing work on this topic and proposed directions for future research efforts. The unified typology of temperament suggested here has well-theorized relationships to neurobiological systems and holds promise for providing a superior description of heterogeneity in ASD compared to current clinical nosologic criteria.

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CHAPTER 2

Editorial Perspective

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Editorial Perspective:
Furthering Research on Temperament in Autism Spectrum Disorder

Lacey Chetcuti[1], Mirko Uljarević[2], Kristelle Hudry[1,3]

[1]Olga Tennison Autism Research Centre, La Trobe University, Australia; [2]Stanford Autism Center, Department of Psychiatry and Behavioral Sciences, Child and Adolescent Psychiatry, School of Medicine, Stanford University, USA; [3]Victorian Autism Specific Early Learning and Care Centre, La Trobe University, Australia.

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2.1. Abstract

Although temperament has been explored in the context of Autism Spectrum Disorder (ASD), research has to date focused almost exclusively on describing group-level differences across samples of participants with and without ASD diagnoses. We argue that it is necessary for ASD research to step away from case-control designs and move towards examining temperament and the clinical phenotype of ASD within an individual differences framework. This approach holds promise for achieving a biologically-based understanding of the pronounced heterogeneity apparent in the clinical manifestation of core and non-core/associated ASD features. We offer methodological suggestions with a view to strengthen and stimulate such work, including: (a) adopting a multi-method/multi-informant measurement approach, which combines both behavioural and biological indicators of temperament, (b) implementing more inclusive sampling/recruitment strategies that move away from traditional DSM categorical boundaries into prospective longitudinal study designs that will enable us to capture a fuller range of the variability inherent in constructs of interest, and (c) moving away from traditional variable centred statistical analyses, and adopting more person-centred approaches to uncover meaningful temperamental subgroups within the ASD-diagnosed population. We conclude by identifying unanswered empirical questions and highlight future directions for the field. This includes specification of the mechanism producing temperament-ASD associations, and investigating interplay between child temperament and the environment.

Heterogeneity is a long-recognized feature of Autism Spectrum Disorder (ASD), observed in the presentation and severity of core/associated symptoms as well as trajectories of symptom onset and lifespan course. *Identifying the sources of variation* in ASD symptomatology and clinical/life outcomes is critical for the development of more targeted and individually-tailored recommendations and interventions that, in turn, will improve life outcomes for individuals with ASD. It is becoming increasingly clear that maintaining the search for disorder-specific sources of heterogeneity may not be an effective means of achieving this goal. Although philosophically different, the developmental psychopathology framework and National Institute of Mental Health's (NIMH) Research Domain Criteria (RDoC; Insel et al., 2010) initiative both emphasise the need to go beyond current symptom-based categorical demarcations of mental health/illness to explain clinical phenomenology at the fundamental biobehavioural level. We propose that captilizing on both traditions holds promise for providing a richer mechanistic understanding of heterogeneity in ASD, and specifically nominate temperament as a relevant construct for future such work.

Temperament reflects early emerging emotional and behavioural traits that result from interactions among genetic, biological, and environmental influences (Shiner et al., 2012). While the structure of temperament remains a topic of continuing debate, we consider temperament to be a composite of three higher-order dimensions: (1) *negative emotionality*, the tendency to experience negative emotions, (2) *sociability*, the tendency to actively and surgently engage with others, and (3) *self-regulation*, the capacity to regulate cognitions, emotions and action. We illustrate in Table 1 how these higher-order dimensions map onto different domains of functioning proposed within the RDoC framework, have distinct neurological substrates, and are encompassed within the dominant theoretical models of temperament (for a review, see Shiner et al., 2012).

Table 1

Unified Higher-Order Framework of Temperament Traits

	Negative Emotionality	Sociability	Self-Regulation
RDoC domain/s of function	Negative valence systems	Positive valence systems Social processes	Cognitive systems (cognitive control construct)
Neural substrates	Bed nucleus of the stria terminalis (BNST) Basolateral and central amygdala Dorsomedial prefrontal cortex	Midbrain ventral tegmental area Ventral striatum (nucleus accumbens) Orbitofrontal cortex	Caudate Anterior Cingulate cortex Dorsolateral prefrontal cortex
Conceptual model			
Alexander Thomas and Stella Chess	Mood Adaptability	Activity Intensity Approach/Withdrawal	Attention Span/Persistence Threshold Distractibility Rhythmicity
Arnold H. Buss and Robert Plomin	Emotionality	Sociability Activity	-
Mary K. Rothbart	Negative Affectivity	Surgency	Effortful Control Orienting/Regulation
H. Hill Goldsmith and Joseph Campos	Anger Proneness	Social Fearfulness Pleasure Activity Level	Interest/Persistence
C. Robert Cloninger	Harm Avoidance	Reward Dependence	Persistence Novelty Seeking

These higher-order temperament dimensions interact in complex ways to affect positive and negative developmental outcomes, such as academic achievement and social-emotional competence (Shiner & Caspi, 2003). Extensive literature also suggests that temperamental variation may be associated with differences in susceptibility and resilience towards psychopathological outcomes. For instance, in two independent samples of children and adolescents, Hankin et al. (2017) found that high negative emotionality and low self-regulation conferred broad-based, transdiagnostic risk toward general psychopathology (i.e., *p* factor). Moreover, low self-regulation was uniquely related to externalizing liability while high negative emotionality and low sociability were linked more specifically to internalizing liability. Considerably less is known, however, about how temperament relates to variance of core and associated ASD features.

We have recently reviewed 40 studies on temperament in the context of ASD and found that much existing research has been descriptive in nature – comparing the temperamental attributes of ASD-diagnosed individuals to those with normative development and/or other clinical/developmental conditions (Uljarević et al., 2018[3]). This conventional strategy of between-group comparison is predicated on the assumption that all individuals with ASD diagnoses share the same temperamental attributes. However, such a possibility seems highly unlikely given that the aetiology and consequent phenotypic expression of ASD symptoms is highly heterogeneous. We therefore argue that there is a need to reorient research efforts towards exploring temperament as a predictor of individual differences *within* the ASD-diagnosed population. As an illustration, we identified a small number of studies reporting concurrent associations between temperament and the severity of core and non-core/associated ASD features (Uljarević et al., under review) – that is, an emerging evidence base broadly supporting our notion that temperament constitutes a *transdiagnostic* factor contributing to heterogeneity in outcomes for both individuals with and without ASD. Nevertheless, this line of research remains in its infancy. Here, we highlight how the RDoC approach may further our understanding of temperament in ASD. We begin by identifying key conceptual and methodological avenues for improvement and conclude by raising some unanswered questions for the field.

There is a need to acknowledge and address confounding in the conceptualization and measurement of temperament and core/associated ASD symptoms. For example, most measures of temperament and internalizing psychopathology tap behaviours related to social withdrawal and inhibition, which form part of the ASD diagnostic criteria. A failure to address such overlap might artificially inflate the strength of associations. While one straightforward solution is to eliminate overlapping items from temperament and outcome measures, we propose that estimates

[3]Citation refers to what is now Chetcuti et al., 2020 [Chapter 1].

of item similarity should be empirically derived (e.g., through joint confirmatory factor analyses) rather than based solely on researcher judgment.

Next, it is crucial to select temperament measures that tap the biologically-based, higher-order traits of negative emotionality, sociability, and self-regulation. Parent-report questionnaires are a longstanding measurement tradition, and those based on Mary Rothbart's conceptualisation represent one such appropriate option. While these set of measures include slightly different fine-grained subscales for specific temperament traits, there is convergence around three overarching dimensions – surgency, negative affectivity, and effortful control (referred to as orienting/regulation in infancy) – that are grounded in biology and align closely with our proposed three-factor taxonomy (Table 1). Nevertheless, we advocate the need to supplement questionnaire information with other, more objective data.

In the context of ASD research, most studies of temperament have relied soley on the parent-report of temperament. These methods offer numerous practical advantages over observational/laboratory-based indices and draw on parents' extensive knowledge of their children to provide a rich picture of behaviour across contexts. However, parental response biases may well be at play. For instance, parent ratings on temperament scales may be influenced by dispositional characteristics, transient mood state, mental health, and perceptions of the parent-child relationship. Research comprising multiplex ASD families – including studies of high-risk infant siblings – should also consider the potential of parents to either inflate (i.e., assimilation effect) or underestimate (i.e., contrasting effect) the degree of temperamental similarity between siblings by evaluating them relative to one another. While this bias likely operates across all parent-rated temperament measures, questionnaires that call for global judgments (e.g., "child cries easily") may be more susceptible than those seeking reports on behaviour within specified contexts (e.g., "child cries before going to sleep"; Saudino, Wertz, Gagne, & Chawla, 2004).

The principal alternative approach is direct observation of child behaviour in the home or during laboratory-based assessments. While these methods may afford greater objectivity than parent-report questionnaires, they nevertheless carry their own limitations in terms of test-retest reliability and ecological validity. Hence, we advocate a multi-method/multi-informant approach to measuring temperament in the context of ASD diagnosis, combining self/other reports and behavioural observations. We also encourage the continuing development of ecologically-valid indices tapping these traits. For example, experience-sampling methods could provide a way of measuring temperament on multiple occasions while 'in-the-moment', circumventing retrospective recall biases and behavioural artefacts created by the laboratory environment.

Moreover, it will be important to incorporate temperament measures across different units of analysis – from observable behaviour to underlying neurobiological systems (i.e., genes, cells, molecules, and circuits; Insel et al., 2010) in order to gain a more *mechanistic* understanding of individual differences in ASD-diagnosed samples. Different neuroimaging modalities capture different structural and functional properties of the brain, and multimodal neuroimaging indices are necessary to achieve a comprehensive understanding of how individual differences in temperament domains map onto variation in the structural and functional integrity of the specific features and circuits. More specifically, while structural magnetic resonance imaging (MRI) and diffusion tensor imaging (DTI) capture structural properties of brain features and connectivity, task evoked and resting state functional MRI capture different aspects of functional dynamics and integrity of particular circuits. Hence, utilizing these methods in isolation to explore, for example, the neurobiological underpinnings of cognitive control will not provide comprehensive mapping across the unit of analysis.

Going beyond the measurement-related issues, the question of precisely *how* temperament and ASD are associated is an important one for the field. Several theoretical models seem plausible: that temperament (a) represents a predisposition towards the development of ASD (i.e., vulnerability association), (b) alters the manifestation of ASD symptoms *after* their onset (i.e., pathoplastic association), or even (c) exists on the same continuum as ASD such that ASD is an extreme variant of continuously-distributed temperament traits (i.e., spectrum association). Shiner and Caspi (2003) provide a detailed review of these competing accounts. Characterizing the nature of the temperament-psychopathology relationship can only be addressed through prospective longitudinal research design. For instance, empirical evidence providing support for the possibility of a spectrum – rather than vulnerability or pathoplastic – association would come from evidence of corresponding longitudinal changes in temperament and ASD features.

We also emphasize that research seeking to understand associations between temperament and features of ASD need not be restricted to the examination of diagnosed individuals who have ‘clinical’ levels of ASD symptoms. There is growing recognition that the ASD phenotype has a spectrum of expression in the neurotypical population and across samples of people with many different neurodevelopmental/psychiatric disorders. That is, the diagnostic features of ASD are themselves *transdiagnostic*. Hence, research on the temperament-ASD relation is well-suited to an RDoC-informed design, involving the recruitment of study participants spanning multiple disorder categories. Even whilst maintaining a core objective of understanding heterogeneity in the context of ASD *diagnosis*, researchers need *not* recruit solely on the basis of DSM-defined diagnostic categories. Rather, recruiting transdiagnostically, the ASD diagnostic label would effectively be invisible allowing the examination of how neural circuits and systems (e.g., temperament) contribute to *individual differences* in social-communicative skills and/or restricted/repetitive behavioural features. While this research design deviates from the between-group comparison approach familiar to researchers with an interest in ASD, it holds the exciting potential to achieve true mechanistic understanding of development that cuts across diagnostic boundaries.

Future research should also employ person-centred statistical techniques to identify ‘natural’ subgroups of individuals who share similar temperamental attributes, rather than maintaining the traditional focus on variable-centred analyses. Person-centred methods – such as cluster and profile analysis – are well-suited to the study of temperament because, unlike variable-centred regression analysis, they take into account the non-orthogonal nature of temperament traits which may be critical in seeking to draw conclusions about predictive associations with other factors within a given sample. The value of this approach has recently been exemplified by Karalunas et al. (2014), who used a community detection clustering technique and identified three temperament subtypes among children with ADHD diagnoses. *Mild*, *Surgent*, and *Irritable* subtypes were distinguished by unique patterns of cardiac physiological response and resting-state functional brain connectivity, stable over time, and predictive of clinical outcomes one year later. Notably, these subtypes were also independent of clinical demarcations of ADHD symptom severity and presentation.

Finally, it will be important to consider the role of the environment on associations among temperament and core/associated features of ASD. In the broader literature, child temperament and parenting behaviours have been shown to shape one another over time and to interact in predicting child outcomes. While the association between temperament and parenting has received little empirical attention in the context of ASD, emerging evidence suggests that dyadic parent-child interaction may be less synchronous when children with ASD have higher negative emotionality and lower self-regulation (e.g., Hirschler-Guttenberg, Golan, Ostfeld-Etzion, & Feldman, 2015). Further longitudinal research is needed to clarify how the interplay of child temperament and the parenting environment contributes to heterogeneity in ASD; specifically, whether parenting practices may attenuate or intensify the effects of child temperament on outcomes, and/or whether the effects of parenting may vary as a function of child temperament.

In conclusion, it is our view that research in the context of ASD lags well behind that being conducted in other clinical fields in maintaining an almost exclusive focus on describing group-level differences in temperament across samples of participants with/without a diagnosis. We call into question the utility of this conventional approach and recommend that future research efforts be directed towards more comprehensive exploration of temperament as a predictor of individual differences. This will necessitate a shift towards a multi-method/multi-informant measurement approach, informed selection of instruments, more person-centred statistical methods, and the application of more rigorous research designs informed by the transdiagnostic RDoC framework.

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CHAPTER 3

Internalizing/Externalizing and Autism

Thus far, this thesis has provided an overview of the existing literature relating to temperament in ASD (Chapter 1) and identified future areas for advancement (Chapter 2). The empirical research presented in this thesis was undertaken to address the identified gap concerning the influence of temperament on individual difference outcomes in the context of autism, focusing specifically on social-emotional functioning – as indexed by levels of internalizing and externalizing symptoms – in early-life. Before proceeding to the empirical chapters, this chapter serves to describe the concepts of internalizing and externalizing, and relevance of these in the context of autism. The chapter concludes with an outline of the specific aims of each of the empirical studies that follow.

3.1. The Internalizing-Externalizing Framework

The terms ‘internalizing’ and ‘externalizing’ are used to describe the underlying (i.e., latent) affective features shared among different forms of social-emotional difficulties and discrete diagnoses. Internalizing symptoms reflect the tendency to direct emotional distress *inwards* as demonstrated through behavioural withdrawal, somatic complaints, anxiety, and/or depression symptoms – including as characteristic of anxiety disorders and depression. Externalizing symptoms reflect behaviours that are directed *outwards* to others and include disruptive, including aggressive, disruptive, hyperactive, antisocial, and delinquent behaviours – as characteristic of oppositional defiant-, conduct-, and attention-deficit/hyperactivity disorders (Achenbach, 1966; APA, 2013). Internalizing and externalizing symptoms are not mutually exclusive, but rather, are moderately and positively correlated in many samples (Achenbach, Ivanova, Rescorla, Turner, & Althoff, 2016). Figure 1 provides a visual depiction.

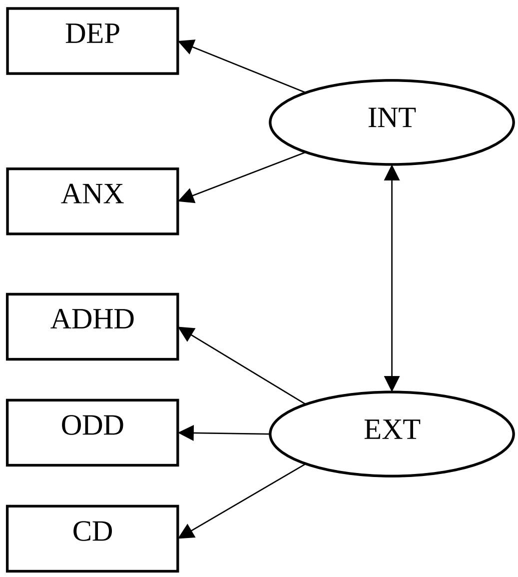

Figure 1. Visual depiction of the higher-order structure of internalizing and externalizing symptoms. Circles represent latent dimensions while squares represent observed variables. Single-headed arrows represent factor loadings and double-headed arrows represent factor correlations. INT = internalizing. EXT = externalizing. DEP = depression. ANX = anxiety. ADHD = attention-deficit/hyperactivity disorder. ODD = oppositional defiant disorder. CD = conduct disorder. Adapted from Eaton, South, and Krueger (2010).

The internalizing/externalizing groupings originated from Achenbach's (1966) factor-analytic work among clinically-referred children and adolescents, and have been well-replicated – including across groups varying by age- (Eaton, Krueger, & Oltmanns, 2011), sex- (Eaton et al., 2012), and cultural background (Eaton et al., 2013), and among those with an autism diagnosis (Rodriguez-Seijas et al., 2020). These have proven useful for classifying social-emotional difficulties in clinical settings – for instance, guiding the organization of disorders within the most recent edition of the Diagnostic and Statistical Manual of Mental Disorders (DSM-5; American Psychiatric Association, 2012) – and provide an overarching framework for understanding factors associated with different forms of difficulties (Achenbach et al., 2016). Furthermore, the broad internalizing/externalizing groupings provide a good starting point for investigations of predictors and may provide a more reliable picture of difficulties in early childhood than do discrete disorders, which may not be fully discernible until later in life.

In terms of measurement, internalizing and externalizing symptoms are most frequently ascertained using Likert-type scales, and assessed according to clinical thresholds (categorical) or by degree of severity (dimensional; Achenbach & Rescorla, 2000; Carter & Briggs-Gowan, 2006). The Child Behavior Checklist (CBCL; (Achenbach & Rescorla, 2003) and Behavior Assessment System for Children (BASC; Reynolds & Kamphaus, 1992) are among the most widely-used measures of internalizing and externalizing symptoms in the general literature (Achenbach et al., 2016), though many other measures are also available. Some behavioural indicators of internalizing and externalizing remain similar across the lifespan (e.g., withdrawal, aggression) while others are more relevant to particular developmental periods – for instance clinging to adults and bedwetting in childhood, and criminal behaviour and suicidal ideation in adolescence/adulthood.

3.2. Prevalence and Relation to Autism

Extensive research suggests that internalizing and externalizing symptoms are experienced by a significant proportion of individuals on the autism spectrum (for a review, see Rosen, Mazefsky, Vasa, & Lerner, 2018; for meta-analyses of anxiety, see van Steensel, Bögels, & Perrin, 2011; van Steensel & Heeman, 2017). Symptoms of clinical concern have been reported in as many as three-quarters of autistic children (Brereton, Tonge, & Einfeld, 2006; Chandler et al., 2016; Ooi, Tan, Lim, Goh, & Sung, 2011) compared to in just 10% of children in the general population (Roberts, Attkisson, & Rosenblatt, 1998). Case-control studies have similarly found more severe internalizing and externalizing symptoms among autistic children compared to those with typical development (Bauminger, Solomon, & Rogers, 2010; Giovagnoli et al., 2015; Horiuchi et al., 2014) and other developmental conditions (Dimitropoulos, Ho, Klaiman, Koenig, & Schultz, 2009). A similar picture is suggested for discrete psychiatric conditions, with one study finding that 95% of clinic referred autistic youth (aged 3 to 17 years) met criteria for three or more additional DSM diagnoses, comparable to referred non-autistic youth (Joshi et al., 2010; for a meta-analysis, see Lugo-Gil & Tamis-LeMonda, 2008). With regard to developmental progression, studies suggest that social-emotional symptoms are apparent among autistic individuals from late infancy/early toddlerhood (Raza et al., 2019; Rescorla et al., 2019), showing gradual decline with age, but nevertheless remaining relatively high into adolescence/adulthood (Gray et al., 2012; Vaillancourt et al., 2016). These results collectively suggest some connection between autism and internalizing/externalizing symptoms. However, the processes underlying this connection have yet to be fully understood.

Several accounts have been put forward to describe the link between autism and social-emotional difficulties. Factor analytic studies have examined how autism traits fit within the internalizing-externalizing framework; specifically, whether autism traits reflect a component of the internalizing and/or externalizing dimension/s. However, this seems not to be the case. That is, autism traits appear to constitute a cluster of features *distinct* from internalizing and externalizing symptoms (Hawks, Marrus, Glowinski, & Constantino, 2019; Noordhof, Krueger, Ormel, Oldehinkel, & Hartman, 2015; White, Bray, & Ollendick, 2012). Other studies have explored whether internalizing and externalizing symptoms relate to the core behavioural features of autism; specifically, whether these symptoms result from challenges with social understanding (e.g., misinterpreting cues) and communication (e.g., conveying needs and wants; Shea, Payne, & Russo, 2018; Volker et al., 2010) and/or restricted/repetitive behaviours and thoughts (Sofronoff, Attwood, & Hinton, 2005). Although some studies have found fewer social-emotional difficulties among autistic children who have more advanced social-communication skills (Saito et al., 2017; Shea et al., 2018) and fewer restricted/repetitive features (Rodgers, Glod, Connolly, & McConachie, 2012), findings are inconsistent (Raza et al., 2019) suggesting that other processes are also at play. It has been proposed that heterogeneity associated with autism – including in the manifestation of internalizing and externalizing symptoms – stems from processes that are not specific to the autistic population, but rather give rise to individual differences in *all* people (i.e., irrespective of clinical status; Insel et al., 2010; Mundy, Henderson, Inge, & Coman, 2007). Several such factors that have been examined in relation to internalizing and externalizing symptoms in the context of autism are considered below.

3.3. The Role of Individual Difference Factors

There is a little consistent evidence that demographic factors influence the presentation of social-emotional difficulties in the autistic population. Some studies have reported sex differences for internalizing and externalizing symptoms – including higher levels of these among autistic males than females (Guerrera et al., 2019) and vice versa (Nordahl et al., 2020). The most consistent finding, however, has been of *non-significant* sex differences (Hartley & Sikora, 2009; Mayes, Castagna, & Waschbusch, 2020; Nasca, Lopata, Donnelly, Rodgers, & Thomeer, 2020; Salomone et al., 2014). With regards to age, existing evidence suggests that internalizing and externalizing symptom levels might vary *across* (e.g., childhood vs adolescence; Salomone et al., 2014), but not *within* developmental stages (Guerrera et al., 2019; Maskey, Warnell, Parr, Le Couteur, & McConachie, 2013). Lastly, studies have reported no differences in internalizing and externalizing symptoms as a function of autistic children's cultural background (Chandler et al., 2016; Hartley & Sikora, 2009), but with some evidence of a negative relation with family sociodemographic status (Chandler et al., 2016; Fanti & Henrich, 2010).

Cognitive/developmental differences are one possible source of variability in the manifestation of social-emotional difficulties in the context of autism, although the direction of effects is uncertain. That is, higher social-emotional difficulties have been reported among autistic children with both lower (Guerrera et al., 2019; Maskey et al., 2013; Salomone et al., 2014) and higher (Gadow, Devincent, Pomeroy, & Azizian, 2005; van Steensel & Heeman, 2017) cognitive/developmental abilities. In any case, evidence of differences in social-emotional functioning between autistic children and those with non-autism developmental delays (Brereton et al., 2006) suggests that internalizing and externalizing difficulties in the autism population are not driven solely by cognitive/developmental ability. Other studies suggest that internalizing and externalizing symptoms might be influenced by the family emotional climate (Romero-Gonzalez, Chandler, & Simonoff, 2018), and by caregivers' manner of interacting with children (Maljaars, Boonen, Lambrechts, Leeuwen, & Noens, 2014) and own psychological symptoms (Yorke et al., 2018). In attempting to understand variability in social-emotional functioning, it might thus be important to consider factors to do with the individual as well as their environment (Mundy et al., 2007).

As illustrated in Chapter 1, temperament has become a topic of growing interest in the literature regarding ASD and has emerged as a significant predictor of internalizing and externalizing symptoms across multiple studies, including over and above any influence of cognitive/developmental ability (e.g., Burrows et al., 2016). Studies of autistic children and adolescents have yielded fairly consistent results; high negative emotionality and low self-regulation have each been related to higher levels of internalizing and externalizing symptoms, both concurrently (Adamek et al., 2011; Burrows, Usher, Schwartz, Mundy, & Henderson, 2016; De Pauw, Mervielde, Leeuwen, & Clercq, 2011; Nazim & Khalid, 2019) and prospectively (Berkovits, Eisenhower, & Blacher, 2017; Bos, Diamantopoulou, Stockmann, Begeer, & Rieffe, 2018; Shephard et al., 2019). Sociability/positive affectivity has been most consistently associated with internalizing symptoms (positive direction; Burrows et al., 2016; Schwartz et al., 2009), but also related to externalizing symptoms (negative direction; Adamek et al., 2011; De Pauw et al., 2011). Yet, little is known about these relations in the context of autism in the early stages of child development.

3.4. The Role of Temperament in Early Childhood

Research in the general population suggests that developmental processes involving temperament can have cascading effects on health and wellbeing beyond early childhood, into adolescence and adulthood (Shiner & Caspi, 2003). In the context of autism, however, little is known about the relation of temperament to social-emotional functioning in infancy and over the toddler years. This is presumably due to the fact that childhood autism is currently diagnosed around mean age 4 years (e.g., Bent, Dissanayake, & Barbaro, 2015). Nonetheless, studies of infants/toddlers at *higher likelihood* of receiving an ASD diagnosis are beginning to clarify the nature of these processes in the context of autism, as the condition begins to unfold.

Shephard et al. (2019) examined whether early-life temperament characteristics (measures across 7, 14, and 24 months of age) predicted mid-childhood anxiety and ADHD symptoms (at age 7 years). The sample comprised children considered to be at higher and lower familial likelihood of ASD (n = 54 and 50), respectively due to having and not having an autistic older sibling. Higher locomotor activity and lower inhibitory control in infancy/toddlerhood were found to predict higher ADHD, while higher infant/toddler fearfulness predicted higher subsequent anxiety. These results were obtained after controlling for mid-childhood levels of autism traits and group status (high vs low ASD likelihood), suggesting associations were similar across the continuum of autism presentation. Hendry et al. (2020) also drew on a sample of children at higher and lower familial likelihood of ASD (*n* = 294 and 412), to explore whether early-childhood trajectories of attentional development predicted subsequent ADHD symptoms. Higher likelihood infants who were later diagnosed with ASD were more likely than non-autistic infants (whether presenting at lower or higher likelihood) to show a plateau in the development of attentional control between 10 and 25 months of age which – across *all* infants showing this developmental pattern – was associated in turn with higher ADHD symptoms at age 3 years.

Some important inferences regarding temperament and social-emotional difficulties can be drawn from these studies comprising infants/toddlers at higher ASD-likelihood. First, temperament characteristics that confer risk towards internalizing and externalizing symptoms may be expressed by infants/toddlers with autism traits before they receive an ASD diagnosis. Second, and consistent with findings in autistic children and adolescents (Burrows et al., 2016; De Pauw et al., 2011), temperament traits may relate in a similar way to internalizing and externalizing symptoms in infants/toddlers irrespective of autism level and diagnostic status. This also corresponds to findings of similar associations between temperament traits and internalizing and externalizing symptoms across children/adolescents from general population samples with varying levels of autism traits (Kamio, Takei, Stickley, Saito, & Nakagawa, 2018). Still, additional longitudinal research should be undertaken in the developmental periods of infancy and toddlerhood, in order to fully capture the relations among temperament and social-emotional difficulties and clarify the developmental processes that give rise to these in the context of autism.

3.5. Objectives of the Present Research

The program of empirical studies presented in this thesis (Chapters 5 to 8) sought to add to emerging knowledge regarding the nature and relation of individual temperament differences to social-emotional outcomes in the context of emerging autism, among higher likelihood infants/toddlers referred from the community. The specific aims and hypotheses of each study are outlined below.

The aim of Study 1 (Chapter 5) was to distinguish distinct temperament subgroups and explore how such differences were related to concurrent social-emotional difficulties. Heightened internalizing symptoms were expected among infants with low sociability-related traits, and elevated internalizing and externalizing symptoms were expected among those with high negative emotionality and low self-regulation. In contrast, the lowest internalizing and externalizing symptom levels were expected among infants with high temperamental sociability and self-regulation.

The aim of Study 2 (Chapter 6) was to explore the continuity of temperament subgroups over repeat assessments, from infancy to toddlerhood, and the relation of these to concurrent social-emotional functioning and autism presentation at each timepoint. Cross-time continuity was broadly expected, but with more pronounced temperament differences arising as children moved from infancy into toddlerhood. Internalizing and externalizing symptoms were expected to present at higher levels, respectively, among temperamentally inhibited and disinhibited toddlers, and at lower levels among well-regulated toddlers. It was also predicted that inhibited toddlers would present with more autism traits, but that there would be no temperament-related differences in child age, sex, or developmental level.

The aim of Study 3 (Chapter 7) was to provide an initial examination of the potential mediating influence of infant temperament on the relations between contemporaneously measured caregiver psychological distress and infant social-emotional difficulties. Infant negative affectivity and self-regulation were expected to mediate the concurrent relation between caregiver psychological distress and both child internalizing and externalizing symptoms, while a mediating effect of sociability was expected only for child internalizing symptoms. A secondary objective was to examine whether the observed pattern of results generalized across infants with varying levels of autism features, with no differential effects expected.

The aim of Study 4 (Chapter 8) was to determine whether reciprocal relations among caregiver psychological distress and child temperament predict the subsequent development of social-emotional difficulties. Parallel pathways were expected to arise from (a) earlier child temperament to subsequent child internalizing and externalizing symptoms through interim caregiver psychological distress, and (b) earlier caregiver psychological distress to subsequent child internalizing and externalizing symptoms through interim child temperament. It was predicted that greater caregiver psychological distress would relate with higher child negative affectivity and lower self-regulation, but not with child sociability. Moreover, it was predicted that greater caregiver psychological distress, higher child negative affectivity, and lower child self-regulation and sociability would be associated with children's higher subsequent social-emotional difficulties. A secondary objective was to examine whether longitudinal pathways involving child temperament and caregiver psychological distress would vary as a function of children's autism symptoms, again with no differential effects expected.

The next chapter provides the general methodology for these four studies, including a description of the participant recruitment procedures, measures, and statistical methods.

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CHAPTER 4

General Method

Each empirical study included in this thesis has been published in, formatted for, or submitted to scientific journals (see page xiii). A streamlined description of the methods used in each study is provided in each relevant chapter/article. The current chapter provides a more comprehensive overview of the research design, participants, measures, and procedures.

4.1. Participant Recruitment and Assessment Procedure

This program of research was embedded within a larger, two-site (Melbourne and Perth, Australia) randomized controlled trial (RCT) of an intervention for infants showing early signs of autism (for a detailed description, see Whitehouse et al., 2019). Conduct of the trial, including data collection reported here, was approved by the Child and Adolescent Health Service Ethics Committee (2016008EP, June 8, 2016), and each caregiver provided written informed consent for their own and their infants' participation.

Participant recruitment occurred between June 2016 and February 2018. Families were invited to participate the larger trial if the following inclusion criteria were met: (a) the infant was aged between 9-14 months and 31 days (corrected for prematurity) at the time of eligibility screening, (b) the child displayed at least three of five key autism features on the Social Attention and Communication Surveillance-Revised (SACS-R; Barbaro & Dissanayake, 2013) 12-month checklist, and (c) the primary caregiver spoke sufficient English to understand study requirements and participate fully. Exclusion criteria were the following: (a) diagnosed comorbidity known to affect child neurological and developmental abilities (including birth at <32 weeks' gestation), and (b) family intention to relocate away from the study site during the 2-year trial follow-up period.

The SACS-R is a revised version of the SACS (Barbaro & Dissanayake, 2010) and includes the following markers for the identification of autism: atypical/absent pointing, waving, imitation, eye contact, response to name (Barbaro & Dissanayake, 2013). When used among 12-month-olds, the SACS-R has an estimated positive predictive value of 72% for subsequent autism diagnosis (Barbaro, Dissanayake, & Sadka, 2018; also see Mozolic-Staunton et al., 2020). The SACS-R was administered by community healthcare professionals directly with infants during routine consultations or completed with caregivers by telephone, with infants showing ≥ 3 markers for autism referred to the study team.

After confirmation of eligibility, families were scheduled a face-to-face assessment session and caregivers were posted a series of questionnaires. Caregivers provided informed consent at the Time 1 visit and a series of behavioural assessments were administered with infants. After Time 1 assessment, families were randomized to receive either the RCT intervention or community treatment as usual. Researchers involved in the administration and coding of assessments remained blind to participant treatment allocation for the trial duration.

Follow-up assessments were completed after delivery of the RCT intervention, at 6- (Time 2) and 12-months (Time 3) post baseline (Time 1 assessment). Outcomes of the RCT intervention were not of interest to the current research program. For studies drawing on longitudinal data (2 and 4), group differences (i.e., between those allocated to the RCT intervention and community treatment as usual) on key independent and dependent variables were explored (and ruled out) before children were combined into a single group for key analysis.

4.2. Sample Characteristics

103 infants (68% male) were recruited into the larger trial and seen at Time 1. Most infants (*n* = 80; 78%) had no family history of autism. An autism diagnosis was reported in the remainder of cases among an older sibling (*n* = 20) or in a cousin (*n* = 3). Hence, this cohort represents a community-based sample of infants with varying family autism histories.

Caregivers were almost exclusively biological mothers (3% biological fathers, 1% other guardian) and of average age 34.28 years (*SD* = 5.05; range 22-50 years) at study entry. With regards to education, 59% of caregivers had a university degree, 16% had a trade/technical certificate or diploma, and 24% had completed secondary education (*n* = 1 missing). Household income was above AUD$2,001 per week (or above AUD$104,000 per annum) for 48% of families, between AUD$1,501 and AUD$2,000 per week (or between AUD$78,000 and AUD$104,000 per annum) for 18% of families, and below AUD$1,00 per week (or AUD$78,000 per annum) for 23% of families (*n* = 11 chose not to provide this information). For context, the median household income for people aged 15 years and over in Australia was AUD$1,438 in 2016 (Australian Bureau of Statistics, 2017); hence this was a varied but generally well-educated and socio-economically secure sample.

Of those 103 families seen at Time 1, 6 (6%) were lost to follow-up at Time 2, and an additional 4 (*n* = 10 total, 10%) were lost to follow-up at Time 3 due to being busy, no longer interested, or dropping out of contact. The mean age of children was 12.39 months (*SD* = 1.97; range 9.07 to 16.33 months) at Time 1, 18.57 months (*SD* = 2.11; range 15.11 to 23.32 months) at Time 2, and 24.67 months (*SD* = 2.19; range 20.37 to 29.76 months) at Time 3.

4.3. Measures

The remainder of this chapter is focused on the methodology of each empirical study included in this thesis. Study 1 (Chapter 5) is cross-sectional, drawing primarily on measures of child temperament and social-emotional difficulties taken at Time 1. Study 2 (Chapter 6) is longitudinal, utilizing repeated measures of child temperament and social-emotional difficulties from Time 1 to Time 3. Study 3 (Chapter 7) is again cross-sectional, drawing on measures of child temperament and child social-emotional difficulties, and introducing measures of caregiver psychological distress, all taken at Time 1. Study 4 (Chapter 8) is then again longitudinal, drawing on measures of temperament and caregiver psychological distress taken at each of Time 1 and Time 2, and the measure of child social-emotional difficulties taken across each of Time 1 to Time 3.

Although not of primary research interest, measures of child autism symptoms, cognitive/developmental abilities, and family demographic characteristics also taken within the protocol for the larger study were variably included in the empirical studies reported here, for sample characterization, exploratory, and control purposes.

4.3.1. Child Temperament

Caregivers completed age-appropriate versions of temperament questionnaires based on Rothbart et al.'s (1981) theoretical approach: the Infant Behavior Questionnaire-Revised (IBQ-R; Gartstein & Rothbart, 2003) at Time 1, and Early Childhood Temperament Questionnaire (ECBQ; Putnam, Gartstein, & Rothbart, 2006) at Time 2 and Time 3. The IBQ-R is a measure of temperament for children aged between 3 and 12 months, and the ECBQ is an ‘upward extension’ of the IBQ-R for children aged 18 to 36 months. The sample included children who did not fit within these instruments’ age brackets; specifically, *n* = 43 (of 103) children at Time 1 were aged over 12 months and *n* = 36 (of 97) children at Time 2 were aged under 18 months. To maintain consistency of measurement across participants at each timepoint, all children at Time 1 were administered the IBQ-R and all children at Time 2 were administered the ECBQ.

IBQ-R items (191) and ECBQ items (201) are presented as questions (e.g., “*When hair was washed, how often did the baby fuss or cry?”*), and the ratings refer to the frequency of the behaviour over the preceding one or two weeks: 1 = *Never*, 2 = *Very Rarely*, 3 = *Less Than Half the Time*, 4 = *About Half the Time*, 5 = *More Than Half the Time*, 6 = *Almost Always*, 7 = *Always,* and NA = *Does Not Apply* (re-coded as missing). IBQ-R/ECBQ items are then averaged into scales representing finer-grained aspects of child temperament. The IBQ-R and ECBQ include many of the same scales: Activity Level, High Intensity Pleasure, Approach, Frustration, Fear, Perceptual Sensitivity, Sadness, Soothability, Cuddliness, Low Intensity Pleasure, and Attentional Focusing (labelled Duration of Orienting on the IBQ-R). The IBQ-R also contains Vocal Reactivity and Smiling and Laughter scales, not included on the ECBQ, and the ECBQ contains additional scales representing later-emerging temperament aspects: Impulsivity, Sociability, Shyness, Discomfort, Motor Activation, Inhibitory Control, and Attentional Shifting.

The IBQ-R and ECBQ scales can be averaged into three higher-order temperament dimensions: (1) Surgency (i.e., social orientation and the experience of positive emotions), (2) Negative Affectivity (i.e., the tendency to experience negative emotions), and (3) Effortful Control (Orienting/Regulation on the IBQ-R; i.e., the capacity to regulate emotions and behaviour)[4]. Most overlapping IBQ-R and ECBQ scales demonstrate a consistent loading on a given dimension, except for Perceptual Sensitivity which loads on the IBQ-R Surgency dimension and ECBQ Negative Affectivity dimension (Putnam et al., 2006). Table 1 provides the definition and higher-order dimension affiliation of each IBQ-R and ECBQ scale.

[4]Given adjustments made to the IBQ-R Orienting/Regulation and ECBQ Effortful Control dimension in Study 4 (i.e., omission of non-overlapping fine-grained scales), this dimension of temperament is referred to in that Study as Self-Regulation.

Table 1

IBQ-R and ECBQ Scale Definitions and Dimension Affiliations

Scale	Definition	IBQ-R	ECBQ	Sur	Neg	Eff
Approach	"Excitement in the anticipation of pleasurable activities."	×	×	×		
Activity Level	"Gross motor activity, including rate and extent of movement."	×	×	×		
Attention Focusing	"Capacity to sustain attention on an object or task."	×	×			×
Attention Shifting	"Ability to transfer attentional focus from one object or task to another."		×			×
Cuddliness	"Desire for, and pleasure in, warmth and closeness with others, independent of shyness or extraversion."	×	×			×
Discomfort	"Negative affect related to sensory qualities of stimulation, including intensity, rate or complexity of light, sound, and texture."		×		×	
Falling Reactivity	"Rate of recovery from peak distress, excitement, or general arousal; ease of falling asleep."	×			×	
Fear	"Negative affect related to anticipated pain, distress and/or threat."	×	×		×	
Frustration	"Negative affect related to confinement, interruption of ongoing tasks or goal blocking."	×	×		×	
High Intensity Pleasure	"Pleasure or enjoyment related to high stimulus intensity, rate, complexity, novelty, and incongruity."	×	×	×	×	
Impulsivity	"Speed of response initiation."		×		×	
Inhibitory Control	"Capacity to suppress inappropriate actions or responses."		×			×
Low Intensity Pleasure	"Pleasure or enjoyment related to low stimulus intensity, rate, complexity, novelty, and incongruity."	×	×			×
Motor Activation	"Repetitive small motor movements; fidgeting."		×		×	
Perceptual Sensitivity	"Detection of slight, low-intensity stimuli from the external environment."	×	×	×	×	
Sadness	"Negative affect, tearfulness or lowered mood related to physical state, disappointment, loss, and/or response to other's suffering."	×	×		×	

Shyness	"Slow or inhibited approach and/or discomfort in social situations."		×		×	
Smiling and Laughter	"Positive affect in response to changes in stimulus intensity, rate, complexity, and incongruity."	×		×		
Sociability	"Seeking and taking pleasure in interactions with others."		×	×		
Soothability	"Reduction of fussing, crying, or distress when soothing techniques are used by the caretaker."	×	×			×
Vocal Reactivity	"Vocalization during daily activities."	×		×		

Note. Scale definitions are from Putnam et al. (2008, p. 17). IBQ-R = Infant Behavior Questionnaire-Revised; ECBQ = Early Childhood Behavior Questionnaire; Sur = Surgency; Neg = Negative Affectivity; Eff = Effortful Control (or Orienting/Regulation).

Several factors guided selection of the IBQ-R and ECBQ for this research. First, the suite of questionnaires based on Rothbart et al.'s (1981) theoretical approach comprise traits and dimensions that are linked to neurobiological process, and thus afford a more mechanistic understanding of individual differences in the context of autism than alternative questionnaire measures based on directly observed child behaviour. Second, their extensive use in the infancy/toddlerhood period in existing studies of autism (see Chapter 1) ensured there was a literature base for empirical comparison. Third, the higher-order three-dimension structure shared by the IBQ-R and ECBQ facilitates examination of temperament across ages and developmental stages and was, thus, well-suited for the planned longitudinal data collection. Fourth, the IBQ-R and ECBQ have evidenced stronger psychometric properties than alternative questionnaire measures derived from the theoretical approaches of Chess and Thomas and colleagues (1968, 1977), Buss and Plomin (1975), and Goldsmith (1987; 1982) (Gartstein, Bridgett, & Low, 2012).

The three-dimensional structure of the IBQ-R and ECBQ has been supported in independent community- and culturally-diverse samples (Casalin et al., 2012; Montirosso et al., 2011; Stępień-Nycz et al., 2018; although see Bosquet Enlow et al., 2016). Moreover, the finer-grained IBQ-R scales and most ECBQ scales have demonstrated adequate internal consistency (Cronbach's alpha coefficients [α] > .70) in community samples (Gartstein et al., 2012; Gartstein & Rothbart, 2003) and for both primary and secondary caregivers (Parade & Leerkes, 2008; Putnam et al., 2006), except for questionable internal consistency reported by Putnam et al. (2006) for ECBQ Impulsivity (α = .57), Activity Level (α = .66), and Attention Shifting (α = .62) scales at child age 18-22 months.

Convergence has been reported, as expected, between observed and caregiver-reported aspects of temperament on the IBQ-R (Gartstein & Marmion, 2008; Parade & Leerkes, 2008) and its predecessor (i.e., IBQ, Rothbart, 1981; Forman et al., 2003; Stifter et al., 2008) and the ECBQ (Mulder et al., 2014). Moreover, there is some support for the specificity of IBQ-R and ECBQ scales (Gartstein & Rothbart, 2003; Putnam et al., 2006) and convergence across scales common to both the IBQ-R and ECBQ (Putnam et al., 2008).

Furthermore, moderate inter-rater agreement has been documented for IBQ-R dimensions (r = 0.31 [Orienting/Regulation] to 0.70 [Negative Affectivity]; Gartstein & Rothbart, 2003) and most scales for primary and secondary caregivers (r's $\geq$ .26 and statistically significant, except for Soothability [.08], High Intensity Pleasure [.12], and Cuddliness [.17]; Parade & Leerkes, 2008), as well as for the ECBQ dimensions (r = 0.31 [Surgency] to 0.45 [Negative Affectivity]) and most scales (r's $\geq$ .30, except for Low Intensity Pleasure [.09], Attention Focusing [.24], and Attention Shifting [.25]; Putnam et al., 2006). Finally, primary caregivers' ratings of child temperament on the ECBQ have shown significant stability over 6-month intervals (Putnam et al., 2006), and significant correlations are apparent among IBQ-R and ECBQ corresponding dimensions (*r* = 0.36 for Surgency, *r* = .36 for Negative Affectivity, and *r* = .41 Effortful Control) and fine-grained scales (*r* = 0.22 [Frustration] to .45 [Perceptual Sensitivity]; Putnam et al., 2008).

All four studies in the current research program included the IBQ-R and/or ECBQ as an independent variable. The IBQ-R and ECBQ fine-grained scales were of primary interest to Studies 1 and 2, given the objective/s to obtain a *nuanced* understanding of the nature of individual temperament differences, whereas the IBQ-R and ECBQ higher-order dimensions were of primary interest to Studies 3 and 4 given the objective/s to more *broadly* characterize developmental pathways implicating child temperament.

4.3.2. Caregiver Psychological Distress

Caregivers completed a short version of the Depression, Anxiety, and Stress Scales (DASS-21; Lovibond & Lovibond, 1995) at Time 1 and Time 2 assessment. DASS-21 items (21) are presented as statements (e.g., “I found it hard to wind down”) and rated for applicability over the preceding week: 0 = *Did not apply to me at* all, 1 = *Applied to me to some degree or some of the time*, 2 = *Applied to me to a considerable degree or a good part of the time*, 3 = *Applied to me very much or most of the time*. DASS-21 items are summed into separate Depression, Anxiety, and Stress scales, each with scores ranging from 0 to 21.

The DASS-21 was specifically selected for this research as it offered a fair balance between brevity (i.e., ease of administration) and psychometric soundness. Specifically, the DASS-21 has been shown to converge with other questionnaire-based measures of psychological distress – including the Beck Anxiety Inventory (BAI; Beck et al., 1988), Beck Depression Inventory-II (BDI-II; Beck et al., 1996), and Positive and Negative Affect Schedule (PANAS-N; Watson et al., 1988) (Gloster et al., 2008; Henry & Crawford, 2005; Norton, 2007) – and to diverge with indices of more broadly conceptualised wellbeing, including positive affect and quality of life (Álvarez et al., 2010; Gloster et al., 2008).

The DASS-21 scales have demonstrated good-to-excellent internal consistency (i.e., α’s > 80) in general population- (Henry & Crawford, 2005; Sinclair et al., 2012), non-Western- (Norton, 2007; Oei et al., 2013), and clinical psychiatric samples (Antony et al., 1998). However, the three-factor structure of the DASS-21 has been challenged by evidence suggesting strong inter-scale correlations (i.e., *r*‘s > .70) and item cross-loadings (Antony et al., 1998; Daza et al., 2002), and presence of a common general factor underlying the three scales (Henry & Crawford, 2005; Osman et al., 2012). Therefore, DASS-21 items may be summed to form an overall total (possible range 0 to 63) representing broad ‘psychological distress’, which has demonstrated stronger internal consistency than the separate scales (i.e., α’s > 90) in general population samples (Asghari et al., 2008; Henry & Crawford, 2005) as well as among parents of children with an autism diagnosis (Falk et al., 2014). Hence, the DASS-21 total score was utilized in this research as an independent variable in Studies 3 and 4.

4.3.3. Child Social-Emotional Functioning.

Caregivers completed the Infant-Toddler Social and Emotional Assessment (ITSEA; Carter & Briggs-Gowan, 2006) at each timepoint. The ITSEA is a clinical tool for identifying social-emotional difficulties among children aged 12 to 35 months. ITSEA items (166) are presented as statements (e.g., “Acts aggressive when frustrated”), and ratings refer to the frequency and intensity of behaviour over the preceding month: 0 = *Not True/Rarely*, 1 = *Somewhat True/Sometimes*, 2 = *Very True/Often*. ITSEA items are averaged within scales representing narrow social-emotional symptoms and competencies, and these can be further averaged across four domains: (1) Internalizing (comprising Depression/Withdrawal, General Anxiety, Separation Distress, and Inhibition to Novelty scales), (2) Externalizing (comprising Activity/Impulsivity, Aggression/Defiance, and Peer Aggression scales), (3) Dysregulation (comprising Sleep, Negative Emotionality, Eating, and Sensory Sensitivity scales), and (4) Competence (comprising Compliance, Attention, Imitation/Play, Mastery Motivation, Empathy, and Prosocial Peer Relations scales). Raw ITSEA domain/scale scores can be converted into standardized *T* scores (M = 50, SD = 10) or percentile rankings, according to child sex and age, with scores at or exceeding the extreme 10^{th} percentile considered to be *Of Concern*.

The ITSEA was specifically selected for this research given its sound psychometric properties and applicability to a wider range of child ages than other questionnaire measures of social-emotional functioning, none of which extend younger than age 18-months (e.g., Child Behavior Checklist [CBCL]; Achenbach & Rescorla, 2003). Specifically, the ITSEA Internalizing and Externalizing domains and subscales have shown convergence with the Ages and Stages Social-Emotional Questionnaires: Social Emotional (ASQ:SE; Squires et al., 2002) Total Score and corresponding Child Behavior Checklist (CBCL 1.5-5; Achenbach & Rescorla, 2003) Composites and Subtests, and the ITSEA Competence domain and subscales have shown convergence with the Adaptive Behavior Assessment System: Second Edition (ABAS-II; Oakland & Harrison, 2008) Social Skill Composite in normative samples (Carter & Briggs-Gowan, 2006). Of interest, low-to-moderate magnitude correlations have been found between the ITSEA scales and Infant Behavior Questionnaire (IBQ; Rothbart & Derryberry, 1981) and Colorado Child Temperament Inventory (CCTI; Buss & Plomin, 1975) scales, suggesting that constructs associated with temperament and social-emotional functioning are distinct (Carter et al., 1999, 2003). Finally, the ITSEA has demonstrated adequate-to-good test-retest reliability over a 44-day interval (*r*’s from 0.82 to 0.90 for domains and from to 0.85 for scales) and inter-rater agreement between mothers and fathers (intra-class correlation coefficients [ICC] ranging from 0.58 to 0.79 for domains and from 0.43 to 0.78 for scales; Carter et al., 2003).

For the current research, within each of Studies 1 through 4, Internalizing and Externalizing domain scores were included as key dependent variables. Study 2 also included the Competence domain. Because $n = 40$ (of 103) children at Time 1 were aged below the lower age limit against which the ITSEA was developed and normed, precluding the computation of standardized scores, raw ITSEA scores were utilized throughout this research. Raw scores also have the advantage of being more wide-ranging than standardized scores and hence can provide more variability for analysis. The proportion of children scoring in the range *Of Concern* was reported in Study 2 for sample characterization purposes only.

4.3.4. Child Autism Features

Children were administered the Autism Observation Scale for Infants (AOSI; Bryson et al., 2008) at Time 1 and Time 2, and the Autism Diagnostic Observation Schedule – 2nd Edition, Toddler Module (ADOS-T; Luyster et al., 2009) at Time 2 and Time 3, to measure behavioural autism traits.

The AOSI is a semi-structured, direct behavioural assessment designed to measure features of autism in infants aged 6- to 18-months. The AOSI is conducted at a table, with the infant seated at on a caregiver’s lap across from an examiner, and includes two short periods of free play with toys and a set of semi-structured activities and presses, lasting a total of 15-20 minutes. Target child behaviours (19; listed in Appendix A) are rated by the examiner on a 2- or 3-point scale where 0 = normative behaviour, 1 = inconsistent, partial, or questionable behaviour, 2 = atypical behaviour, 3 = total lack of the behaviour. AOSI scores are derived from 16 (of 19) behavioural ratings. Items with a rating above 0 are tallied to yield a marker count (range 0 to 16) and summed to create a total score (range 0 to 38), with higher scores indicating more autism features.

AOSI marker counts and total scores, respectively, have demonstrated excellent inter-rater reliability at infant ages 6 (Cohen’s kappa coefficient [*k*] = .68 and .74), 12 ($k = .92$ and .93), and 18 months ($k = .93$ and .94) and adequate-to-good two-week test-retest reliability at infant age 12-months (intra-class correlation coefficient [ICC] = .68 and .61; Bryson et al., 2008). Moreover, AOSI scores early in the second year of life have been shown to predict subsequent ADOS total scores (Gammer et al., 2015) and autism classification (Zwaigenbaum et al., 2005), supporting the predictive validity of these for identifying autism traits in early-life. Hudry et al. (2020) have reported sound psychometric properties for the AOSI in the current sample, including good-to-excellent intra-rater reliability (i.e., across video- and live-coding approaches; ICC = 0.88 at Time 1 and 0.92 at Time 2) and inter-rater agreement (ICC = 0.83 at Time 1 and 0.88 at Time 2), and convergence with concurrent ADOS-T total algorithm scores at Time 2 ($r = 0.41$, $p < .001$).

The ADOS-T is a semi-structured, direct behavioural assessment designed to measure features of autism in children aged 12 to 30 months. The ADOS-T is conducted at a child-sized table and on the floor and includes a period of free-play and a set of semi-structured activities and presses, lasting a total of 40-60 minutes. Target child behaviours (41; listed in Appendix B) are rated by the examiner on a 3- or 4-point scale, where – similarly to the AOSI – a score of 0 represents typical behaviour and higher scores reflect progressively more atypical behaviour. Select items are summed, depending on child age and expressive language ability (i.e., child age 12-20 months or nonverbal [12-20/NV] versus child age 21-30 months and verbal [21-30/V]; see Appendix B), to yield Social Affect (SA) and Restricted and Repetitive Behavior (RRB) domain scores and an overall ADOS total score (SA + RRB; range 0 to 28), which may be converted to range of concern: *little-to-no concern* (total score ≤ 9 [12-20/NV] or ≤ 7 [21-30/V], *mild-to-moderate concern* (total score between 10-13 [12-20/NV] or 8-11 [21-30/V]), and *moderate-to-severe Concern* (total score ≥14 [12-20/NV] or ≥12 [21-30/V]).

The ADOS-T has shown strong diagnostic validity; specifically, a total cut-off score of 12 [12-20/NV] or 10 [21-30/V] has yielded sensitivity and specificity values greater than 80% for autism versus non-autism classification (Esler et al., 2015; Luyster et al., 2009). Further, Guthrie et al. (2013) reported that 95% of children with ADOS-T scores in the moderate-to-severe range were diagnosed with autism 1-2 years later, while 83% of children in the little-to-no concern range were not subsequently diagnosed with autism. Further, Macari et al. (2018) found that clinicians' ADOS-T ratings of infant social-communication behaviour were well-aligned with parents responses on the First Year Inventory (FYI; Baranek et al., 2003), with the exception that amount social babbling was rated lower by clinicians than parents. Estimates of internal consistency are excellent for the ADOS-T SA domain (α = .88 [12-20/NV] and .90 [21-30/V]) albeit lower for the RRB domain (α = .50 [for 12-20/NV and 21-30/V]; Luyster et al., 2009). Finally, the ADOS-T total scores and domain scores have demonstrated strong inter-rater reliability (.93 > ICC > .90 [12-20/NV] and .99 > ICC > .74 [21-30/V]) and 2-month test-retest reliability (.86 > ICC > .75 [12-20/NV] and .95 > ICC > .60 [21-30/V]; Luyster et al., 2009).

AOSI and ADOS-T assessments were administered and scored by examiners who met standard requirements for research reliability on each of these tools. Time 1 AOSI scoring was completed live by the administering examiner, while Time 2 AOSI and ADOS-T scoring was completed via videotape by an alternate-site examiner to guarantee blindness to participant treatment allocation (given the context of the larger intervention trial). A subset of AOSI (*n* = 22 at Time 1, *n* = 20 at Time 2) and ADOS-T assessments (*n* = 16) were double- or consensus-scored to check examiners' administration fidelity and scoring reliability. The key examiners responsible for AOSI and ADOS-T administration maintained an average of at least 80% agreement with one another or consensus for the duration of the data collection period (for more details, see Hudry et al., 2020).

ADOS-T and/or AOSI total scores were explored as secondary dependent variables in Studies 1 and 2, and as potential moderator variables in Studies 3 and 4.

4.3.5. Child Cognitive/Developmental Level

Children were administered the Mullen Scales of Early Learning (MSEL; Mullen, 1995) at each timepoint. The MSEL is a standardized, examiner-administered assessment of child cognitive/developmental functioning suitable for use from birth to 68-months of age. It includes a Gross Motor scale and four cognitive scales: Visual Reception, Fine Motor, Receptive Language, and Expressive Language. MSEL scale raw scores may be converted into standardized t scores (M = 50, SD = 10), percentile ranks, and age equivalents, and t scores for the four cognitive scales can be summed and converted into an Early Learning Composite (ELC; M = 100, SD = 15) representing general level of functioning.

The MSEL was standardized on 1,849 children from the general population (excluding those with known disabilities) and demonstrated sound psychometric properties, including good 2-week test-retest reliability (i.e., r's > .70) and construct validity (Mullen, 1995). Although not yet normed for clinical samples, the MSEL has shown convergence with the original and revised Differential Ability Scales (Elliott, 1990, 2007) (Bishop et al., 2011; Farmer et al., 2016) and divergence with factors composed of autism symptom and social-emotional functioning measures in samples with autism, non-autism delays/disorders, and normative development (Swineford et al., 2015). Further, factor analytic results suggest the MSEL scales relate to the same, single latent construct (similar to the ELC) in autism and non-autism groups, supporting construct validity (Swineford et al., 2015).

The MSEL ELC was explored as a secondary dependent variable in Studies 1 and 2.

4.3.6. Demographic Characteristics

Caregivers completed a demographic questionnaire at Time 1 to provide information concerning caregiver age, education level, annual household income, and family medical histories.

4.4. Statistical Procedure

4.4.1. IBQ-R/ECBQ and ITSEA item overlap

Researchers have suggested that relations between temperament and social-emotional functioning may be inflated due to the overlap in items across measures of these constructs (Frick, 2004; Nigg, 2006). To address this potential issue, a side-by-side comparison of the IBQ-R/ECBQ and ITSEA was undertaken to identify items phrased around the same or similar child behaviours. A total of 17 ITSEA items (listed in Table 2) were identified as overlapping with IBQ-R and/or ECBQ items: within the ITSEA Internalizing domain, n = 10 items (of n = 30) overlapped with the IBQ-R and (n = 5) / or (n = 5) ECBQ; within the ITSEA Externalizing domain, n = 3 items (of n = 24) overlapped with the IBQ-Q and (n = 1) / or (n = 2) ECBQ; within the ITSEA Competence domain, n = 5 items (of n = 37) overlapped with the ECBQ (no items from this domain overlapped with the IBQ-R). ITSEA items that overlapped with IBQ-R and/or ECBQ items were removed prior to analysis on a study-by-study basis, depending on what temperament data was used: Studies 1 and 3 drew only upon IBQ-R data (hence n = 5 ITSEA items removed), Study 2 drew only upon ECBQ data (hence n = 17 ITSEA items removed), while Study 4 drew upon IBQ-R and ECBQ data but did not consider the ITSEA Competence domain (hence n = 12 ITSEA items removed).

4.4.2. Preliminary data handling and assumption testing

Hardcopy assessment data were entered into a purpose-built, password-protected Research Electronic Data Capture (REDCap; Harris et al., 2009) system hosted at La Trobe University, and subsequently imported into the Statistical Package for Social Sciences (SPSS; IBM Corp Armonk, NY, US) for preliminary data checking. Out-of-range errors were detected through computation of descriptive statistics and verified against hardcopy data. The assumption of multivariate normality was assessed for each questionnaire (IBQ-R, ECBQ, DASS-21, ITSEA) and assessment (MSEL, AOSI, ADOS-T) by dividing kurtosis and skewness values by their respective standard errors, with a normal bell-shaped curve indicated by a z score within ± 1.96. Extreme kurtosis and/or positive skew were apparent for some IBQ-R (Falling Reactivity, Soothability [Time 1]) and ECBQ (Distress to Limitations, Fear, Motor Activation [Time 2-3], Perceptual Sensitivity [Time 3, only]) scales, the ECBQ Negative Affectivity dimension (Time 2), DASS-21 total scores (Time 1-2), ITSEA Internalizing (Time 1-2) and Externalizing (Time 1-3) domains, and AOSI (Time 1-2) and ADOS-T (Time 2) total scores. Moreover, negative skew was apparent for other IBQ-R (Smiling and Laughter, High Intensity Pleasure, Approach [Time 1]) and ECBQ (Approach [Time 3, only]) scales.

Square root, logarithmic, and inverse transformation procedures did not transform these data to normality, hence departures from multivariate normality were handled in two ways: (1) using the maximum likelihood (MLR) estimator for analyses in M*plus* – which provides parameter estimates with standard errors and χ^2 statistics that are robust to non-normality (Muthén, 2002) and is appropriate for small-to-medium sample sizes (Yuan & Bentler, 2000), and (2) using a bootstrap procedure for analyses in SPSS – which resamples the dataset and repeats the analysis a specified number of times (typically >1,000) to generate an overall summary estimate for which the multivariate normality assumption does not apply – with 95% confidence intervals (CIs) obtained using the bias-corrected and accelerated (BCa) method to correct for bias and skewness of bootstrap estimates.

Next, Cronbach's alpha coefficients (α) were computed to evaluate internal consistency of key questionnaire measures (IBQ-R, ECBQ, DASS-21, ITSEA) in the present dataset. The results are presented in each study Chapter but repeated here for convenience. The IBQ-R and ECBQ dimensions demonstrated good-to-excellent internal consistency ($.93 > \alpha > .83$; as reported in Study 4 [Chapter 8]), while the range of internal consistency estimates was wider for the IBQ-R scales ($.89 > \alpha > .69$; see Study 1 [Chapter 5]) and ECBQ scales ($.94 > \alpha > .58$; see Study 2 [Chapter 6]) compared to the questionnaire developers (Gartstein & Rothbart, 2003; Putnam et al., 2006), and internal consistency for the ECBQ Impulsivity scale was in the questionable range ($\alpha = .46$). The DASS-21 total score demonstrated excellent internal consistency ($\alpha = .92$ at both timepoints).

Internal consistency was evaluated for the ITSEA before and after the removal of items overlapping with the IBQ-R and/or ECBQ. Cronbach's α estimates for the unaltered ITSEA domains were as follows: Internalizing ($\alpha_{t1} = .77$; $\alpha_{t2} = .85$; $\alpha_{t3} = .80$); Externalizing ($\alpha_{t1} = .84$; $\alpha_{t2} = .90$; $\alpha_{t3} = .92$); Competence ($\alpha_{t1} = .82$; $\alpha_{t2} = .89$; $\alpha_{t3} = .93$). Cronbach's α estimates were lower for the altered ITSEA domains (i.e., post-item removal) but still in the acceptable range at each timepoint ($\alpha > .70$) with the exception of Internalizing at Time 1 ($\alpha < .60$; refer to Studies 1-4 for more details). Inspection of the item-total correlations revealed that the item *"Wakes up from scary dreams or nightmares"*, negatively correlated with the full scale, was due at least in part, to the majority of responses being *Not True/Rarely*. This item was retained in the Internalizing domain for Study 4 to maintain consistency of measurement across timepoints but removed from the Internalizing domain for studies that drew only upon cross-sectional Time 1 data (i.e., Study 1 and Study 3) to increase the value of α above .60.

The extent of missing data was examined at each timepoint. Time 1 data were available for $n = 96$ on the IBQ-R (6.8% missing), $n = 95$ on DASS-21 (7.8% missing), and $n = 88$ for the ITSEA (14.6% missing). Time 2 data were available for $n = 90$ on the ECBQ (12.7% missing), $n = 91$ on the DASS-21 (11.7% missing), and $n = 88$ for the ITSEA (14.6% missing). Time 3 data were available for $n = 81$ on the ECBQ (21.4% missing) and $n = 80$ on the ITSEA (22.4% missing). Pertaining to other (non-key) measures: Time 1 MSEL and AOSI data were available for the full sample of $n = 103$; Time 2 MSEL, AOSI, and ADOS-T data were available for $n = 96$ (7.8% missing); and Time 3 MSEL and ADOS-T data were available for $n = 92$ (10.7% missing). These missing data were handled in statistical analyses using default software procedures: full information maximum likelihood (FIML; Schafer & Graham, 2002) estimation in M*plus* (i.e., drawing complete-data inferences from available information), and listwise deletion in SPSS (i.e., removing cases with incomplete data).

Table 2

Overlapping IBQ-R/ECBQ and ITSEA Items

IBQ-R item	ECBQ item	ITSEA item removed
When introduced to an unfamiliar adult, how often did the baby cling to a parent? When in the presence of several unfamiliar adults, how often did the baby cling to a parent?	When approached by an unfamiliar person in a public place (for example, the grocery store), how often did your child cling to a parent?	Hangs onto you or wants to be in your lap when with other people Is shy with new adults
How often during the last week did the baby play with one toy or object for 5-10 minutes?	When playing alone, how often did your child become easily distracted?	Goes from toy to toy faster than other children his or her age
For no apparent reason, how often did your baby appear sad?	During everyday activities, how often did your child become sad or blue for no apparent reason?	Looks unhappy or sad without any reason
When visiting a new place, how often did the baby continue to be upset for 10 minutes or more?	When visiting a new place, how often did your child not want to enter?	Takes a while to feel comfortable in new places (10 minutes or more)
When visiting a new place, how often did the baby move about actively when s/he is exploring new surroundings?	In situations where s/he is meeting new people, how often did your child become quiet?	Is quiet or less active in new situations?
	During everyday activities, how often did your child rock back and forth while sitting?	Is restless and can't sit still
	While visiting relative or adult family friends s/he sees infrequently, how often did your child stay back and avoid eye contact?	Does not make eye contact
	When approaching unfamiliar children playing, how often did your child seem uncomfortable?	Is shy with new children

	During everyday activities, how often did your child seem full of energy, even in the evening?	Seems to have no energy
	When s/he asked for something and you said "no", how often did your child have a temper tantrum?	Has temper tantrums
	In situations where s/he is meeting new people, how often did your child become quiet?	Takes a while to speak in unfamiliar situations
	During everyday activities, how often did your child become distressed when his/her hands were dirty and/or sticky?	Is *very* worried about getting dirty
	When engaged in an activity requiring attention, how often did your child stay involved for 10 minutes or more?	Can pay attention for a long time (other than watching TV)
	When asked to do so, how often was your child able to lower his or her voice?	Quiets down when you say "Shh"
	When engaged in play with his/her favourite toy, how often did your child play for 5 minutes or less?	Plays with toys for 5 minutes or longer
	When looking at picture books on his/her own, how often did your child enjoy looking at the books?	Looks at picture books by himself or herself
	When being dressed or undressed, how often did your child stay still?	Stays still while being changed, dressed, or bathed

Note. Colours represent the domain affiliation of ITSEA items: Internalizing; Externalizing; Competence.

4.4.3. Analytic strategy

The empirical objectives of this research were addressed using the following set of analyses, performed in SPSS (IBM Corp Armonk, NY, US) or M*plus* Version 8 (Muthén & Muthén, 1998-2017):

- Descriptive statistics analysis (Studies 1-4; SPSS);
- Latent profile analysis (Studies 1 and 2; M*plus*);
- One-way analysis of variance (Studies 1, 2, and 4) and analysis of covariance (Study 2; SPSS);
- Cross-tabulation analysis (Study 2; SPSS);
- Independent samples *t*-tests (Studies 2 and 4; SPSS);
- Pearson product-moment correlation coefficients (Studies 3 and 4; SPSS);
- Mediation and moderated mediation analysis (Study 3; SPSS);
- Cross-lagged path modelling (Study 4; M*plus*).

Alpha was set at 0.05 for each analysis conducted in SPSS, unless otherwise stated, and BCa 95% CIs not spanning zero taken as indicative of the significance of post-hoc pairwise comparisons (in ANOVA and *t*-tests) and of indirect effects (in mediation/moderated mediation analyses). Effect size was measured using eta squared (η^2) for ANOVA/ANCOVA, with .01 interpreted as small, .06 medium, and .14 large (Cohen, 1988). A set of statistical fit indices and criteria provided indication of goodness-of-fit for models tested in M*plus*, and these are described in turn.

4.4.3.1. Studies 1 and 2

Latent profile analysis (LPA) was conducted to identify subgroups of children according to temperament based on IBQ-R data at Time 1 (Study 1) and ECBQ data at Time 2 and Time 3 (Study 2). Like hierarchical cluster analysis, the goal of LPA is to identify unobserved or 'latent' categories of individuals in a population with respect to a set of continuous indicators – here, scores on the fine-grained IBQ-R or ECBQ scales. However, the procedure for generating and exploring categorical subgroups differs between methods; specifically, hierarchical cluster analysis simultaneously generates a series of models with subgroup solutions from 1 (no heterogeneity, all individuals in one subgroup) to *n* (no homogeneity, each individual is discrete), whereas the recommended procedure for LPA is to estimate a comparative baseline model with a single subgroup (i.e., *k*) and then increase the number of subgroups in the model by 1 (i.e., *k* + 1) until convergence issues are encountered, or until the increase in subgroups no longer merits a reduction in parsimony (Nylund-Gibson & Choi, 2018). On the basis of previous findings from normative development, models with one through five temperament subgroups were examined in the present research. The main advantage of LPA over hierarchical cluster analysis is that it provides more objective criteria from which to determine the number of subgroups; specifically, selection of subgroup solution is informed by statistical fit indices in LPA but relies on visual inspection of a dendrogram in hierarchical cluster analysis, which can sometimes be ambiguous and subjective.

Because the fit indices provided in LPA do not often converge on a single subgroup solution, the recommended procedure is to consider these jointly (Nylund-Gibson & Choi, 2018). In the current research, the number of temperament subgroups was decided through consideration of (a) information criteria – the Akaike Information Criterion (AIC; Akaike, 1987), Bayesian Information Criterion (BIC; Schwarz, 1978), and Adjusted BIC (Sclove, 1987) – where lower values indicate superior fit, (b) likelihood-based tests – the Lo-Mendell-Rubin test (LMRT; Lo, Mendell, & Rubin, 2001) and Bootstrapped Likelihood Ratio test (BLRT; McLachlan, 1987) – where a significant *p* value suggests fit improvement compared to a model with one less subgroup (i.e., k vs $k - 1$), and (c) the entropy statistic (Celeux & Soromenho, 1996), where a value closer to 1 indicates better classification accuracy. Number of subgroups was also guided by non-statistical criteria, including theoretical meaningfulness and parsimony (i.e., favouring simplicity and accuracy; Morgan, 2015).

After selection of the final LPA solution, children were allocated to subgroups based on highest posterior membership probabilities (range 0-1) and analysis of variance (ANOVA) and post-hoc tests were conducted in SPSS to determine the nature of between-subgroup differences in IBQ-R or ECBQ scale scores. A Bonferroni correction for multiple comparisons was applied to control familywise Type 1 error rate, resulting in an alpha level of 0.004 (0.05/14) and 0.003, respectively, for ANOVA comparing subgroup IBQ-R or ECBQ scale scores. Each temperament subgroup was allocated a descriptive label based on its qualitative temperament characteristics.

An additional objective of Study 2 was to explore temperament subgroup classifications over time. This was achieved using cross-tabulations with Bonferroni post-hoc tests, to examine relations among temperament subgroup classifications identified at Time 1 and 2 and at Time 2 and 3.

One-way ANOVA/ANCOVA were then performed to explore between-subgroup differences in concurrent behavioural/clinical phenotypic characteristics (chronological age, sex ratio, MSEL ELC score, AOSI and/or ADOS-T Total score) and social-emotional functioning (ITSEA Internalizing, Externalizing, and Competence domain scores [while controlling for ADOS-T total score in Study 2]). Exploratory *t*-tests were also conducted in Study 2 to explore differences in Time 3 ITSEA domain scores between children who maintained versus shifted their temperament subgroup classification from Time 2 to 3.

4.4.3.2. Studies 3 and 4

An initial examination of zero-order bivariate correlations was undertaken to examine relations between IBQ-R/ECBQ Surgency, Negative Affectivity, and Effortful Control (Orienting/Regulation) dimension scores, DASS-21 total scores, and ITSEA Internalizing and Externalizing domain scores concurrently (Studies 3 and 4) and across time (Study 4, only).

Study 3 used the SPSS PROCESS macro (Hayes, 2018) to perform mediation analyses on Time 1 data; examining the indirect effect of caregiver psychological distress (DASS-21 total score) on child social-emotional difficulties (ITSEA Internalizing and Externalizing domain scores) via child temperament (IBQ-R dimension scores). Moderated mediation analyses were subsequently performed to determine if indirect effects varied according to AOSI Total score.

In Study 4, cross-lagged path analyses were conducted to explore the directionality of longitudinal effects between caregiver psychological distress and child temperament, in the prediction of child social-emotional difficulties. Specifically, cross-lagged pathways were specified from (a) Time 1 DASS-21 total to Time 2 ECBQ dimensions to Time 3 ITSEA Internalizing/Externalizing domains, and (b) from Time 1 IBQ-R dimensions to Time 2 DASS-21 total to Time 3 ITSEA Internalizing/Externalizing domains. Within-time covariances (i.e., concurrent relations between variables at Time 1 and Time 2) and autoregressive effects (i.e., cross-time relations of the *same* construct) were estimated simultaneously, thereby ‘partialling out’ these effects that may have otherwise accounted for cross-lagged pathways. Further, ANOVA and *t*-tests examining the effects of putative covariates led to the inclusion of annual household income in each model. Cross-lagged path models were estimated separately for each IBQ-R/ECBQ dimension and ITSEA domain.

The goodness-of-fit of each cross-lagged path model was assessed using the χ^2 statistic (Jöreskog, 1969), root mean square error of approximation (RMSEA; Steiger, 1990), Comparative Fit Index (CFI; Bentler, 1990), Tucker-Lewis index (TLI; Tucker & Lewis, 1973), and standardized root mean square residual (SRMR; Bentler, 1995). ‘Good’ model fit was ascertained according to conventional criteria, including a non-significant χ^2 statistic, RMSEA ≤ 0.06, CFI and TLI ≥ 0.90, and SRMR < 0.08 (Hooper et al., 2008).

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CHAPTER 5

Study 1

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Chetcuti, L., Uljarević, M., Varcin, K. J., Boutrus, M., Wan, M. W., Green, J., ... & AICES Team. (2020). Subgroups of temperament associated with social–emotional difficulties in infants with early signs of autism. *Autism Research*, *13*(12), 2094-2101. https://doi.org/10.1002/aur.2381

Subgroups of Temperament Associated with Social-Emotional Difficulties in Infants with Early Signs of Autism

Lacey Chetcuti[1,2], Mirko Uljarević[3], Kandice Varcin[4], Maryam Boutrus[2,4,5], Ming Wai Wan[6], Jonathan Green[7,8], Teresa Iacono[9], Cheryl Dissanayake[2,10], Andrew J. O. Whitehouse[2,4], Kristelle Hudry[1], and the AICES Team[11]

[1]School of Psychology and Public Health, La Trobe University, AUS; [2]Cooperative Research Centre for Living with Autism (Autism CRC), AUS; [3]Melbourne School of Psychological Sciences, the University of Melbourne, Melbourne, Australia; [4]Telethon Kids Institute, AUS; [5]University of Western Australia, School of Psychological Science, AUS; [6]Division of Neuroscience and Experimental Psychology, School of Health Sciences, University of Manchester, UK; [7]Division of Neuroscience and Experimental Psychology, School of Biological Sciences, University of Manchester, UK; [8]Manchester Academic Health Science Centre, Manchester University NHS Foundation Trust, Greater Manchester Mental Health NHS Trust, UK; [9]La Trobe Rural Health School, AUS; [10]Olga Tennison Autism Research Centre, School of Psychology and Public Health, La Trobe University, AUS; [11]the AICES team in alphabetical order: Josephine Barbaro, Stefanie Dimov, Murray Maybery, Michelle Renton, Nancy Sadka, Leonie Segal, Vicky Slonims, Scott Wakeling, and John Wray.

5.1. Abstract

Links between temperament and social-emotional difficulties are well-established in normative child development but remain poorly characterized in autism. We sought to characterize distinct temperament subgroups and their associations with concurrent internalizing and externalizing symptoms in a sample of 103 infants (M_{age} = 12.39 months, SD = 1.97; 68% male) showing early signs of autism. Latent profile analysis was used to identify subgroups of infants with distinct temperament trait configurations on the Infant Behavior Questionnaire-Revised. Derived subgroups were then compared in terms of internalizing and externalizing symptoms on the Infant-Toddler Social and Emotional Assessment. Three distinct temperament subgroups were identified: (1) *inhibited/low positive* (n = 22), characterized by low Smiling and Laughter, low High Intensity Pleasure, low Vocal Reactivity, and low Approach, (2) *active/negative reactive* (n = 23), characterized by high Activity Level, high Distress to Limitations, high Sadness, high Fear, and low Falling Reactivity, and (3) *well-regulated* (n = 51), characterized by high Cuddliness, high Soothability, and high Low Intensity Pleasure. There were no differences in infant sex ratio, mean age or developmental/cognitive ability. Inhibited/low positive infants had significantly more behavioural autism signs than active/negative reactive and well-regulated infants, who did not differ. Inhibited/low positive and active/negative reactive infants had higher internalizing symptoms, relative to well-regulated infants, and active/negative reactive infants also had higher externalizing symptoms. These findings align closely with those garnered in the context of normative child development, and point to child temperament as a putative target for internalizing and externalizing interventions.

5.2. Lay Summary

This study explored whether infants with early signs of autism could be grouped according to temperament characteristics (i.e., emotional, behavioural, and attentional traits). Three subgroups were identified that differed with respect to emotional and behavioural difficulties. Specifically, ‘inhibited/low positive’ infants had high emotional difficulties, ‘active/negative reactive’ infants had high emotional *and* behavioural difficulties, while ‘well-regulated’ infants had the lowest difficulties.

5.3. Introduction

Symptoms of autism spectrum disorder (hereafter, autism) co-occur at high rates with internalizing (anxiety and/or depression) and externalizing (inattentive/hyperactive, oppositional, and/or aggressive behaviour) symptoms, at both a subclinical and clinical level (Lundström et al., 2011; Joshi et al., 2010). Social-emotional difficulties are heightened among children with autism from very early childhood (Rescorla et al., 2019), and may contribute to functional impairment (Chiang & Gau, 2016), prognosis and differential treatment response (Vivanti, Prior, Williams, & Dissanayake, 2014). Therefore, it is critical to identify, early on in life, those children with autism features at greatest risk of internalizing and/or externalizing symptoms so appropriate supports can be allocated.

Existing literature on normative development suggests that individual variation in children's temperament may be associated with social-emotional difficulties; that is, early-emerging emotional and behavioural traits in domains of *negative emotionality*, the tendency to experience negative emotions, *sociability*, the tendency to engage actively with others, and *self-regulation*, the capacity to regulate emotions and action (Chetcuti, Uljarević, & Hudry, 2018). High negative emotionality and low self-regulation confer susceptibility towards both internalizing and externalizing symptoms, whereas low sociability more strongly relates to internalizing symptomatology (De Pauw & Mervielde, 2010; De Pauw, Mervielde, & Leeuwen, 2009). A similar pattern of relations has been reported among school-aged children and adolescents with autism (Burrows, Usher, Schwartz, Mundy, & Henderson, 2016; De Pauw & Mervielde, 2010; Schwartz et al., 2009). However, no studies have explored associations between temperament and social-emotional difficulties in infancy, when key differences in temperament associated with autism first become apparent (Clifford et al., 2013).

Furthermore, studies of normative development provide some indication that person-centered statistical methods (cluster/profile analysis) may be a useful alternative means of characterising relations among temperament and social-emotional difficulties (Chetcuti et al., 2018). In the seminal work of Thomas, Chess, and Birch (1968), three subgroups were identified by (top-down) qualitative analysis of temperament data collected through clinical observations and interviews with parents of 141 normative infants. Temperamentally *difficult* children were characterized by high and intense negative emotionality and activity, low sociability, and low self-regulation, while *easy* children showed the opposite trait pattern – low negative emotionality, high sociability, and high self-regulation. *Slow-to-warm-up* children showed a qualitatively different trait configuration – high negative emotionality (but of lesser intensity than difficult children), low sociability and activity, and average self-regulation. This typology was subsequently supported through factor analysis (Thomas & Chess, 1977) and replicated using data-driven (bottom-up) statistical techniques (Mcdevitt & Carey, 1978). Using person-centered statistical methods, recent studies have identified thematically similar temperament subgroups among other normative cohorts (e.g., Robins, John, Caspi, Moffitt, & Stouthamber-Loeber, 1996) that meaningfully map onto internalizing and externalizing outcomes. A slow-to-warm-up disposition appears to confer susceptibility towards internalizing symptoms/disorders, while a difficult temperament is associated with heightened externalizing symptoms/disorders. Temperamentally difficult children also appear more susceptible to both co-occurring internalizing *and* externalizing symptoms, while children with an easy disposition seem least prone towards the development of either (Putnam & Stifter, 2005; Robins et al., 1996; Thomas et al., 1968).

Only a few studies have examined patterns of multiple temperament traits in the context of autism. Kasari and Sigman (1997) found that children with an autism diagnosis scored higher than normative children and children with Down syndrome on a composite score reflecting difficult temperament (a constellation of irregularity, withdrawal from new stimuli, low adaptability, high intensity, and negative mood). Similarly, Chuang et al. (2012) found that a higher percentage of children with autism had a difficult temperament trait constellation (34.3%) than children with normative development (18.2%). To our knowledge, only one study has characterized children into temperament subgroups that were not predefined by existing theory, but rather emerged ‘bottom-up’ from the analyzed data. Garon et al. (2009) used discriminant function analysis to identify temperament trait constellations that prospectively distinguished infants who did and did not go on to receive an autism diagnosis at preschool-age. Two temperament functions differentiated children with autism from normative children at 24-months: lower scores were apparent among children with autism for a ‘behavioural approach’ function reflecting sensitivity to social reward cues, and ‘effortful emotion regulation’ function reflecting the ability to manage negative emotions and behaviour. Garon et al. (2009) also investigated whether temperament function scores differed within their autism-diagnosed sample according to timing of autism diagnosis. A combination of higher autism symptoms, lower IQ, and lower behavioural approach was found to differentiate among children with autism diagnosed earlier vs later in life.

Taken together, evidence from existing studies suggests differences across multiple temperament traits among children with autism compared to non-autism controls, and according to timing of autism diagnosis. Apart from Garon et al. (2009), there have been no other efforts to characterize temperamentally distinct subgroups of children with autism features or explore the potential relevance of such subgroups for explaining variability in children’s social-emotional outcomes. Therefore, among a unique cohort of infants referred with early autism signs we sought to (a) identify temperament subgroups using person-centered methods and (b) explore associations between these and concurrent social-emotional difficulties. We expected heightened internalizing symptoms among infants presenting with low sociability-related temperament traits, and elevated internalizing and externalizing symptoms among those with high negative emotionality and low self-regulation. In contrast, we expected the lowest internalizing and externalizing symptom levels among infants with high temperamental sociability and self-regulation.

5.4. Method

Participants were 103 infants aged 9-16 months (*M* = 12.39, *SD* = 1.97; 68% male) recruited into a larger study (citations withheld), for which prospective ethical approval was granted by institutional review boards. Referral to the study was by community healthcare providers, on the basis of infants showing ≥3 (of 5) key autism behaviours on the Social Attention and Communication Surveillance-Revised (SACS-R) tool (i.e., atypical/absent pointing, waving, imitation, eye contact, response to name; Barbaro & Dissanayake, 2013). The SACS-R is a revised version of the SACS (Barbaro & Dissanayake, 2010) designed as an autism surveillance tool for implementation by primary health professionals during routine well-child checks. The original SACS tool has excellent estimated sensitivity (84%) and specificity (99%) for detecting autism in childhood (based on a general population prevalence estimate of 1:100; Barbaro & Dissanayake, 2010). Similarly, in a more recent study, the SACS-R has shown good positive predictive value (72%) for subsequent autism diagnosis among 12-month-olds (Barbaro, Dissanayake, & Sadka, 2018; also see Mozolic-Staunton, Donelly, Yoxall, & Barbaro, 2020). Each infant was administered the Mullen Scales of Early Learning (MSEL; Mullen, 1995) to ascertain cognitive/developmental level, and the Autism Observation Scale for Infants (AOSI; Bryson et al., 2008) to quantify early behavioural autism signs.

Caregivers (72% mothers) completed the Infant-Toddler Social and Emotional Assessment (ITSEA; Carter & Briggs-Gowan, 2006) to ascertain infant symptoms in Internalizing and Externalizing domains, and the Infant Behavior Questionnaire-Revised (IBQ-R; Gartstein & Rothbart, 2003) to measure fine-grained temperament traits: Activity Level, Smiling and Laughter, High Intensity Pleasure, Vocal Reactivity, Approach, Perceptual Sensitivity (reflecting aspects of sociability), Distress To Limitations, Fear, Sadness, Falling Reactivity (aspects of negative emotionality), Duration Of Orienting, Low Intensity Pleasure, Cuddliness, and Soothability (aspects of self-regulation).

To address the issue of measurement confounding, ITSEA items that were conceptually and semantically similar to IBQ-R items were removed prior to calculation of ITSEA domain scores (Appendix A). Internal consistency was good for both scales of the IBQ-R (α=.65-.89) and domains of the ITSEA (Externalizing α=.82; Internalizing α=.62).

5.4.1. Analytic Strategy

Latent profile analysis (LPA) was conducted in M*plus* (Muthén & Muthén, 1998-2017) using the robust maximum likelihood estimator. Model fit concerning temperament subgroups identified from the 14 IBQ-R scales was assessed with the Akaike Information Criterion (AIC), Bayesian Information Criterion (BIC), and Adjusted BIC, where lower values indicate better fit, and statistically significant Lo-Mendell-Rubin (LMRT) and Bootstrapped Likelihood Ratio tests (BLRT) indicate fit improvement with an additional subgroup (*k* vs *k*–1). Subgroup classification quality was assessed with the entropy statistic, with a value closer to 1 indicating less uncertainty. Model selection was also guided by parsimony and interpretability (Bauer & Curran, 2003). Once extracted, subgroup-level differences in mean IBQ-R scale scores were determined via bootstrapped (2,000 resamples) one-way analysis of variance (ANOVA) with a Bonferroni correction applied for multiple comparisons (i.e., alpha-level of 0.05/14 = 0.0036) and post-hoc tests. Pearson's chi-square tests and one-way ANOVAs were then performed to explore differences in infant clinical characteristics and ITSEA domain scores as a function of temperament subgroup. Eta squared (η^2) was the effect size measure computed for each ANOVA, with .01 interpreted as small, .06 medium, and .14 large.

5.5. Results

Table 1 summarises model fit indices. The three-subgroup model was selected as the best fitting solution, with lowest-value BIC and statistically significant BLRT. Although the four- and five-subgroup solutions also had statistically significant BLRT and lower AIC and Adjusted BIC values, Nylund, Asparouhov and Muthén, (2007) advocate better performance of the BIC in smaller samples. Further, the three-subgroup solution was most parsimonious, with accurate subgroup classification (i.e., entropy >.80; mean posterior membership probabilities >.70 [Profile 1=.97, 2=.92, 3=.98]; Clark, 2010; Nagin, 2005).

Table 1

Comparison of Five LPA Models for Infant Temperament

#of subgroups	*n* for each subgroup	AIC	BIC	Adjusted BIC	LMRT *p*-value	BLRT *p*-value	Entropy
1	n_1=96	3775.87	3847.67	3759.26	-	-	-
2	n_1=20 n_2=76	3603.34	3713.61	3577.84	<.001	<.001	.95
3	n_1=22 n_2=23 n_3=51	3506.26	3654.99	3471.86	.056	<.001	.92
4	n_1=15 n_2=23 n_3=20 n_4=38	3474.53	3661.72	3431.23	.471	<.001	.90
5	n_1=19 n_2=10 n_3=15 n_4=42 n_5=10	3454.23	3679.88	3402.03	.293	<.001	.93

Note. AIC = Akaike Information Criterion; BIC = Bayesian Information Criterion; LMRT = Lo-Mendell-Rubin; BLRT = Bootstrapped Likelihood Ratio Test.

Infants were assigned to temperament subgroups based on maximum probability of membership. Figure 1 shows IBQ-R scale mean scores for infants in the three identified temperament subgroups with ANOVA results in Table 2. The first subgroup (n=22) was characterized by low Smiling and Laughter, low High Intensity Pleasure, low Vocal Reactivity and low Approach; hereafter, labelled inhibited/low positive. The second (n=23) was labelled active/negative reactive, given high Activity Level, high Distress to Limitations, high Sadness, and high Fear, and low Falling Reactivity. The third (n=51), with high Cuddliness, high Soothability, and high Low Intensity Pleasure, was labelled well-regulated.

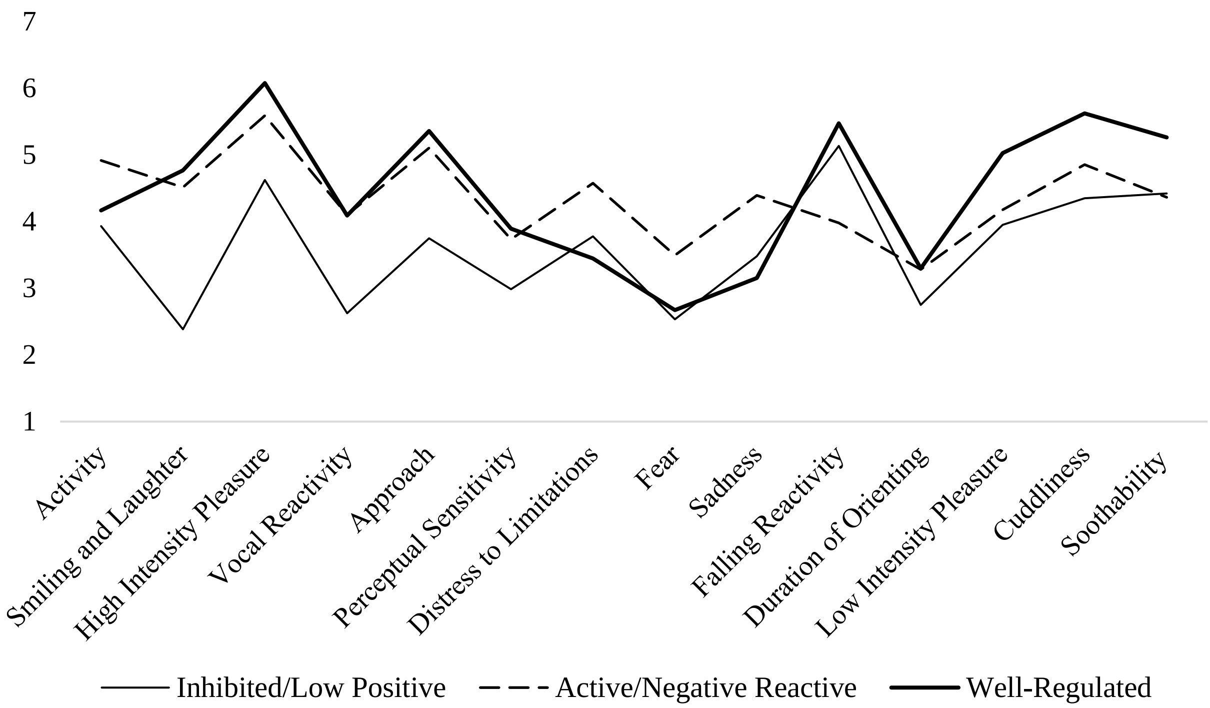

Figure 1. Infant Behavior Questionnaire-Revised (IBQ-R) scale mean scores for each temperament subgroup.

Table 2

ANOVA Results Showing Mean IBQ-R Scale Scores for Infants in Each Temperament Subgroup

IBQ-R Scale	Inhibited/ Low Positive M (SD)	Active/Negative Reactive M (SD)	Well-Regulated M (SD)	F	p	η^2	BCa 95% CI Contrast *a*	Contrast *b*	Contrast *c*
Activity	3.93 (0.70)	4.92 (0.65)	4.17 (0.61)	15.23	<.001	.25	**-1.38, -0.58**	**0.43, 1.04**	-0.1, 0.59
Smiling and Laughter	2.38 (0.66)	4.51 (0.71)	4.77 (0.80)	87.34	<.001	.66	**-2.52, -1.74**	-0.66, 0.04	**2.07, 2.79**
High Intensity Pleasure	4.62 (0.70)	5.59 (0.68)	6.08 (0.55)	41.92	<.001	.48	**-1.38, -0.56**	**-0.81, -0.17**	**1.13, 1.78**
Vocal Reactivity	2.63 (0.72)	4.1 (0.96)	4.09 (0.95)	22.09	<.001	.32	**-1.98, -0.97**	-0.47, 0.46	**1.05, 1.87**
Approach	3.75 (1.04)	5.11 (0.74)	5.36 (0.86)	25.95	<.001	.36	**-1.89, -0.82**	-0.63, 0.14	**1.11, 2.11**
Perceptual Sensitivity	2.98 (1.35)	3.74 (1.10)	3.89 (1.28)	3.88	.024	.08	**-**	-	**-**
Distress to Limitations	3.78 (1.01)	4.57 (0.75)	3.45 (0.92)	11.86	<.001	.20	**-1.35, -0.28**	**0.69, 1.52**	-0.82, 0.21
Fear	2.54 (0.87)	3.49 (0.93)	2.67 (0.86)	8.40	<.001	.15	**-1.43, -0.46**	**0.34, 1.23**	-0.29, 0.61
Sadness	3.48 (0.78)	4.39 (0.79)	3.15 (0.97)	14.82	<.001	.24	**-1.37, -0.46**	**0.81, 1.64**	-0.75, 0.14
Falling Reactivity	5.14 (0.96)	3.98 (0.8)	5.47 (0.55)	33.20	<001	.42	**0.63, 1.69**	**-1.83, -1.14**	-0.07, 0.74
Duration of Orienting	2.75 (0.76)	3.28 (0.87)	3.3 (1.18)	2.27	.109	.05	**-**	-	**-**
Low Intensity Pleasure	3.95 (0.85)	4.18 (0.72)	5.03 (0.81)	18.46	<.001	.29	-0.69, 0.25	**-1.24, -0.50**	**0.70, 1.49**
Cuddliness	4.35 (0.79)	4.85 (0.73)	5.63 (0.71)	27.25	<.001	.37	**-0.99, -0.01**	**-1.13, -0.45**	**0.91, 1.70**
Soothability	4.42 (0.77)	4.37 (0.48)	5.26 (0.5)	27.60	<.001	.38	-0.34, 0.42	**-1.14, -0.65**	**0.5, 1.20**

Note. Contrast *a* = Inhibited/Low Positive vs. Active/Negative Reactive. Contrast *b* = Active/Negative Reactive vs. Well-Regulated. Contrast *c* = Well-Regulated vs. Inhibited/Low Positive. Bolded BCa 95% CIs do not span zero, signifying statistical significance. ITSEA = Infant-Toddler Social and Emotional Assessment. BCa = bias-corrected and accelerated. CI = confidence interval.

Between-subgroup differences are presented in Table 3. There were no differences in infant sex ratio, mean age[5] or developmental/cognitive ability (MSEL). *Inhibited/low positive* infants had significantly more behavioural autism signs (AOSI) than *active/negative reactive* and *well-regulated* infants, who did not differ. Infants classified as either *inhibited/low positive* or *active/negative reactive* had significantly higher Internalizing symptoms than *well-regulated* infants. *Active/negative reactive* infants had higher Externalizing symptoms than *well-regulated* infants. Those classified as *inhibited/low positive* had intermediate Externalizing symptoms but did not differ from the other two subgroups

[5]Non-significant correlation coefficients were obtained between infant age and each of the 14 IBQ-R subscale continuous scores (r =.000 [Cuddliness] to .175 [Vocal Reactivity])

Table 3

Sample and Temperament Subgroup Characteristics and Between-Subgroup Comparisons

	Full sample (N = 103)	Inhibited/Low Positive (n = 22)	Active/Negative Reactive (n = 23)	Well-Regulated (n = 51)	Between Subgroup Comparisons			BCa 95% CI		
	M (*SD*)	*M* (*SD*)	*M* (*SD*)	*M* (*SD*)	χ^2/F	*p*	$\varphi/\ \eta^2$	Contrast *a*	Contrast *b*	Contrast *c*
Male (%)	70 (68)	17 (77.27)	17 (77.27)	31 (60.78)	2.44	.295	0.16	-	-	-
Age	12.39 (1.97)	12.13 (2.18)	12.61 (2.16)	12.39 (1.76)	0.34	.713	0.01	-	-	-
MSEL ELC	86.02 (16.76)	82.95 (20.44)	84.13 (12.66)	88.18 (13.73)	0.88	.418	0.02	-	-	-
AOSI Total[6]	8.90 (4.31)	10.91 (4.63)	7.30 (3.56)	7.45 (3.61)	7.73	.001	0.14	**1.38, 5.97**	-1.96, 1.63	**-5.93, -1.24**
ITSEA Int	0.38 (0.23)	0.45 (0.25)	0.50 (0.23)	0.28 (0.17)	7.04	.002	.17	-0.22, 0.12	**0.09, 0.34**	**-0.30, -0.02**
ITSEA Ext	0.32 (0.25)	0.33 (0.24)	0.42 (0.27)	0.27 (0.23)	7.16	.002	.18	-0.27, 0.01	**0.09, 0.34**	-0.18, 0.02

Note. Contrast *a* = Inhibited/Low Positive vs. Active/Negative Reactive. Contrast *b* = Active/Negative Reactive vs. Well-Regulated. Contrast *c* = Well-Regulated vs. Inhibited/Low Positive. Bolded BCa 95% CIs do not span zero, signifying statistical significance. MSEL = Mullen Scales of Early Learning. ELC = Early Learning Composite. AOSI = Autism Observation Schedule for Infants. ITSEA = Infant-Toddler Social and Emotional Assessment. INT = Internalizing. EXT = Externalizing. BCa = bias-corrected and accelerated. CI = confidence intervals.

[6]AOSI temperament items (Reactivity and Transitions) were removed from the computation of total scores counts prior to ANOVA

5.6. Discussion

The aim of this study was to characterize associations between temperament and concurrent internalizing/externalizing symptomatology among a community-referred cohort of infants presenting with early autism symptoms. Three temperament subgroups were identified using a person-centered approach – *inhibited/low positive*, *active/negative reactive,* and *well-regulated* –that aligned closely with those observed in normative samples (e.g., Robins et al., 1996; Thomas et al., 1968, 1977).

The *active/negative reactive* subgroup showed close alignment with Thomas et al.'s (1968, 1977) difficult subgroup, sharing a tendency toward temperamental negative affect and self-regulation difficulties. Indeed, such a profile has been consistently replicated (e.g., Beekman et al., 2015; Prokasky et al., 2017). Similarly, the *well-regulated* subgroup was characterized by effective self-regulation; an attribute shared by Thomas et al.'s easy subgroup and similar other subgroups identified in the literature (Gartstein et al., 2017; Robins et al., 1996). The *inhibited/low positive* subgroup shared the low sociability characteristics of Thomas et al.'s slow-to-warm-up subgroup. However, previously identified low-sociability subgroups have also encompassed high trait self-regulation, which was not the case here. Rather, traits related to self-regulation – Low Intensity Pleasure, Cuddliness, and Soothability – were found to be comparable or even lower among *inhibited/low positive* infants relative to the remainder of the cohort. Alternatively, high self-regulation may not emerge among *inhibited/low positive* infants until later childhood, when attention comes under greater effortful control (Posner & Rothbart, 2006).

A further aim was to investigate whether temperament subgroup membership predicted variability in social-emotional difficulties in our cohort of infants showing early autism symptoms. Infants classified as *inhibited/low positive* and *active/negative reactive* had more co-occurring internalizing symptoms compared to *well-regulated* infants. Externalizing symptoms were similarly elevated in the *active/negative reactive* subgroup, relative to *well-regulated* infants, while *inhibited/low positive* infants had intermediate externalizing symptom levels which were not significantly different to the two other subgroups. These results are consistent with literature on normative development, suggesting that slow-to-warm-up children are prone towards internalizing symptoms while difficult children are prone towards both internalizing and externalizing symptoms. Moreover, the finding of fewer co-occurring internalizing/externalizing symptoms among well-regulated infants is consistent with findings pertaining to an easy temperament in normative development (Robins et al., 1996; Thomas et al., 1968).

Infants classified as *inhibited/low positive* presented with more behavioural signs of autism compared to *active/negative reactive* or *well-regulated* infants. This is consistent with evidence that autism severity is negatively associated with temperamental sociability (Kamio, Takei, Stickley, Saito, & Nakagawa, 2018) and scores on the behavioural approach discriminant function identified by Garon et al. (2009). The precise nature of associations between temperament and autism features has yet to be elucidated. It may be that low sociability-related temperament traits (characteristic of the *inhibited/low positive* subgroup) increase vulnerability towards emergent autism symptoms (i.e., vulnerability association) or, alternatively, exist on the same continuum as autism such that autism represents an extreme variant of low temperamental sociability (i.e., spectrum association; see Chetcuti et al., 2019). Another possible explanation is that similarities in the behavioural expression and measurement of social interest/motivation deficits and temperament-related social reticence created a biased inflation of autism symptom ratings among *inhibited/low positive* infants. The presence of co-occurring social-emotional difficulties might also contribute to differences in autism severity, such that the heightened internalizing symptoms experienced by *inhibited/low positive* infants might exacerbate their autism-related difficulties (Duvekot, Ende, Verhulst, & Greaves-Lord, 2018). Conversely, autism-related difficulties might contribute to the development of internalizing symptoms over time (Pickard, Rijsdijk, Happé, & Mandy, 2017).

This study has several limitations. First, given the relatively modest sample size, replication across larger and phenotypically diverse samples is needed in order to evaluate the robustness of the three-subgroup solution. Second, temperament and social-emotional difficulties were both measured via parent-report; thus, the observed associations may be inflated through common-method variance. A related issue concerns conceptual overlap between temperament and internalizing/externalizing symptoms. Although the sample size precluded formal statistical testing of item-content, ITSEA items that were conceptually and semantically similar to IBQ-R items were removed to minimise measurement confounding. Moreover, previous studies have yielded significant associations after conceptual overlap was empirically determined through factor analysis (Lemery et al., 2002). Next, it is not possible to draw causal conclusions from the current cross-sectional results. While we conclude that temperament characteristics confer risk towards later social-emotional difficulties through evidence of concurrent associations, it is equally possible that social-emotional difficulties influence the expression of child temperament (see Shiner & Caspi, 2003). Finally, it remains unknown what proportion or which infants in our sample will go on to receive an autism diagnosis and/or other clinical diagnoses; nonetheless, comparison of AOSI characterisation data obtained here (see Table 3) and in familial ‘at-risk’ infants who went on to autism diagnostic outcome (Gammer et al., 2015) gives us encouragement that infants at elevated likelihood of autism diagnosis were successfully recruited. Future work should explore potential predictive relations between temperament patterns in infancy and clinical outcomes in childhood among large, well characterised, general-population samples.

The clinical implication of these findings is that inhibited*/low positive* and *active/negative reactive* infants with autism features might benefit most from interventions addressing social-emotional difficulties that target *specific* patterns of maladaptive temperamental responding. For example, INSIGHTS into Children's Temperament is a temperament-tailored intervention designed to equip caregivers with child management techniques that 'fit' a child's temperament type (McClowry, 2003), and more successfully reduces externalizing symptoms in children with normative development than a comparison program (McClowry, Snow, & Tamis Le-Monda, 2005). No such temperament-based interventions have been developed or trialled in the context of autism. Nonetheless, the apparent convergence of findings here with studies of normative development suggest a similar treatment approach might also be useful among children with autism features.

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5.8. Appendix

Table A1

Overlapping IBQ-R and ITSEA Items

IBQ-R items	**ITSEA items removed**
How often during the last week did the baby play with one toy or object for 5-10 minutes?	Goes from toy to toy faster than other children his or her age
For no apparent reason, how often did your baby appear sad?	Looks unhappy or sad without any reason
When introduced to an unfamiliar adult, how often did the baby cling to a parent? When in the presence of several unfamiliar adults, how often did the baby cling to a parent?	Hangs onto you or wants to be in your lap when with other people Is shy with new adults
When visiting a new place, how often did the baby continue to be upset for 10 minutes or more?	Takes a while to feel comfortable in new places (10 minutes or more)
When visiting a new place, how often did the baby move about actively when s/he is exploring new surroundings	Is quiet or less active in new situations

CHAPTER 6

Study 2

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Continuity of Temperament Subgroup Classifications from Infancy to Toddlerhood in the Context of Emerging Autism

Lacey Chetcuti[1,2], Mirko Uljarević[3,4], Kandice J. Varcin[5,6], Maryam Boutrus[2,5], Stefanie Dimov[1], Sarah Pillar[5], Josephine Barbaro[2,7], Cheryl Dissanayake[2,7], Jonathan Green[8,9], Andrew J. O. Whitehouse[2,5], Kristelle Hudry[1], & the AICES Team[10]

[1]School of Psychology and Public Health, La Trobe University, Australia; [2]Cooperative Research Centre for Living with Autism (Autism CRC), Long Pocket, Brisbane, Queensland, Australia; [3]Stanford Autism Center, Department of Psychiatry and Behavioral Sciences, Child and Adolescent Psychiatry, School of Medicine, Stanford University, USA; [4]Melbourne School of Psychological Sciences, Faculty of Medicine, Dentistry and Health Sciences, The University of Melbourne, Victoria, Australia; [5]Telethon Kids Institute, University of Western Australia; [6]School of Allied Health Sciences, Griffith University, Gold Coast, Australia; [7]Olga Tennison Autism Research Centre, School of Psychology and Public Health, La Trobe University, Australia; [8]Division of Neuroscience and Experimental Psychology, School of Biological Sciences, University of Manchester, Manchester, UK; [9]Manchester Academic Health Science Centre, Manchester University NHS Foundation Trust, Greater Manchester Mental Health NHS Trust, Manchester, UK; [10]the AICES Team in alphabetical order: Teresa Iacono, Murray Maybery, Michelle Renton, Nancy Sadka, Leonie Segal, Vicky Slonims, Scott Wakeling, Ming Wai Wan, and John Wray.

6.1. Abstract

Objective: To explore (a) the continuity of temperament subgroup classifications from infancy to toddlerhood in the context of autism traits and (b) the relation of temperament subgroups to differences in child behavioural/clinical phenotypic presentation.

Method: 103 infants (68% male) showing early signs of autism were referred to the study by community healthcare professionals and seen for assessments when aged around 12-months (Time 1), 18-months (Time 2), and 24-months (Time 3). Child temperament and social-emotional functioning were caregiver-reported, and child developmental level and autism traits were assessed directly. Latent profile analysis was used to identify temperament subgroups at each timepoint, and cross-tabulations were used to explore the continuity of subgroup classification over time. Between-subgroup differences in child phenotypic presentation were explored at each timepoint using analysis of variance/covariance and *t*-tests. This research expands upon an initial cross-sectional analysis of Time 1 data reported previously (Chetcuti et al., 2020).

Results: *Inhibited/low positive, active/negative reactive*, and *sociable/well-regulated* subgroup classifications were delineated at each timepoint, and there was a significant likelihood of consistent classification of children within subgroups from one timepoint to the next. However, a *reactive/regulated* subgroup was uniquely identified at Time 3, and membership here was not associated with any subgroup classification 6-months prior. Temperament subgroups were associated with child social-emotional functioning and autism traits, but unrelated to child age, sex, or developmental level.

Conclusions: Temperament subgroup classifications might represent a reliable and very early indicator of autism characteristics and social-emotional functioning among infants/toddlers with autism traits.

6.3. Introduction

Temperament represents an interrelated system of attentional, emotional, and behavioural traits that work separately and jointly to influence how an individual perceives and relates to the world (Shiner et al., 2012). Accordingly, there may be greater utility in examining temperament traits in combination with one another rather than in isolation (Chetcuti et al., 2019; Cloninger & Zwir, 2018). Indeed, research in typical samples suggests that children can be classified into distinct subgroups based on configurations of multiple temperament traits, which show incremental value for predicting social-emotional outcomes over and beyond that of discrete traits (Hart, Hofmann, Edelstein, & Keller, 1997; but see Costa, Herbst, McCrae, Samuels, & Ozer, 2002). Inhibited and *dis*inhibited temperament types appear to confer susceptibility towards internalizing (anxiety and/or depression) and externalizing (inattentive/hyperactive, oppositional, and/or aggressive behaviour) symptoms in children with typical development, respectively (Putnam & Stifter, 2005; Robins et al., 1996; Thomas et al., 1968). Emerging evidence suggests that the construct of temperament may also provide a useful framework for understanding variability in samples with non-typical development.

Research into autism spectrum disorder (hereafter autism) suggests early temperament characteristics may prospectively predict subsequent clinical diagnosis among infants at elevated familial likelihood (i.e., with a diagnosed older sibling; Clifford et al., 2013; Garon et al., 2009, 2016). Among diagnosed individuals, temperament characteristics have also been found to predict heterogeneity in core social-communication and restricted/repetitive behavioural traits (Chuang et al., 2012) and co-occurring internalizing and externalizing outcomes (Burrows, Usher, Schwartz, Mundy, & Henderson, 2016; Schwartz et al., 2009; see also Chetcuti et al., 2020, for a systematic review). However, only a few studies – including a recent study from our group – have used a subgrouping approach to examine individual difference in relation to temperament among children with autism traits (Chetcuti et al., 2020; Lee et al., 2020).

In our study (Chetcuti et al., 2020), three temperament subgroups were identified among infants with early signs of autism around the first birthday: a *well-regulated* subgroup (n = 51) characterized by high self-regulation capacities, an *inhibited/low positive* subgroup (n = 22) characterized by low positive affectivity and sociability, and an *active/negative reactive* subgroup (n = 23) characterized by intense and prolonged negative affectivity. Another study by Lee et al. (2020) found that children on the autism spectrum could be classified into two temperament subgroups in middle childhood: a *reactive* subgroup (n = 112) was characterized by lower levels of behavioural and emotional regulation and higher negative affectivity compared to an *even* subgroup (n = 73).

The subgroup classifications identified by us (Chetcuti et al., 2020) and Lee et al. (2020) shared some common attributes but differed in number and composition. Specifically, our *active/negative reactive* subgroup comprised around one-quarter of infants while their qualitatively similar *reactive* subgroup comprised over half of their sample. Moreover, Lee et al. (2020) did not identify an *inhibited/low positive* subgroup classification. These discrepancies could be ascribed to differences in methodology (e.g., questionnaire measure) or analytic technique (e.g., latent profile vs cluster analysis, respectively). However, it may also be that maturational changes in temperament trait expression (Putnam et al., 2008) and trait levels (Roberts & DelVecchio, 2000) result in qualitatively different subgroups and/or intra-individual differences in subgroup classification at different ages. This question has yet to be explored in the context of autism but has been addressed in typical samples, as detailed below.

Studies of children with typical development have characterized temperament subgroups across multiple timepoints, and found moderate-to-high intra-individual continuity of subgroup membership. Janson and Mathiesen (2008) identified five temperament subgroups in a population-based sample of children assessed at four timepoints from age 18-months through to 9 years. Classifications of *undercontrolled, confident, unremarkable, inhibited,* and *uneasy* showed moderate stability across adjacent ages. For example, 44% of children remained in the same subgroup between ages 18 and 30 months. However, the proportion of children within each subgroup changed markedly with child age, such that the *inhibited* and *unremarkable* subgroups went from least prevalent at 18-months (5% and 14% of the cohort, respectively) to most prevalent at 8-9 years (30% and 39%, respectively). van den Akker et al. (2010) similarly identified subgroups in a non-clinical sample assessed at four timepoints: from age 30- through to 42-months. Here, 68-71% of children retained their classifications of *typical, expressive,* or *fearful* across adjacent ages. Common to Janson and Mathiesen (2008) and van den Akker et al.'s (2010) approaches was the use of all available information across repeated measurements of temperament to derive subgroup solutions presumed to ‘fit’ the whole sample across the entire developmental period studied. Stability estimates might have therefore been higher for van den Akker et al. (2010), because they measured temperament across a shorter developmental period (i.e., 12 months; vs. 7.5 years for Janson and Mathiesen [2008]), deriving fewer and more clearly differentiated subgroups strongly tied to the toddlerhood period.

Just as temperament traits are not static, but rather shaped by context and experience (Kiff et al., 2011), the ways in which temperament traits ‘group’ together may also change over the life course. This may be particularly true of the period of developmental transition from infancy to toddlerhood, when self-regulation extends from early reactive/bottom-up processes (e.g., attentional capture) to include deliberate/top-down operations (e.g., attentional inhibition). Such maturation of self-regulation processes might, in turn, change the attributional properties of temperament subgroups identified in infancy. For example, an *overcontrolled* subgroup distinguished by high agreeableness and conscientiousness in middle/late childhood (Robins et al., 1996) originates in infancy but is at that point distinguished by below average activity and positive affectivity (Komsi et al., 2006). Moreover, 'new' subgroups might emerge in toddlerhood as the expression of emotion becomes more explicit, and social vs non-social fearfulness (i.e., shyness) become discernible (Beekman et al., 2015).

The identification of temperament subgroups *separately* at different developmental stages might better account for maturational changes. Beekman et al. (2015) adopted this method to identify temperament subgroups among children with typical development at each of ages 9-, 18-, and 27-months. *Negative reactive* and *positive reactive* subgroups were identified at all ages and showed significant cross-time stability, such that 51% of *negative reactive* and 78% of *positive reactive* children retained their classification over the study period. *Typical-low expressive* and *typical-expressive* subgroups – characterized by a steady magnitude of traits and no discernible pattern of 'highs and lows' – were identified at 9-months only, whereas *active reactive* and *fearful* subgroups emerged from only 18-months. With respect to membership stability, toddlers classified as *fearful* at 18-months were significantly likely to retain this classification at 27-months. *Active reactive* toddlers at 18-months, however, had an essentially equal likelihood of retaining their classification (29%) or moving to *positive reactive* (34%) or *negative reactive* (37%) classifications at 27-months, indicating significant variability of discrete traits within this subgroup over the developmental course.

Overall, existing studies on typical child development suggest moderate-to-high intra-individual continuity of temperament classifications in childhood. A greater number of differentiated subgroups emerged at older ages (e.g., Beekman et al., 2015; see also Gartstein et al., 2017), suggesting temperament classifications might become increasingly complex and heterogeneous over time. Subgroups of temperament have only been identified among children with autism traits at single timepoints (Chetcuti et al., 2020; Lee et al., 2020); therefore, the developmental progression of subgroup classifications remains to be elucidated.

The present study investigated the continuity of temperament subgroup classifications to around age 18- and 24-months among a cohort of children presenting with early signs of autism for whom we recently reported temperament subgroup classifications at the start of study enrolment at 12-months of age (Chetcuti et al., 2020). Broad continuity in the qualitative features of temperament subgroups was anticipated, with continuity in children's classification among these subgroups expected over time. In addition, it was expected that new subgroups might emerge as children aged from infancy to toddlerhood. Previously we showed that the children's 12-month temperament subgroup classifications were associated with differences in their concurrent social-emotional functioning and autism presentation. Hence, an ancillary aim in the current follow-up study was to explore how temperament subgroup classifications identified at the subsequent timepoints, around 6- and 12-months later, might be related to variability in social-emotional functioning and phenotypic characteristics at those same later timepoints. Consistent with our earlier analysis, we expected higher internalizing and externalizing symptoms to present, respectively, among toddlers classified within temperamentally inhibited and disinhibited subgroups. Fewer social-emotional difficulties were expected among toddlers classified as well-regulated. These differences were expected after controlling for the effects of autism traits on social-emotional functioning. In line with our earlier findings at the 12-month assessment, we predicted a greater number of autism traits amongst the toddlers belonging to a temperamentally inhibited subgroup at later visits, but no between-subgroup differences in child age, sex, or developmental level.

6.4. Method

6.4.1. Study design

As previously detailed (Whitehouse et al., 2019), 103 infants aged 9-14 months (M = 12.39, SD = 1.97; 68% male) were enrolled in a larger study on the basis of presenting with at least three (of five) behavioural signs of autism on the Social Attention and Communication Surveillance (SACS; Barbaro & Dissanayake, 2010, 2013; Mozolic-Staunton, Donelly, Yoxall, & Barbaro, 2020) 12-month checklist (i.e., atypical/absent pointing, waving, imitation, eye contact, response to name). Exclusion criteria included the presence of a diagnosed condition known to affect neurological and developmental abilities (including <32 weeks' gestation) and intention to relocate during the 2-year study period. A battery of standardized behavioural assessments and caregiver-report questionnaires were completed for each infant around 2-weeks after study enrolment (M = 2.53, SD = 1.50; Time 1 assessment visit). After the Time 1 assessment, infants were randomly allocated to receive either a novel trial intervention (n = 50) or community treatment-as-usual (n = 53) as part of the larger study. Post-intervention follow-up assessments were conducted for each infant 6- and 12-months after the Time 1 assessment (Time 2 and Time 3, respectively). Preliminary analyses suggested no substantive effects of intervention group allocation (intervention versus control) on variables relevant to the current study so participants were treated as a single group.

6.4.2. Measures

Child temperament was assessed using the caregiver-report Infant Behavior Questionnaire-Revised (IBQ-R; Gartstein & Rothbart, 2003) at Time 1, and Early Childhood Behavior Questionnaire (ECBQ; Putnam, Gartstein, & Rothbart, 2006) at Time 2 and Time 3. IBQ-R items (191) and ECBQ items (201) are presented as questions (e.g., "When being dressed or undressed, how often did your child squirm and try to get away?") and caregivers rate the frequency of the behaviour over the preceding one or two weeks (1 = *Never* to 7 = *Always*). The ECBQ is an upward extension of the IBQ-R utilized at Time 1 and thus includes many of the same scales – Activity Level, High Intensity Pleasure, Approach, Frustration, Fear, Perceptual Sensitivity, Sadness, Soothability, Cuddliness, Low Intensity Pleasure, and Attentional Focusing – and additional later-developing aspects of Impulsivity, Sociability, Shyness, Discomfort, Motor Activation, Inhibitory Control, and Attentional Shifting. Equivalent IBQ-R and ECBQ scales were significantly correlated across adjacent time points (r = .20-.78) and internal consistency was adequate/good for most IBQ-R (α = .65-.89; see [Chetcuti et al., 2020]) and ECBQ scales (α = .58-.94; see Appendix B). Cronbach's α was .46 for the Impulsivity scale at Time 2; however, this scale was retained unaltered to maintain consistency of measurement across time, and given it was not found to differentiate among identified Time 2 subgroups (see below). Impulsivity also generated a low α coefficient in testing by instrument developers (α = .58 at 18- to 22-months; Putnam et al., 2006), and has been used unaltered in other studies (Chetcuti et al., 2020).

Child social-emotional functioning was assessed using the caregiver-report Infant-Toddler Social and Emotional Assessment (ITSEA; Carter & Briggs-Gowan, 2006) at all timepoints. ITSEA items (166) are presented as statements (e.g., "Cries or hangs onto you when you try to leave") and caregivers rate the applicability of behavioural descriptions to their child over the preceding month (1 = *Not True/Rarely* to 3 = *Very True/Often*). Raw subscale means were summed to form Internalizing (including Depression/Withdrawal, General Anxiety, Separation Distress, and Inhibition to Novelty), Externalizing (including Activity/Impulsivity, Aggression/Defiance, and Peer Aggression), and Competence (including Compliance, Attention, Mastery Motivation, Imitation/Play, Empathy, and Prosocial Peer Relations) domain composite scores. These were converted to standardized *t*-scores at Time 2 and Time 3 (not possible at Time 1 as some children were aged <12-months) to determine the proportion of children scoring in the 'Of Concern' range (extreme 10th percentile), but analysed in raw form in relation to temperament subgroup membership. To reduce measurement confounding, ITSEA items that were conceptually and semantically similar to ECBQ items were excluded from the computation of domain composite raw scores prior to the analysis of between-subgroup differences (see Appendix A), as was the entire Inhibition to Novelty subscale. ITSEA domains have good inter-rater agreement (r = .70 to .78; Carter & Briggs-Gowan, 2006) and the modified domains demonstrated good internal consistency at all three timepoints in the current dataset (α = .62 to α = .93).

Child developmental level was assessed using the Mullen Scales of Early Learning (MSEL; Mullen, 1995) at all timepoints. An Early Learning Composite (ELC; M = 100, SD = 15) was derived from Visual Reception, Fine Motor, Receptive Language, and Expressive Language subscales. The Autism Observation Scale for Infants (AOSI; Bryson, Zwaigenbaum, McDermott, Rombough, & Brian, 2008) was administered at Time 1 and Time 2 and the Autism Diagnostic

Observation Schedule-2nd Edition, Toddler Module (ADOS-T; Luyster et al., 2009) at Time 2 and Time 3 to assess child autism traits. Higher AOSI total scores (range 0 to 38) and ADOS-T total scores (range 0 to 28) indicated more autism traits.

6.4.3. Participant Characterization

Among those children with valid ITSEA data, 'Of Concern' scores were reported in the Internalizing domain for 16.5% (n = 17) at Time 2 and 17.5% (n = 18) at Time 3; in the Externalizing domain for 6.8% (n = 7) at Time 2 and 7.8% (n = 8) at Time 3; and in the Competence domain for 31.1% (n = 32) at Time 2 and 38.8% (n = 40) at Time 3. The MSEL indicated somewhat below-average developmental abilities for the group as a whole, at Time 1 (M = 86.02, SD = 16.76), Time 2 (M = 85.97, SD = 17.14), and Time 3 (M = 89.41, SD = 21.31). Moderate autism traits were found across Time 1 (AOSI M = 8.90, SD = 4.31), Time 2 (AOSI M = 8.49, SD = 4.61; ADOS-T M = 10.02, SD = 5.57), and Time 3 (ADOS-T M = 10.11, SD = 6.08). Considerable heterogeneity was also apparent, however, with autism presentation spanning the full range of possible scores, from (putatively) subclinical to clinical levels. Whitehouse et al. (2019) and Hudry et al. (2020) provide detailed descriptions of the sample behavioural/clinical phenotypic characteristics.

6.4.4. Statistical Analyses

Latent profile analysis (LPA) was used to identify child subgroups with distinct constellations of temperament traits at each timepoint. This was conducted in M*plus* Version 8 (Muthén & Muthén, 1998-2017) using the robust maximum likelihood estimator. One through five subgroup solutions were estimated (per our Time 1 procedure) from the 18 ECBQ scales, separately at each of Time 2 (n = 90 available) and Time 3 (n = 81 available). Model fit was assessed with the Akaike Information Criterion (AIC), Bayesian Information Criterion (BIC), and Adjusted BIC (ABIC), where lower values indicate superior fit. The Lo-Mendell-Rubin Likelihood Ratio test (LMRT) and Bootstrapped Likelihood Ratio test (BLRT) compare fit of neighbouring solutions (i.e., k vs k–1; where $p < .05$ suggests improvement), and the entropy statistic assesses classification quality (where >.80 suggests 'good'; Clark, 2010). Analyses of variance (ANOVA) were used to compare the temperament qualities across the identified subgroups of children, with a Bonferroni correction applied for multiple comparisons (i.e., alpha level of 0.05/18 = 0.0027) and post-hoc tests. Each subgroup was then allocated an appropriate descriptive label (carried forward from Time 1 if qualitatively similar). Cross-tabulations were computed, with Bonferroni-corrected post-hoc tests, to explore intra-individual shifts in subgroup classification across adjacent timepoints. One-way bootstrapped ANOVA/ANCOVA (2,000 resamples) and exploratory t-tests were then performed to explore differences in behavioural/clinical phenotypic characteristics and social-emotional functioning (controlling for autism traits) between subgroups at a given timepoint and as a function of subgroup classification over time. Eta squared (η^2) was the effect size measure computed for each ANOVA/ANCOVA, with .01 interpreted as small, .06 medium, and .14 large (Cohen, 1988).

6.5. Results

6.5.1. Characterization of Temperament Subgroups at Each Timepoint

Fit statistics/indices for the LPA models under comparison are shown in Table 1, with those from our Time 1 analysis (originally reported in Chetcuti et al., 2020). Entropy was high for all subgroup solutions at each of the three timepoints. The AIC and ABIC were lowest for the five-subgroup solution at both time points, whereas the BIC favoured a three-subgroup solution at Time 2 and a four-subgroup solution at Time 3. This solution was accepted in the interest of interpretability and having sufficient power to explore associated factors, and given evidence that BIC outperforms other fit indices in modest sample sizes such as this (Nylund et al., 2007).

Table 1

Fit Statistics and Indices for Time 1, Time 2, and Time 3 LPA Models

# of subgroups	AIC	BIC	ABIC	LMRT *p*-value	BLRT *p*-value	Entropy
Time 1						
1	3775.87	3847.67	3759.26	-	-	-
2	3603.34	3713.61	3577.84	<.001	<.001	.95
3	3506.26	3654.99	3471.86	.056	<.001	.92
4	3474.53	3661.72	3431.23	.471	<.001	.90
5	3454.23	3679.88	3402.03	.293	<.001	.93
Time 2						
1	4518.90	4608.90	4495.28	-	-	-
2	4318.84	4456.33	4282.75	.067	<.001	0.97
3	4236.97	4421.96	4188.41	.476	<.001	0.93
4	4201.76	4434.24	4140.73	.573	<.001	0.94
5	4191.71	4471.69	4118.21	.750	.071	0.96
Time 3						
1	4274.79	4360.99	4247.46	-	-	-
2	4033.10	4164.79	3991.34	.175	<.001	0.98
3	3961.65	4138.84	3905.46	.315	<.001	0.99
4	3906.76	4129.45	3836.16	.599	<.001	0.95
5	3867.47	4135.65	3782.44	.534	<.001	0.95

Note. The final subgroup solution is shaded. AIC = Akaike Information Criterion; BIC = Bayesian Information Criterion; LMRT = Lo-Mendell-Rubin Test; BLRT = Bootstrapped Likelihood Ratio Test.

ANOVAs revealed significant between-subgroup differences on 12 (of 14) IBQ-R subscales at Time 1 (see Chetcuti et al., 2020) and here, on 16 (of 18) ECBQ subscales at Time 2 and on all 18 ECBQ subscales Time 3 (see Tables 2 and 3). At Time 2, Subgroup 1 (*n* = 54; 60%) was distinguished by children with the highest levels of Sociability, Soothability, Attention Shifting, Inhibitory Control, and Low Intensity Pleasure, and with the lowest Sadness and Frustration levels. Subgroup 2 (*n* = 12; 13%) was characterized by children with the highest Motor Activation, Discomfort, Fear, Frustration, Perceptual Sensitivity, and Sadness scores. Subgroup 3 (*n* = 24; 27%) was characterized by children with the lowest levels of High Intensity Pleasure, Low Intensity Pleasure, and Approach.

At Time 3, Subgroup 1 (*n* = 27; 33%) was characterized by children with high Sociability, Soothability, Attention Shifting, Cuddliness, and Low Intensity Pleasure, and with low Motor Activation. Subgroup 2 (*n* = 11; 14%) was distinguished by children with the highest Activity, Discomfort, Frustration, and Sadness, coupled with the lowest Attention Shifting and Cuddliness. This subgroup also comprised children with the highest Fear, Motor Activation, and Perceptual Sensitivity and lowest Attention Focusing, Soothability, and Inhibitory Control; however, only certain contrasts reached statistical significance (see Table 3). Subgroup 3 (*n* = 8; 10%) included children with the lowest levels of Impulsivity, Approach, and Sociability. Finally, Subgroup 4 (*n* = 35; 43%) comprised children with lower self-regulation-related attributes than Subgroup 1 (but mostly higher than the other subgroups) and levels of Positive Anticipation and High Intensity Pleasure comparable to those of children in Subgroup 2.

The allocation of subgroup descriptive labels was informed by visual inspection and comparison of line graphs with IBQ-R/ECBQ subscale mean scores for each subgroup, at each timepoint (see Figure 1). Subgroup 1 at both Time 2 and Time 3 had the highest Sociability, Attention Shifting, Soothability, and Low Intensity Pleasure. These subgroups were considered qualitatively similar to the Time 1 *well-regulated* subgroup – also distinguished by high Soothability and Low Intensity Pleasure – albeit with emerging high Sociability at Time 2 (not measured on the Time 1 IBQ-R). Hence, Subgroup 1 at both Time 2 and Time 3 was labelled *sociable/well-regulated.* Subgroup 2 at both Time 2 and Time 3 was characterized by the highest Discomfort, Frustration, and Sadness. The Time 1 *active/negative reactive* subgroup was also characterized by the highest Sadness and Discomfort; hence, these subgroups were allocated the same label: *active/negative reactive.* Subgroup 3 at Time 2 and Time 3 had the lowest Approach, as did the *inhibited/low positive* subgroup at Time 1; therefore, these subgroups were given the same label: *inhibited/low positive*. Subgroup 4 appeared uniquely at Time 3 and was labelled *reactive/regulated.*

Table 2

ANOVA Results Showing Mean ECBQ Scale Scores for Time 2 Temperament Subgroups

							BCa 95% Confidence Interval		
	SWR	ANR	ILP	*F*	η^2	*p*	SWR vs ANR	ANR vs ILP	ILP *vs* SWR
ACT	4.68	4.93	5.00	1.53	0.03	.222			
HPL	4.57	4.73	3.89	5.27	0.11	.007	-0.74, 0.43	**0.04, 1.56**	**-1.11, -0.18**
IMP	4.91	4.65	4.64	1.57	0.04	.215			
APP	4.06	4.45	2.67	19.29	0.31	<.001	-0.97, 0.24	**1.07, 2.43**	**-1.81, -0.93**
SOC	5.10	3.29	3.37	25.64	0.38	<.001	**1.27, 2.39**	-0.87, 0.77	**-2.43, -1.12**
DIS	1.58	3.12	1.57	55.88	0.57	<.001	**-1.91, -1.19**	**1.16, 1.98**	-0.23, 0.20
FEA	2.20	3.52	2.08	15.14	0.26	<.001	**-2.10, -0.64**	**0.68, 2.29**	-0.45, 0.22
FRU	3.03	4.82	3.80	14.53	0.26	<.001	**-2.50, -0.95**	**0.04, 2.11**	**0.06, 1.17**
MOT	1.80	3.29	1.93	23.37	0.35	<.001	**-2.11, -0.95**	**0.85, 2.00**	-0.22, 0.39
PSE	3.01	4.12	2.56	11.18	0.21	<.001	**-1.67, -0.49**	**0.83, 2.25**	-0.91, 0.06
SAD	2.55	3.86	3.11	11.05	0.21	<.001	**-1.97, -0.59**	**0.10, 1.57**	**0.09, 0.83**
SHY	3.17	4.32	3.52	7.11	0.14	.002			
SOO	5.90	4.60	5.06	21.59	0.34	<.001	**0.65, 1.90**	-1.05, 0.14	**-1.22, -0.46**
ATF	3.71	3.23	3.09	5.37	0.11	.007			
ATS	4.50	3.55	3.30	44.50	0.47	<.001	**0.60, 1.36**	-0.18, 0.76	**-1.57, -0.98**
CUD	5.13	4.28	4.16	12.97	0.22	<.001	**0.22, 1.46**	-0.62, 0.91	**-1.44, -0.54**
INH	3.80	2.94	2.70	12.15	0.23	<.001	**0.13, 1.64**	-0.62, 0.97	**-1.46, -0.66**
LPL	4.97	4.45	3.47	29.79	0.39	<.001	**0.08, 1.00**	0.50, 1.59	**-1.97, -1.19**

Note. SWR = sociable/well-regulated; ANR = active/negative reactive; ILP = inhibited/low positive; BCa = bias corrected and accelerated; ACT = Activity Level; HPL = High Intensity Pleasure; IMP = Impulsivity; APP = Approach; SOC = Sociability; DIS = Discomfort; FEA = Fear; FRU = Frustration; MOT = Motor Activation; PSE = Perceptual Sensitivity; SAD = Sadness; SHY = Shyness; SOO = Soothability; ATF = Attentional Focusing; ATS = Attentional Shifting; CUD = Cuddliness; INH = Inhibitory Control; LPL = Low Intensity Pleasure.

Table 3

ANOVA Results Showing Mean ECBQ Scale Scores for Time 3 Temperament Subgroups

								BCa 95% Confidence Interval					
	SWR	ANR	ILP	RRE	*F*	η^2	*p*	SWR vs ANR	ANR vs ILP	ILP *vs* SWR	RRE *vs* SWR	RRE *vs* ANR	RRE *vs* ILP
ACT	4.25	5.85	4.22	4.94	16.77	0.37	<.001	**-2.11, -1.01**	**0.93, 2.27**	-0.54, 0.46	**0.37, 1.01**	**-1.43, -0.31**	**0.22, 1.23**
HPL	4.14	5.07	3.36	4.81	9.136	0.26	<.001	**-1.53, -0.26**	**0.59, 2.67**	-1.63, 0.18	**0.27, 1.07**	-0.83, 0.41	**0.46, 2.28**
IMP	5.06	5.00	3.65	4.74	8.069	0.27	<.001	-0.54, 0.65	**0.63, 2.04**	**-1.96, -0.80**	-0.70, 0.04	-0.81, 0.27	0.49,1.58
APP	4.16	4.51	1.97	4.77	17.802	0.22	<.001	-1.17, 0.54	**1.52, 3.45**	**-2.89, -1.37**	**0.11, 1.08**	-0.50, 1.06	**2.07, 3.42**
SOC	5.34	3.35	2.4	4.72	23.465	0.38	<.001	**1.28, 2.69**	**0.07, 1.80**	**-3.60, -2.27**	**-1.10, -0.10**	**0.66, 2.14**	**1.62, 2.98**
DIS	1.53	3.51	1.85	2.07	20.512	0.32	<.001	**-2.65, -1.29**	**0.57, 2.73**	-0.30, 1.00	**0.26, 0.79**	**-2.12, -0.75**	-0.47, 0.83
FEA	2.04	3.40	2.33	2.69	6.021	0.07	.001	**-2.22, -0.53**	-0.15, 2.33	-0.53, 1.22	**0.29, 0.99**	-1.65, 0.18	-0.57, 1.21
FRU	2.62	4.94	3.25	3.98	24.178	0.20	<.001	**-2.87, -1.79**	**0.53, 2.74**	-0.18, 1.51	**1.00, 1.74**	**-1.53, -0.38**	-0.28, 1.66
MOT	1.49	3.42	2.67	1.80	21.443	0.39	<.001	**-2.71, -1.24**	-0.29, 1.77	**0.47, 1.88**	**0.07, 0.55**	**-2.43, -0.90**	**-1.64, -0.09**
PSE	2.84	4.02	2.39	3.39	6.25	0.09	.001	**-1.85, -0.47**	**0.78, 2.48**	-1.13, 0.24	**0.05, 1.02**	-1.30, 0.04	**0.42, 1.54**
SAD	2.19	4.18	2.72	3.01	21.409	0.29	<.001	**-2.46, -1.41**	**0.64, 2.21**	**0.01, 1.09**	**0.49, 1.13**	**-1.64, -0.60**	-0.30, 0.91
SHY	2.94	3.91	4.17	4.17	6.905	0.07	<.001	**-1.68, -0.20**	-1.70, 1.18	-0.03, 2.41	**0.76, 1.69**	-0.46, 1.04	-1.16, 1.17
SOO	5.89	4.26	4.31	5.36	17.808	0.37	<.001	**0.96, 2.27**	-0.86, 0.78	**-2.17, -0.94**	**-0.86, -0.19**	**0.42, 1.77**	**0.46, 1.62**
ATF	4.14	2.60	3.38	3.92	9.266	0.33	<.001	**0.89, 2.11**	-1.63, 0.11	-1.65, 0.10	-0.67, 0.21	**0.71, 1.86**	-0.20, 1.29
ATS	4.70	3.07	3.81	4.29	17.42	0.39	<.001	**1.14, 2.14**	**-1.28, -0.23**	**-1.33, -0.43**	**-0.78, -0.06**	**0.77, 1.68**	**0.11, 0.80**
CUD	5.41	3.29	4.40	4.95	14.887	0.40	<.001	**1.49, 2.73**	**-2.15, -0.07**	**-1.93, -0.08**	**-0.86, -0.04**	**1.06, 2.26**	-0.40, 1.50
INH	4.40	2.27	3.37	3.22	14.341	0.17	<.001	**1.48, 2.77**	-2.41, 0.03	-2.11, 0.08	**-1.65, -0.69**	**0.35, 1.53**	-1.29, 0.88
LPL	5.29	3.49	3.31	4.87	27.031	0.48	<.001	**1.40, 2.20**	-0.37, 0.73	**-2.52, -1.44**	**-0.77, -0.06**	**1.00, 1.75**	**1.00, 2.11**

Note. SWR = sociable/well-regulated; ANR = active/negative reactive; ILP = inhibited/low positive; RRE = reactive/regulated; BCa = bias corrected and accelerated; ACT = Activity Level; HPL = High Intensity Pleasure; IMP = Impulsivity; APP = Approach; SOC = Sociability; DIS = Discomfort; FEA = Fear; FRU = Frustration; MOT = Motor Activation; PSE = Perceptual Sensitivity; SAD = Sadness; SHY = Shyness; SOO = Soothability; ATF = Attentional Focusing; ATS = Attentional Shifting; CUD = Cuddliness; INH = Inhibitory Control; LPL = Low Intensity Pleasure.

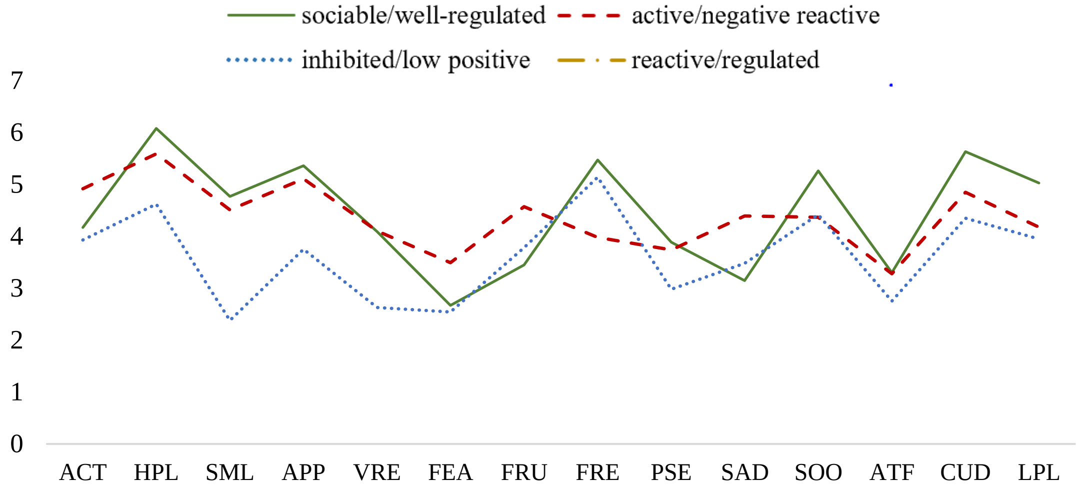

Figure 1a. IBQ-R scale means for subgroups at Time 1.

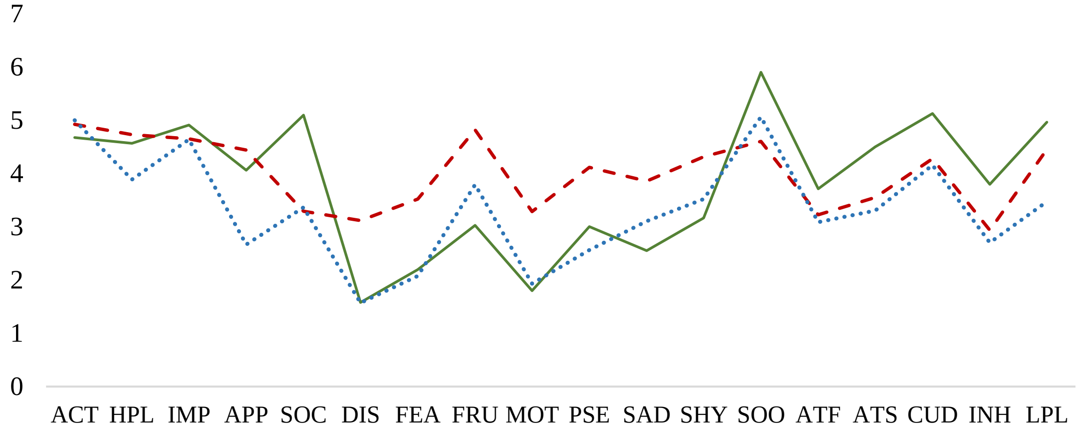

Figure 1b. ECBQ scale means for subgroups at Time 2.

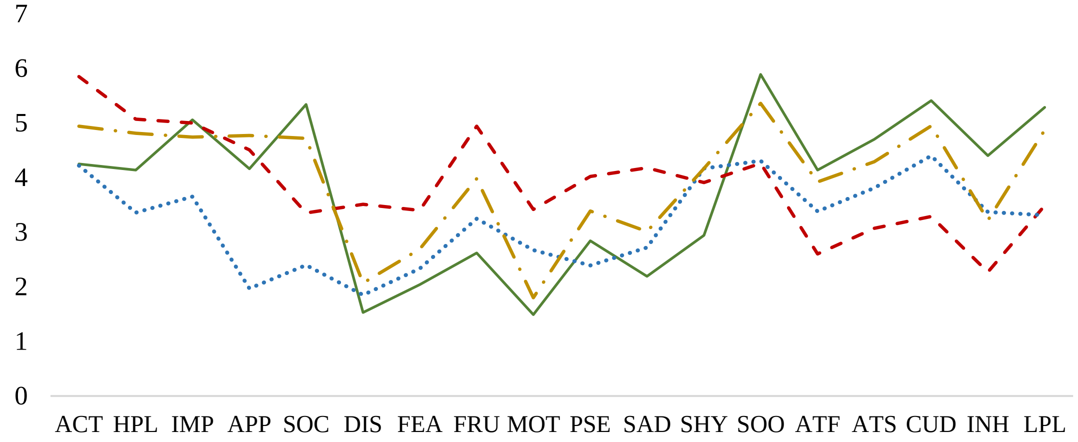

Figure 1c. ECBQ scale means for subgroups at Time 3.

Note. ACT = Activity Level; HPL = High Intensity Pleasure; SML = Smiling and Laughter; VRE = Vocal Reactivity; FRE = Falling Reactivity; IMP = Impulsivity; APP = Approach; SOC = Sociability; DIS = Discomfort; FEA = Fear; FRU = Frustration; MOT = Motor Activation; PSE = Perceptual Sensitivity; SAD = Sadness; SHY = Shyness; SOO = Soothability; ATF = Attentional

Focusing; ATS = Attentional Shifting; CUD = Cuddliness; INH = Inhibitory Control; LPL = Low Intensity Pleasure.

6.5.2. Intra-Individual Continuity of Temperament Subgroup Classification

Cross-tabulation analyses showed significant associations between individual children's temperament subgroup classifications across adjacent ages; from Time 1 to Time 2, χ_2 (4, *N* = 87) = 36.80, *p* < .001, and from Time 2 to Time 3, χ_2 (6, *N* = 80) = 56.88, *p* < .001. Results are depicted in Figure 2, with solid arrows between the stacked columns representing time-to-time sequences that occurred more often than expected by chance (and *n* representing raw numbers of children). There was a significant likelihood of Time 1 *well-regulated* infants belonging to the *sociable/well-regulated* subgroup at Time 2 (*z* = 5.04, *p* < .001), and of children being consistently classified *sociable/well-regulated* at Time 2 and Time 3 (*z* = 4.58, *p* < .001). Likewise, there was a significant likelihood of children being consistently classified *active/negative reactive* at Time 1 and Time 2 (*z* = 3.30, *p* < .001) and at Time 2 and Time 3 (*z* = 5.17, *p* < .001), and *inhibited/low positive* at Time 1 and Time 2 (*z* = 4.58, *p* < .001) and at Time 2 and Time 3 (*z* = 4.15, *p* < .001). However, there was no association of particular Time 2 subgroup classification with Time 3 *reactive/regulated* classification; that is, *sociable/well-regulated* (*z* = 0.46, *p* = .646), *active/negative reactive* (*z* = -0.53, *p* = .595), and *inhibited/low positive* (*z* = -0.10, *p* = .924) toddlers at Time 2 all had equal likelihood of being classified *reactive/regulated* at Time 3.

Time-to-time sequences of temperament subgroup classifications that occurred significantly *less* often than expected by chance (depicted in Figure 2 with dashed arrows) include: movement from Time 1 *well-regulated* to Time 2 *inhibited/low positive* (*z* = -.398, *p* < .001; *n* = 4 children) or *active/negative reactive* (*z* = -2.08, *p* < .05; *n* = 3); from Time 1 *active/negative* reactive to Time 2 *sociable/well-regulated* (*z* = -2.08, *p* < .05; *n* = 7); from Time 1 *inhibited/low positive* to Time 2 *sociable/well-regulated* (*z* = -3.06, *p* < .001; *n* = 6); from Time 2 *sociable/well-regulated* to Time 3 *active/negative reactive* (*z* = -4.37, *p* < .001; no cases) or *inhibited/low positive* (*z* = -2.89, *p* < .01; *n* = 1); from Time 2 *active/negative reactive* to Time 3 *sociable/well-regulated* (*z* = -2.48, *p* < .05; no cases); and from Time 2 *inhibited/low positive* to Time 3 *sociable/well-regulated* (*z* = -3.16, *p* < .01; *n* = 1).

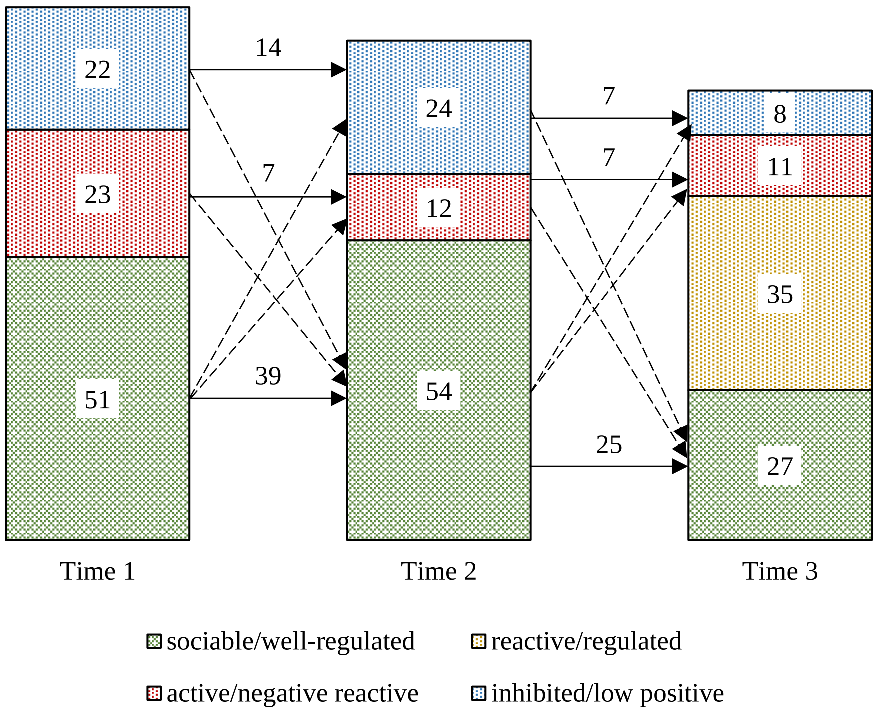

Figure 2. Number of children classified in each temperament subgroup at each timepoint, and results of cross-tabulation analyses. Solid arrows indicate time-to-time sequences of subgroup classification observed *more* often than expected, and numbers at arrows indicate the number of children in each cross-tabulation. Dashed arrows indicate time-to-time sequences of subgroup classification that occurred *less* often than expected by chance.

6.5.3. Temperament Subgroups in Relation to Phenotypic Characteristics and Social-Emotional Functioning

Table 4 presents ANOVA results demonstrating no significant differences between temperament subgroups with regard to child age, sex ratio, or developmental level at either timepoint, or for autism traits at Time 2. The four subgroups at Time 3 differed with regard to concurrent ADOS-T total scores, with post-hoc pairwise comparisons revealing that *inhibited/low positive* children had the highest autism traits. Further, a trend-level difference was observed in the sex composition of Time 3 subgroups.

ANCOVA revealed significant between-subgroup differences for concurrent ITSEA domain scores at both Time 2 and Time 3, after controlling for ADOS-T total score (see Figure 3). Time 2 ADOS-T total score was not significantly associated with Internalizing, F (1,82) = 2.88, p = .094 η^2 = 0.03, Externalizing, F (1,82) = 0.00, p = .951 η^2 = 0.00, or Competence, F (1,80) = 1.95, p = .167 η^2 = 0.02. Time 3 ADOS-T total score was significantly associated with

Internalizing, F (1,73) = 4.77, p = .034, η^2 = 0.06, and Competence, F (1,72) = 6.68, p = .012, η^2 = 0.09, but not Externalizing, F (1,73) = 1.00, p = .320, η^2 = 0.01.

Post-hoc pairwise comparisons of Time 2 ITSEA domain scores among the three subgroups showed that Internalizing symptoms were highest among *active/negative* children, intermediate for *inhibited/low positive* children, and lowest among the *sociable/well-regulated* subgroup. The *sociable/well-regulated* subgroup had lower Externalizing symptoms than the *active/negative reactive* and *inhibited/low positive* subgroups, which did not differ from one another. *Inhibited/low positive* children had lower Competence than the *sociable/well-regulated* subgroup but did not differ from the *active/negative* subgroup, nor was there a significant difference in Competence between children classified *sociable/well-regulated* or *active/negative*.

Pairwise comparisons of Time 3 ITSEA domain scores among the four subgroups revealed that children classified as either *active/negative reactive, inhibited/low positive,* or *reactive/regulated* had significantly higher Internalizing symptoms than *sociable/well-regulated* infants. *Reactive/regulated* children had lower Internalizing symptoms than *active/negative reactive* and *inhibited/low positive* children, who did not differ from one another. *Active/negative reactive* children had the highest Externalizing symptoms. The *reactive/regulated* subgroup had higher Externalizing symptoms than *sociable/well-regulated* children but did not differ from the *inhibited/low positive* subgroup. There were no differences in Externalizing symptoms between the *sociable/well-regulated* and *inhibited/low positive* subgroups. Children classified as *sociable/well-regulated* had the highest levels of Competence. The *reactive/regulated* subgroup had significantly higher Competence relative to the *active/negative reactive* and *inhibited/low positive* subgroups, which did not differ from one another.

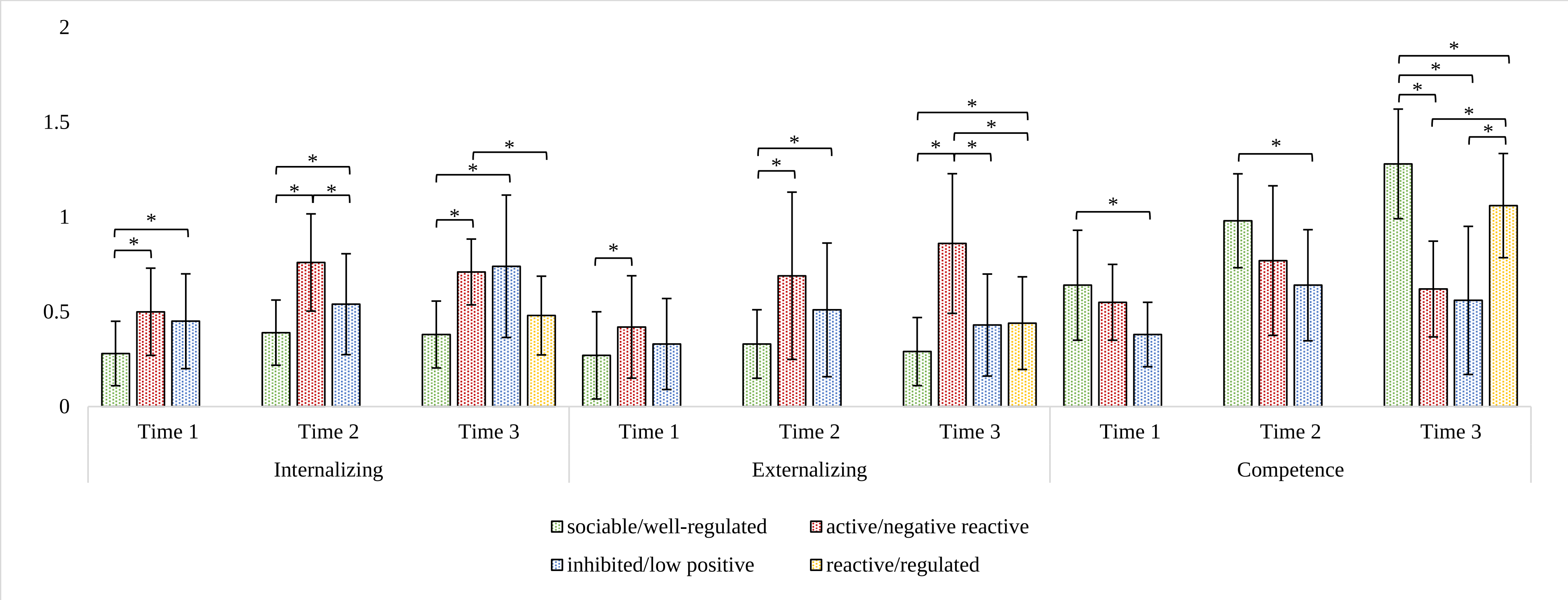

Figure 3. ITSEA domain scores for each temperament subgroup at Time 1 and Time 2 and Time 3. Bars represent the mean (± standard deviation). Bracketed bars with an asterisk (*) are significantly different.

Table 4

Between-Subgroup Comparisons of Age, Sex, Phenotypic Characteristics, and Social-Emotional Functioning at Each Timepoint

								BCa 95% Confidence Interval					
	SWR	ANR	ILP	RRE	χ^2/F	φ/ η^2	*p*	SWR vs ANR	ANR vs ILP	ILP *vs* SWR	RRE *vs* SWR	RRE *vs* ANR	RRE *vs* ILP
Time 1													
Age (months)	12.39	12.61	12.13		0.34	0.01	.713						
Sex (% male)	61	77	77		2.44	0.16	.295						
AOSI Total	7.45	7.30	10.91		7.73	0.14	<.01	-1.56, 1.86	**-3.50, -1.00**	**0.82, 2.94**			
MSEL ELC	88.18	84.13	82.95		0.88	0.02	.418						
ITSEA Int	0.28	0.50	0.45		7.04	0.17	<.01	**-0.34, -0.09**	-0.12, 0.22	**0.03, 0.31**			
ITSEA Ext	0.27	0.42	0.33		7.16	0.18	<.01	**-0.34, -0.07**	-0.01, 0.27	-0.01, 0.17			
ITSEA Com	0.64	0.55	0.38		7.76	0.16	<.01	-0.03, 0.20	-0.20, 0.03	**-0.37, -0.15**			
Time 2													
Age (months)	18.47	19.32	18.52		0.94	0.02	.936						
Sex (% male)	69	67	63		0.27	0.06	.873						
AOSI Total	7.61	9.25	9.43		1.57	0.04	.214						
ADOS-T Total	9.52	10.33	10.30		0.21	0.00	.812						
MSEL ELC	86.35	83.25	88.17		0.31	0.01	.735						
ITSEA Int	0.39	0.77	0.52		17.19	0.30	<.001	**-0.55, -0.22**	**0.08, 0.42**	**0.02, 0.24**			
ITSEA Ext	0.33	0.69	0.52		9.43	0.19	<.001	**-0.62, -0.10**	-0.13, 0.47	**0.06, 0.32**			
ITSEA Com	0.98	0.77	0.66		10.78	0.21	<.001	-0.04, 0.45	-0.14, 0.37	**-0.45, -0.19**			
Time 3													
Age (months)	24.38	25.45	26.10	24.30	2.19	0.08	.096						

Sex (% male)	67	82	25	69	7.26	0.30	.064						
ADOS-T Total	9.00	7.63	16.29	11.14	5.29	0.17	.002	-6.72, 3.98	**14.52, 0.06**	**2.31, 15.00**	-0.32,7.34	-3.03, 7.31	-11.33, 1.05
MSEL ELC	89.93	83.27	79.59	92.29	1.15	0.04	.337						
ITSEA Int	0.36	0.70	0.89	0.49	15.66	0.39	<.001	**-0.45, -0.21**	-0.44, 0.06	**0.25, 0.79**	**0.03, 0.22**	**-0.34, -0.08**	**-0.63, -0.16**
ITSEA Ext	0.30	0.86	0.44	0.44	13.49	0.36	<.001	**-0.82, -0.36**	**0.12, 0.75**	-0.07, 0.38	**0.04, 0.23**	**-0.69, -0.22**	-0.23, 0.19
ITSEA Com	1.24	0.60	0.68	1.08	16.89	0.41	<.001	**0.44, 0.83**	-0.38, 0.27	**-0.89, -0.28**	**-0.31, -0.02**	**0.31, 0.64**	**0.12, 0.71**

Note. SWR = sociable/well-regulated; ANR = active/negative reactive; ILP = inhibited/low positive; RRE = reactive/regulated; BCa = bias corrected and accelerated; ITSEA = Infant-Toddler Social and Emotional Assessment; Int = Internalizing; Ext = Externalizing; Com = Competence; AOSI = Autism Observation Scale for Infants; ADOS-T = Autism Diagnostic Observation Schedule, Toddler Module; MSEL = Mullen Scales of Early Learning; ELC = Early Learning Composite.

Next, exploratory *t*-tests were conducted to compare Time 3 ITSEA domain scores for children with a consistent classification at Time 2 and Time 3 versus those classified within the new *reactive/regulated* subgroup at Time 3. Given only a small subset of Time 2 *active/negative reactive* (n = 4) and *inhibited/low positive* (n = 7) children were subsequently classified *reactive/regulated* at Time 3 – and that both of these subgroups were broadly associated with social-emotional difficulties – this comparison reflected those who (a) had a consistent *active/negative reactive* or *inhibited/low positive* classification at Time 2 and Time 3 (n = 14) versus (b) were classified either *active/negative reactive* or *inhibited/low positive* at Time 2 and *reactive/regulated* at Time 3 (n = 11). Significant differences were apparent such that children with a consistent Time 2 and Time 3 temperament classification had higher Time 3 Internalizing symptoms (t = 2.25, p < .05, mean difference = 0.21, BCa 95% CI 0.04 to 0.39) and lower Time 3 Competence than children classified *reactive/regulated* (t = -3.18, p < .01, mean difference = -0.38, BCa 95% CI -0.63 to -0.14). There were no significant differences in Time 3 Externalizing domain scores, t = 1.69, p = .104. Significant differences were also apparent between *sociable/well-regulated* children classified the same (n = 25) versus *reactive/regulated* (n = 20) from Time 2 to Time 3, with the latter demonstrating higher Time 3 Externalizing levels, t = -3.65, p < .01, mean difference = -0.20, BCa 95% CI -0.31 to -0.09, and lower Time 3 Competence, t = 2.24, p < .05, mean difference = 0.19, BCa 95% CI 0.02 to 0.35. There were no significant differences in Time 3 Internalizing domain scores, t = -0.751, p = .457.

6.6. Discussion

The main aim of this study was to explore the continuity of temperament subgroup classifications among children with early signs of autism as they moved out of infancy and into toddlerhood and toward the point of potential autism diagnosis. An ancillary aim was to explore the relation of temperament subgroup classifications to variability in child social-emotional functioning (internalizing, externalizing, and competence) and behavioural/clinical phenotypic characteristics (autism traits, developmental level).

We had previously reported classifications for this cohort of infants – into *well-regulated, active/negative reactive,* and *inhibited/low positive* subgroups – at around 12-months of age (Time 1; Chetcuti et al., 2020), and here applied the same procedure to identify temperament subgroups at two subsequent timepoints. We found the Time 1 subgroup classifications to be broadly replicated when children were aged around 18-months (Time 2) and 24-months (Time 3). There was a significant likelihood of children having a recurrent subgroup classification from one timepoint to the next, and no apparent patterns to the movement of children who did change from one subgroup to another over time. An additional profile emerged, uniquely apparent at Time 3, which we labelled *reactive/regulated*. Classification in this subgroup was not associated with any subgroup classification 6-months prior.

There were no differences between subgroups with respect to child age, sex ratio, or developmental level at any timepoint. By contrast, *inhibited/low positive* children had the highest autism traits in infancy and toddlerhood. Consistent across timepoints, children classified as *active/negative reactive* or *inhibited/low positive* had the highest-reported social-emotional difficulties, whereas *sociable/well-regulated* children had high social-emotional competence. Children classified as *reactive/regulated* had intermediate social-emotional functioning – higher than children classified as *active/negative reactive* and *inhibited/low positive* children but lower than *sociable/well-regulated* children.

6.6.1. Continuity of Temperament Subgroup and Intra-Individual Classifications

Given that the expression of traits has been shown to differ depending on child developmental stage (Putnam et al., 2008), temperament subgroups were identified separately when children were aged around 12-, 18-, and 24-months. Nevertheless, consistency was apparent in the way fine-grained temperament traits grouped together to define each subgroup, even despite differences in child age and questionnaire version across timepoints (i.e., IBQ-R at Time 1 vs ECBQ at Time 2 and Time 3). That is, at each timepoint, an *inhibited/low positive* subgroup was characterized by a trait constellation corresponding to inhibited social approach, and an *active/negative reactive* subgroup was characterized by high negative affectivity-related traits. A *sociable/well-regulated* subgroup was characterized at all timepoints by a constellation of high self-regulation-related traits, coupled with high sociability at Time 2 and Time 3.

The proportion of children classified as *active/negative reactive* or *inhibited/low positive* decreased from around one-quarter at Time 1 to one-tenth by Time 3. This is in line with Janson and Mathiesen (2008) who found that the proportion of children with typical development classified as temperamentally *undercontrolled* – bearing resemblance to the present *active/negative reactive* subgroup – decreased from 25% at age 18-months to just 8% at 8-9 years. However, van den Akker et al. (2010) found the proportion of children with typical development classified as *expressive* – also similar to the current *active/negative reactive* subgroup – remained stable from around 30- to 42-months. Further, Janson and Mathiesen (2008) found that an increasing proportion of children were classified as *inhibited* – bearing resemblance to the present *inhibited/low positive* subgroup – over the study period. Some difference in findings might be attributable to the use of different measurement and subgrouping techniques. However, a small body of evidence suggests a genuinely differential pattern of change in discrete temperament traits among children with autism compared to children with non-autism developmental delays and typical development (Del Rosario et al., 2014; Pijl et al., 2019; Reyes et al., 2019). Therefore, the differential continuity of temperament subgroup classifications in the context of diagnosed autism vs typical development could be an interesting area of further enquiry.

Our finding of decreasing *active/negative reactive* subgroup membership is also somewhat contrary to Lee et al.'s (2020) finding which suggested the majority of school-aged children on the autism spectrum have a *reactive* temperament. The frequency of children displaying 'extreme' temperamental reactivity types may follow a non-linear trajectory; decreasing from infancy to the toddlerhood years as children become more adept at regulating their affect, behaviour, and arousal, and then increasing as children enter school and are exposed to a wider variety of emotion-eliciting situations. Further longitudinal research over a longer time frame would thus improve understanding of the developmental progression of temperament in the context of autism.

As predicted, there was a significant likelihood of recurrent subgroup classification from timepoint-to-timepoint. A total of 76% of Time 1 *well-regulated* infants were classified as *sociable/well-regulated* at Time 2, among whom 46% were subsequently re-classified as *sociable/well-regulated* at Time 3. 30% of Time 1 *active/negative reactive* infants were classified *active/negative reactive* at Time 2, with 58% of these children re-classified as such at Time 3. Finally, 64% of Time 1 *inhibited/low positive* infants were classified *inhibited/low positive* at Time 2, among whom 29% were again classified *inhibited/low positive* at Time 3. By contrast, infants/toddlers belonging to the *sociable/well-regulated* subgroup were unlikely to become subsequent members of either the *active/negative reactive* or *inhibited/low positive* subgroup, and vice versa. Among children with typical development, Beekman et al. (2015) found that 62-69% of 9-month-old infants were re-classified in the same (*positive*- or *negative reactive*) subgroup at 18-months, and 30-76% of 18-month-old toddlers retained their original (*fearful*, *positive*- or *negative*- or *active reactive*) subgroup membership 9-months later. Together these findings suggest that children's temperament qualities are unlikely to undergo extensive transformations as they move out of infancy and into toddlerhood.

At Time 3, an additional temperament subgroup labelled *reactive/regulated* comprised 43% of toddlers and was characterized by children with high arousal of positive affect and intermediate level negative affectivity- and self-regulation attributes. Both greater number of, and more differentiated, temperament subgroups have also been identified among older compared to younger children with typical development (Beekman et al., 2015; Gartstein et al., 2017), suggesting greater temperamental heterogeneity later in development. Seemingly contrary to this notion, Lee et al. (2020) identified only two temperament subgroups of children with autism at school-age. However, it is difficult to compare and draw overall conclusions across from this and Lee et al.'s (2020) study given differences in sample characteristics (i.e., community-referred/undiagnosed versus autism-diagnosed), methodology (i.e., temperament questionnaire), and analytic approach (i.e., cluster analysis versus LPA) differences, which can lead to different subgroup solutions.

Children’s classification in the Time 3 *reactive/regulated* subgroup was not associated with classification in any particular Time 2 subgroup. Therefore, this subgroup could be conceived as comprising: (a) Time 2 *sociable/well-regulated* toddlers with slower-to-develop self-regulation than their counterparts subsequently retaining *sociable/well-regulated* classification at Time 3, (b) Time 2 *active/negative reactive* toddlers with self-regulatory gains surpassing those of toddlers retaining *active/negative reactive* classification at Time 3, and (c) Time 2 *inhibited/low positive* toddlers with heightened social-approach and attentional focus than those retaining their former *inhibited/low positive* classification at Time 3.

6.6.2. Temperament Subgroups in Relation to Social-Emotional Functioning and Phenotypic Characteristics

As predicted from the results of our Time 1 analysis (Chetcuti et al., 2020), higher social-emotional difficulties and lower social-emotional competence were reported among *active/negative reactive* and *inhibited/low positive* toddlers, relative to *sociable/well-regulated* toddlers at Time 2 and Time 3. These results are consistent with the literature on typical child development suggesting a promotive role of child self-regulation and positive emotionality for social-emotional development and, conversely, risk conferred by negative emotionality and dysregulation (e.g., Cassiano, Gaspardo, Furini, Martinez, & Linhares, 2016; Edwards & Hans, 2015; Gartstein, Putnam, & Rothbart, 2012; also see reviews by Davis & Suveg, 2014; De Pauw & Mervielde, 2010; Muris & Ollendick, 2005; Sanson, Hemphill, & Smart, 2004) and an inhibited or disinhibited temperament type (Putnam & Stifter, 2005; Robins et al., 1996; Thomas et al., 1968). However, the mean level of internalizing symptoms, externalizing symptoms, and social-emotional competence associated with each subgroup classification differed somewhat according to assessment timepoint/child age.

The *active/negative reactive* and *inhibited/low positive* subgroups had significantly higher internalizing symptoms than the *sociable/well-regulated* subgroup at all timepoints. Internalizing symptoms were equivalent for the *active/negative reactive* and *inhibited/low positive* subgroups at Time 1 and Time 3, but significantly higher for the *active/negative reactive* subgroup at Time 2. Upon visual inspection of Figure 3 it seems both *active/negative reactive* and *inhibited/low positive* subgroups were associated with a higher magnitude of internalizing symptoms at later timepoints, relative to Time 1. However, internalizing symptoms were roughly equivalent for the *active/negative reactive* subgroup at Time 2 and Time 3, but higher at Time 3 relative to Time 2 for the *inhibited/low positive* subgroup.

As for externalizing symptoms, the *active/negative reactive* subgroup had the highest reported levels at each timepoint but the difference relative to the *inhibited/low positive* subgroup reached significance only at Time 3. Again, the mean level of externalizing symptoms associated with *active/negative reactive* subgroup classification was higher at later timepoints relative to Time 1, but slightly lower for the *inhibited/low positive* and *sociable/well-regulated* subgroups. Finally, the highest competence was reported for children characterized within the *well-regulated* subgroup at Time 1 and *sociable/well-regulated* subgroup at Time 2 and Time 3. The level of competence associated with *inhibited/low positive* and *active/negative reactive* classification was broadly even at Time 2 and Time 3, but higher for the *sociable/well-regulated* subgroup at Time 3 relative to Time 2.

These findings suggest that temperament subgroup classifications relate to variation in social-emotional functioning in a broadly consistent way during infancy and toddlerhood. The varying level of internalizing and externalizing symptoms and competence associated with each temperament subgroup at each timepoint suggests that children with different trait constellations might vary in their capacity to adapt their behaviour in response to increasing environmental and functional demands, resulting in more pronounced between-subgroup differences at older ages. Alternatively, it may be that only those 'most' *inhibited/low positive* or *active/negative reactive* infants were recurrently classified in these subgroups across timepoints – as opposed to being subsequently classified *sociable/well-regulated* or *reactive-regulated* – resulting in smaller proportion of membership among these over time, despite evidence of higher associated levels of internalizing and/or externalizing symptoms.

As already noted, and consistent with our Time 1 analysis, there were no differences between temperament subgroups with respect to mean age, sex ratio, or developmental level at either Time 2 or Time 3. However, there was a trend-level difference in the sex composition of Time 3 subgroups; females comprised three-quarters of *the inhibited/low positive* subgroup, compared to around one-third of the *sociable/well-regulation* and *reactive/regulated* subgroups and one-fifth of the *active/negative reactive* subgroup. Moreover, higher autism traits were apparent among *inhibited/low positive* infants relative to those classified as *active/negative reactive* or *sociable/well-regulated* at Time 1 and Time 3. This finding is consistent with evidence that autism severity is positively associated with continuous ratings of temperamental sociability (Kamio et al., 2018) and observed intensity of joy in response to positive induction probes (Macari et al., 2018). However, there were no differences in autism traits among temperament subgroups at Time 2. This finding is not easy to explain as measures of autism traits used at this timepoint were also used at Time 1 (i.e., AOSI) and Time 3 (i.e., ADOS-T). The difficulties of disentangling social interest/motivation deficits from temperament-related social reticence in infancy might have created a biased inflation of autism feature ratings among *inhibited/low positive* infants at Time 1, but not at Time 2 when greater child mobility and communication capabilities make this distinction more explicit. That is, a genuine influence of temperament on the expression of autism might only become apparent in later toddlerhood when symptoms are more consolidated.

6.6.3. Study Limitations and Future Directions

Conducting the LPA using all 18 ECBQ (and 14 IBQ-R) fine-grained subscales permitted a full and nuanced description of temperamental heterogeneity within our cohort. Most previous studies of typical development characterized temperament subgroups on the basis of global constructs representing an aggregation of multiple finer-grained traits, which may have obscured meaningful variability. However, the resulting number of trait comparisons required by our approach – within and across timepoints – presented a challenge for the interpretation of subgroup equivalence. Advancement from the IBQ-R to ECBQ further compounded this challenge, as Time 1 subgroups were identified on the basis of a somewhat different set of traits compared to those identified at Time 2 and Time 3. Thus, the *sociable/well-regulated, active/negative reactive,* and *inhibited/low positive* subgroups identified at each timepoint – whilst assigned the same descriptive label – included slightly differing configurations of specific finer-grained traits. Nevertheless, cross-time similarities were apparent when subgroup characteristics were abstracted at a higher-level (i.e., broadly in terms of levels of surgency-, negative affectivity-, and self-regulation-related traits), and putative subgroup analogues showed similar patterns of relations with other measures at each timepoint (ITSEA, MSEL), lending confidence to our interpretation that *sociable/well-regulated, active/negative reactive,* and *inhibited/low positive* subgroups were identified recurrently.

The use of caregiver-report questionnaires is another limitation, given the potential for respondent biases as well as shared variance between the ECBQ and ITSEA due to common-method and/or confounding in item content. The ECBQ item/response format (Putnam et al., 2006) and interspersion of ITSEA symptom and competence items (Carter & Briggs-Gowan, 2006) partially protects against bias, however, and we sought to actively reduce measurement confounding by removing ITSEA items that were conceptually and semantically similar to ECBQ items. Nonetheless, a multimethod/multi-informant measurement approach should be used in future research to circumvent such potential issues.

The modest size of the current sample precluded examination of individual trajectories of change within each subgroup, which might have helped clarify differential patterns of membership across timepoints. For instance, inspection of subgroup means suggests comparable Activity Level for the *active/negative reactive* subgroup as identified at Time 1 and Time 2, but higher Activity Level for the other subgroups at Time 2 relative to Time 1. Activity Level was then higher for the *active/negative reactive* subgroup at Time 3 but lower for the *sociable/well-regulated* and *inhibited/low positive* subgroups at Time 3, relative to previous timepoints. The lack of between-subgroup differences in Activity Level at Time 2 might, therefore, be attributable to differences in the developmental course of this trait. However, the varying patterns of subgroup classification from timepoint-to-timepoint indicate that children *within* each subgroup did not follow the same trajectory. Studies comprising children with typical development suggest that attributes of the caregiver and caregiving environment may shape child temperament characteristics (Karreman et al., 2006; Paulussen-Hoogeboom et al., 2007) and subgroup membership (Beekman et al., 2015; Hart et al., 1997; van den Akker et al., 2010). Research is needed to determine whether such factors exert a differential influence depending on temperament subgroup classification and/or other individual difference characteristics, such as the presence of autism traits.

Since this study did not include a typical comparison sample, it is not known whether children with autism traits differ with regard to temperament subgroup classifications and continuity. Nonetheless, the extent of heterogeneity within, and overlap among, DSM-/ICD-defined disorder categories has drawn question to the validity of the traditional case-control approach and prompted research to shift towards a more dimensional conceptualization of symptoms and behaviours (Hudry, Pellicano, Uljarevic & Whitehouse, 2020; Insel et al., 2010). Complementary to this, sampling beyond the boundaries of diagnostic autism criteria ensured the present sample spanned the full range of variation in autism presentation (see Hudry et al., 2020), from subclinical traits through to overt symptoms likely warranting future diagnosis. Beyond the scope of this study, the question of whether temperament has differential continuity or influence depending on the specific constellation and clinical salience of autism traits also warrants consideration in future work.

6.6.4. Conclusions

This study extended our initial examination of temperament subgroups in a large cohort of referred children with autism traits by examining the continuity of classifications across multiple timepoints. The nature of temperament subgroup classifications was relatively consistent at around 12, 18, and 24 months of age, and there was moderate intra-individual continuity of classification over time. *Active/negative reactive* and *inhibited/low positive* temperament classifications were associated with a relatively consistent pattern of social-emotional difficulties, whereas a *sociable/well-regulated* classification was associated with superior social-emotional competence. Taken together, these findings suggest that the nature and expression of ‘problematic’ temperament attributes among children in whom early autism traits may also be emerging is unlikely to be transient and may provide a reliable and very early indicator of children’s social-emotional functioning outcomes.

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6.8. Appendices

Table A1

Overlapping ECBQ and ITSEA Items

ECBQ item	ITSEA item removed
When playing alone, how often did your child become easily distracted?	Goes from toy to toy faster than other children his or her age
During everyday activities, how often did your child become sad or blue for no apparent reason?	Looks unhappy or sad without any reason
When approached by an unfamiliar person in a public place (for example, the grocery store), how often did your child cling to a parent?	Is shy with new adults
During everyday activities, how often did your child rock back and forth while sitting?	Is restless and can't sit still
While visiting relative or adult family friends s/he sees infrequently, how often did your child stay back and avoid eye contact?	Does not make eye contact
When visiting a new place, how often did your child not want to enter?	Takes a while to feel comfortable in new places (10 minutes or more)
In situations where s/he is meeting new people, how often did your child become quiet?	Is quiet or less active in new situations?
When approaching unfamiliar children playing, how often did your child seem uncomfortable?	Is shy with new children
During everyday activities, how often did your child seem full of energy, even in the evening?	Seems to have no energy
When s/he asked for something and you said "no", how often did your child have a temper tantrum?	Has temper tantrums
In situations where s/he is meeting new people, how often did your child become quiet?	Takes a while to speak in unfamiliar situations

During everyday activities, how often did your child become distressed when his/her hands were dirty and/or sticky?	Is *very* worried about getting dirty
When engaged in an activity requiring attention, how often did your child stay involved for 10 minutes or more?	Can pay attention for a long time (other than watching TV)
When asked to do so, how often was your child able to lower his or her voice?	Quiets down when you say “Shh”
When engaged in play with his/her favourite toy, how often did your child play for 5 minutes or less?	Plays with toys for 5 minutes or longer
When looking at picture books on his/her own, how often did your child enjoy looking at the books?	Looks at picture books by himself or herself
When being dressed or undressed, how often did your child stay still?	Stays still while being changed, dressed, or bathed

Table A2

IBQ-R/ECBQ Scale Time-to-Time Correlations and ECBQ Internal Consistency

	Time 1 IBQ-R – Time 2 ECBQ	Time 2 ECBQ – Time 3 ECBQ	Cronbach's α Time 2/Time 3
Activity Level	.20†	.63**	.68 / .75
High Intensity Pleasure	.20†	.53**	.77 / .81
Approach	.35**	.55**	.87 / .90
Frustration	.44**	.63**	.89 / .89
Fear	.40**	.66**	.71 / .86
Perceptual Sensitivity	.47**	.58**	.77 / .82
Sadness	.45**	.64**	.85 / .83
Soothability	.46**	.62**	.86 / .87
Cuddliness	.63**	.78**	.89 / .93
Low Intensity Pleasure	.43**	.68**	.84 / .85
Attentional Focusing	.24*	.60**	.83 / .88
Sociability	-	.70**	.93 / .94
Shyness	-	.64**	.85 / .88
Impulsivity	-	.64**	.46 / .71
Discomfort	-	.58**	.58 / .86
Motor Activation	-	.57**	.79 / .85
Inhibitory Control	-	.66**	.88 / .91
Attentional Shifting	-	.63**	.77 / .83

Note. †p = .06. *p < .05. **p < .01.

CHAPTER 7

Study 3

This paper has been published in *Autism Research.* The accepted manuscript version is included in this Chapter; the final publication is reproduced, with the permission of Wiley the copyright holder, in Appendix F.

Chetcuti, L., Uljarević, M., Varcin, K. J., Boutrus, M., Wan, M. W., Slonims, V., ... the AICES Team (2020). The role of negative affectivity in concurrent relations between caregiver psychological distress and social-emotional difficulties in infants with early signs of autism. *Autism Research*, *13*(8), 1349-1357. https://doi.org/10.1002/aur.2296

The Role of Negative Affectivity in Concurrent Relations between Caregiver Psychological Distress and Social-Emotional Difficulties in Infants with Early Signs of Autism

Lacey Chetcuti[1,2], Mirko Uljarević[3,4], Kandice Varcin[5], Maryam Boutrus[2,5,6], Ming Wai Wan[7], Vicky Slonims[8], Jonathan Green[9,10], Leonie Segal[11], Teresa Iacono[12], Cheryl Dissanayake[1,2], Andrew J.O. Whitehouse[2,5], Kristelle Hudry[1], and the AICES Team[13]

[1]School of Psychology and Public Health, La Trobe University, Australia; [2]Cooperative Research Centre for Living with Autism (Autism CRC), Long Pocket, Brisbane, Queensland, Australia; [3]Stanford Autism Center, Department of Psychiatry and Behavioral Sciences, Child and Adolescent Psychiatry, School of Medicine, Stanford University, USA; [4]Melbourne School of Psychological Sciences, Faculty of Medicine, Dentistry and Health Sciences, The University of Melbourne, Victoria, Australia; [5]Telethon Kids Institute, University of Western Australia; [6]School of Psychological Science, University of Western Australia, Australia; [7]Division of Neuroscience & Experimental Psychology, School of Health Sciences, University of Manchester; [8]Children's Neurosciences, Evelina London Children's Hospital, Institute of Psychiatry, Psychology & Neuroscience, Kings College London, London, UK; [9]Division of Neuroscience & Experimental Psychology, School of Biological Sciences, University of Manchester; [10]Manchester Academic Health Science Centre, Manchester University NHS Foundation Trust, Greater Manchester Mental Health NHS Trust, Manchester, UK; [11]Australian Centre for Precision Health, School of Health Sciences, University of South Australia, Adelaide, SA; [12]La Trobe Rural Health School, Bendigo, VIC, AUS; [13]the AICES team in alphabetical order: Josephine Barbaro, Stefanie Dimov, Murray Maybery, Michelle Renton, Nancy Sadka, Scott Wakeling, and John Wray.

7.1. Abstract

Recent evidence suggests the link between caregiver psychological distress and offspring social-emotional difficulties may be accounted for by offspring temperament characteristics. However, existing studies have only focused on neurotypical children; thus, the current study sought to provide an initial examination of this process among children with varying levels of early autism features. Participants included 103 infants aged 9-16 months (*M* = 12.39, *SD* = 1.97; 68% male) and their primary caregiver (96% mothers) referred to a larger study by community healthcare professionals. We utilized caregiver-reported measures of psychological distress [Depression Anxiety Stress Scales], infant temperament [Infant Behavior Questionnaire-Revised] and internalizing and externalizing symptoms [Infant-Toddler Social and Emotional Assessment] and administered the Autism Observation Schedule for Infants (AOSI) at an assessment visit to quantify autism features. Infant negative affectivity was found to mediate positive concurrent relations between caregiver psychological distress and infant internalizing and externalizing symptoms, irrespective of the infants' AOSI score. While preliminary and cross-sectional, these results replicate and extend previous findings suggesting that the pathway from caregiver psychological distress to negative affectivity to social-emotional difficulties might also be apparent among infants with varying levels of autism features. More rigorous tests of causal effects await future longitudinal investigation.

7.2. Lay Summary

Offspring of caregivers experiencing psychological distress (i.e., symptoms of depression, anxiety, and/or stress) may themselves be at increased risk of poor mental health outcomes. Several previous studies conducted with neurotypical children suggest that this link from caregiver-to-child may be facilitated by children's temperament qualities. This study was a preliminary cross-sectional exploration of these relationships in infants with features of autism. We found that infants' elevated negative emotions were involved in the relation between caregiver heightened psychological distress and children's mental health difficulties, consistent with neurotypical development.

7.3. Introduction

There is a well-established link between caregiver psychological distress and heightened risk towards internalizing (anxiety and/or depression) and externalizing (inattention/hyperactivity, oppositional, and/or aggressive behavior) symptoms among offspring (for meta-analyses, see Goodman et al., 2011, and Lawrence, Murayama, & Creswell, 2018). However, the nature of these associations is currently unclear. One potential mechanism that may account for the relation between caregiver psychological distress and child social-emotional difficulties is children's individual temperament characteristics, defined as biologically-based differences in reactivity and self-regulation (Rothbart & Derryberry, 1981). While early theories of temperament emphasized the genetic etiology and stability of traits across developmental periods (Goldsmith et al., 1987), there is growing recognition that temperament is malleable to environmental experience. Indeed, research has shown that caregiver psychological distress symptoms are associated with children's temperamental difficulties (Hanington, Ramchandani, & Stein, 2010), which in turn may confer risk towards child social-emotional difficulties (Hankin et al., 2017). Nevertheless, few existing studies have specifically tested this pathway.

Among 97 mother-child dyads, Suveg, Shaffer, Morelen, and Thomassin (2011) found that the links between maternal psychological distress and children's internalizing and externalizing symptoms were mediated by child self-regulation (i.e., the capacity to suppress or modulate emotions and behavior). Similar results were garnered by Choe, Shaw, Brennan, Dishion, and Wilson (2014) in a large sample of 677 toddlers and their mothers. Specifically, low levels of self-regulation at age 3 years was found to mediate the association between maternal depression at age 2 and toddler oppositionality at age 4. Nevertheless, Choe et al. did not explore the relevance of this pathway to children's internalizing symptoms. Allen, Oshri, Rogosch, Toth, and Cicchetti (2018) found that low child self-regulation mediated the link between maternal depression and child social-emotional difficulties. High levels of child negative affect also acted as a mediator of this association, although there was no effect of offspring positive affect/sociability. Nevertheless, the composite measure of both internalizing *and* externalizing utilized by Allen et al. may have obscured the presence of specific internalizing versus externalizing pathways. Indeed, emerging evidence suggests that low positive affect/sociability may confer internalizing-specific risk (Hankin et al., 2017).

The current study is an initial attempt to extend empirical work on this topic to the context of autism. Our primary objective was to examine whether variation in child temperament is relevant to the links between contemporaneously measured caregiver psychological distress and child social-emotional difficulties in a sample of young infants with features of autism. Examining the relevance of this pathway to autism is important given there is a higher prevalence of internalizing and externalizing symptoms/disorders among autistic individuals than in the general population. Indeed, it is estimated that over 90% of individuals with autism meet DSM criteria for a co-occurring psychiatric disorder (Joshi et al., 2010; Salazar et al., 2015), and although these are not typically diagnosed in children under the age of 2, associated social-emotional difficulties can be identified at a very young age (Briggs-Gowan, Carter, Bosson-Heenan, Guyer, & Horwitz, 2006) suggesting potential for pre-emptive intervention.

While yet to be empirically tested, several lines of evidence suggest that the aforementioned pathway identified in neurotypical children – from caregiver psychological distress to child social-emotional difficulties through child temperament – might extend to young infants with features of autism. Symptoms of psychological distress are higher among caregivers of autistic children than comparison samples (Hayes & Watson, 2013; Yirmiya & Shaked, 2005), and positively associated with children's internalizing and externalizing symptomatology (Carter, Martínez-Pedraza, & Gray, 2009; Herring et al., 2006). Moreover, autistic children demonstrate higher negative affect, lower positive affect/sociability, and lower self-regulation than non-autistic comparison groups (Chetcuti et al., 2019) – a temperament pattern associated with heightened levels of both caregiver psychological distress (Britton, 2011; Olino et al., 2011) and child social-emotional difficulties (Eisenberg et al., 2001, 2009). Prospective studies of infants at higher familial likelihood of developing autism (by virtue of having an older autistic sibling) indicate that a temperament profile consisting of higher negative affect, lower positive affect/sociability, and lower self-regulation might predict subsequent autism diagnosis in toddlerhood (Clifford et al., 2013; Garon et al., 2015; Del Rosario, Gillespie-Lynch, Johnson, Sigman, & Hutman, 2014; Paterson et al., 2019; for a review, see Chetcuti et al., 2019). These findings suggest there may be an early-emerging profile of temperamental susceptibility towards caregiver psychological distress and social-emotional difficulties in autism. However, the relation of temperament characteristics to social-emotional difficulties or caregiver psychological distress has yet to be explored early on in development, among infants with early autism signs.

The establishment of temporal or causal processes is beyond the scope of cross-sectional research. Nevertheless, caregiver-to-child effects were hypothesised and modelled, as studies with longitudinal measures more consistently found an effect of early caregiver attributes on subsequent child temperament than the reverse, when cross-sectional associations and stability of constructs were controlled for (Hanington, Ramchandani, & Stein, 2010; Pesonen et al., 2008), particularly in early life (Eisenberg et al., 2010). In light of evidence suggesting temperament traits function similarly across clinical and non-clinical groups (Burrows, Usher, Schwartz, Mundy, & Henderson, 2016; Schwartz et al., 2009), we expected to replicate the results obtained by Suveg et al. (2011), Choe et al. (2014), and Allen et al. (2018) in a sample of infants with autism features. Specifically, infant negative affectivity and self-regulation were expected to mediate the concurrent relation between caregiver psychological distress and both internalizing and externalizing symptoms, while we anticipated a mediating effect of surgency only for internalizing. A secondary objective was to examine whether results generalize across infants with varying levels of autism features, though we predicted no such effects.

7.4. Method

7.4.1. Participants

Participants were 103 infants aged 9-16 months (M = 12.39, SD = 1.97; 68% male) and their primary caregivers recruited into a larger study [reference withheld for blinded review]. Referral to the study was by community healthcare providers, on the basis of infants showing ≥3 of 5 behavioural markers autism on the Social Attention and Communication Surveillance-Revised (SACS-R) tool (i.e., atypical/absent pointing, waving, imitation, eye contact, response to name; Barbaro & Dissanayake, 2013). The SACS-R is a revised version of the SACS (Barbaro & Dissanayake, 2010) designed as an autism surveillance tool for implementation during routine well-child checks. The SACS-R has an estimated positive predictive value of 72% when used with 12-month-olds for subsequent autism diagnosis (Barbaro, Dissanayake, & Sadka, 2018). Other inclusion criteria were child chronological age between 9- and 14-months 31 days (corrected for prematurity) and caregivers having sufficient English to understand study requirements and participate fully. Exclusion criteria were diagnosed comorbidity known to affect infant neurological and developmental abilities (including gestation <32 weeks) or family intention to relocate within 2 years of enrolment. Caregivers were on average 34.28 years old (SD = 5.05) and predominantly biological mothers (3% biological fathers, 1% guardians). Most infants (n = 80; 78%) had no family history of autism and, among others, an autism diagnosis was reported for an older sibling/s (n = 20) or cousin (n =3).

7.4.2. Procedure and Measures

This study draws on a subset of the data collected at the baseline assessment for the larger study, for which ethical approval was granted by institutional review boards. Baseline assessments occurred an average of 2.53 weeks (SD = 1.50) after eligibility screening. Caregivers provided informed consent and completed a series of questionnaires.

A short form of the Depression Anxiety Stress Scales (DASS-21; Lovibond & Lovibond, 1995) was used to measure caregiver self-reported psychological distress. DASS-21 items (21) are rated on a 4-point Likert scale, ranging from 0 (*Did not apply to me at all) to* 3 (*Applied to me very much or most of the time*). Responses across three subscales (depression, anxiety, stress) were summed to yield an overall score (range 0 to 63).

The Infant-Toddler Social and Emotional Assessment (ITSEA; Carter & Briggs-Gowan, 2006) was used to assess infant internalizing and externalizing symptoms. ITSEA items (170) are rated by caregivers on a 3-point Likert scale ranging from 0 (*Not true/rarely*) to 3 (*Very true/often*), and domain subscale mean scores are averaged to form composite internalizing (consisting of depression/withdrawal, general anxiety, separation distress, and inhibition to novelty) and externalizing (consisting of activity/impulsivity, aggression/defiance, peer aggression) scores (range 0 to 2).

The Infant Behavior Questionnaire-Revised (IBQ-R; Gartstein & Rothbart, 2003) was used to measure child temperament. IBQ-R items (191) are rated by caregivers on a 7-point Likert scale for frequency, ranging from 1 (*Never*) to 7 (*Always*), and fine-grained subscales are averaged to form three higher-order dimension scores: surgency/extraversion (consisting of activity level, smiling and laughter, high intensity pleasure, vocal reactivity, approach, perceptual sensitivity), negative affectivity (consisting of distress to limitations, fear, sadness, falling reactivity) and orienting/regulation (consisting of duration of orienting, low intensity pleasure, cuddliness, and soothability).

Overlapping item content between the ITSEA and IBQ-R was removed to reduce measurement confounding, including the entire inhibition to novelty subscale which measures a temperament-based construct (for more details, see Whitehouse et al., 2020).

Autism features were measured by the Autism Observation Scale for Infants (AOSI; Bryson, Zwaigenbaum, McDermott, Rombough, & Brian, 2008), a direct observational measure that includes a standard set of semi-structured activities. Examiner ratings of (16) target social-communicative, sensory-motor, attentional, and play behaviours, ranging from 0 to 2 or 3, are summed to create a total score (maximum 38). Higher scores on all metrics denoted greater expression of the measured construct(s), including more autism-related behaviour.

7.5. Results

Descriptive statistics and bivariate correlations are presented in Table 1. Child age and sex were considered as potential covariates but were mostly unrelated to other variables (see Table 1)[7]. There were significant inter-correlations among caregiver psychological distress, child social-emotional difficulties (internalizing, externalizing), and negative affectivity in the expected direction. Orienting/regulation and child internalizing and externalizing were negatively correlated, although neither orienting/regulation nor surgency/extraversion were related to parent depression.

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[7]Child age was significantly correlated with externalizing, $r = .26$, $p < .05$. Inclusion of age as a covariate in the mediation model with externalizing as the dependent variable and AOSI Total score as a moderator did not substantively change the results, F (2,88) = 6.35, $R^2 = .36$, $p < .01$. The mediation effect remained significant (B = 0.004, 95% bootstrap CI 0.001 to 0.008), and the direct effect of caregiver psychological distress remained non-significant (B = 0.005, 95% bootstrap CI -0.002 to 0.011). Child age had a significant direct effect on child externalizing, $B = 0.03$, t (85) = 2.54, p <. 05.

Table 1

Descriptive Statistics and Bivariate Correlations Between Study Variables (N = 103)

	n data	α	*n* (%) or *M* (SD)	Range	1	2	3	4	5	6
Child sex (male)	103	-	70 (68%)	-	.05 [-.17, .26]	.02 [-.19, .24]	-.01 [-.22, .20]	.03 [-.24, .18]	-.01 [-.21, .20]	.02 [-.19, .24]
Child age at baseline (months)	103	-	12.39 (1.97)	9.10-16.30	-.10 [-.32, .09]	.06 [-.15, .25]	.26* [.08, .42]	.07 [-.13, .27]	.08 [-.14, .29]	.04 -.18, .25]
SACS-R	103	-		3-5						
3 markers			32 (31%)							
4 markers			34 (33%)							
5 markers			37 (36%)							
1. DASS-21 Total	95	.86	9.41 (7.84)	0-39	-					
2. ITSEA Internalizing	91	.62[a]	0.38 (0.23)	0.00-0.99	.37** [.15, .56]	-				
3. ITSEA Externalizing	88	.82	0.32 (0.25)	0.00-1.21	.24* [-.04, .48]	.23* [.04, .43]	-			
4. IBQ-R Surgency/Extraversion	96	.77	4.40 (0.73)	1.88-5.22	-.05 [-.29, .16]	-.11 [-.33, .11]	.07 [-.19, .31]	-		
5. IBQ-R Negative Affectivity	96	.78	3.28 (0.76)	1.88-5.22	.34** [.12, .53]	.58** [.41, .72]	.45** [.28, .60]	.09 [-.11, .29]	-	
6. IBQ-R Orienting/Regulation	96	.63	4.43 (0.62)	2.95-6.41	-.11 [-.30, .07]	-.21* [-.40, -.01]	-.23* [-.45, .01]	.53** [.37, .67]	-.34** [-.51, -.15]	-
7. AOSI Total	103	.66	8.90 (4.31)	1-28	.07 [-.21, .33]	.29** [.11, .45]	-.07 [-.27, .13]	-.36** [-.54, -.15]	.03 [-.19, .22]	-.05 [-.24, .14]

Note. Correlation coefficients were bootstrapped (5,000 resamples) to account for distributional non-normality. SACS-R = Social Attention and Communication Surveillance-Revised; DASS-21 = Depression Anxiety Stress Scales-21; ITSEA = Infant-Toddler Social and Emotional Assessment; IBQ-R = Infant Behavior Questionnaire-Revised; AOSI = Autism Observation Scale for Infants.

[a] Removal of the item with the lowest corrected item-total correlation increased the value of Cronbach's *α* from .56 to .62 for the ITSEA Internalizing domain.

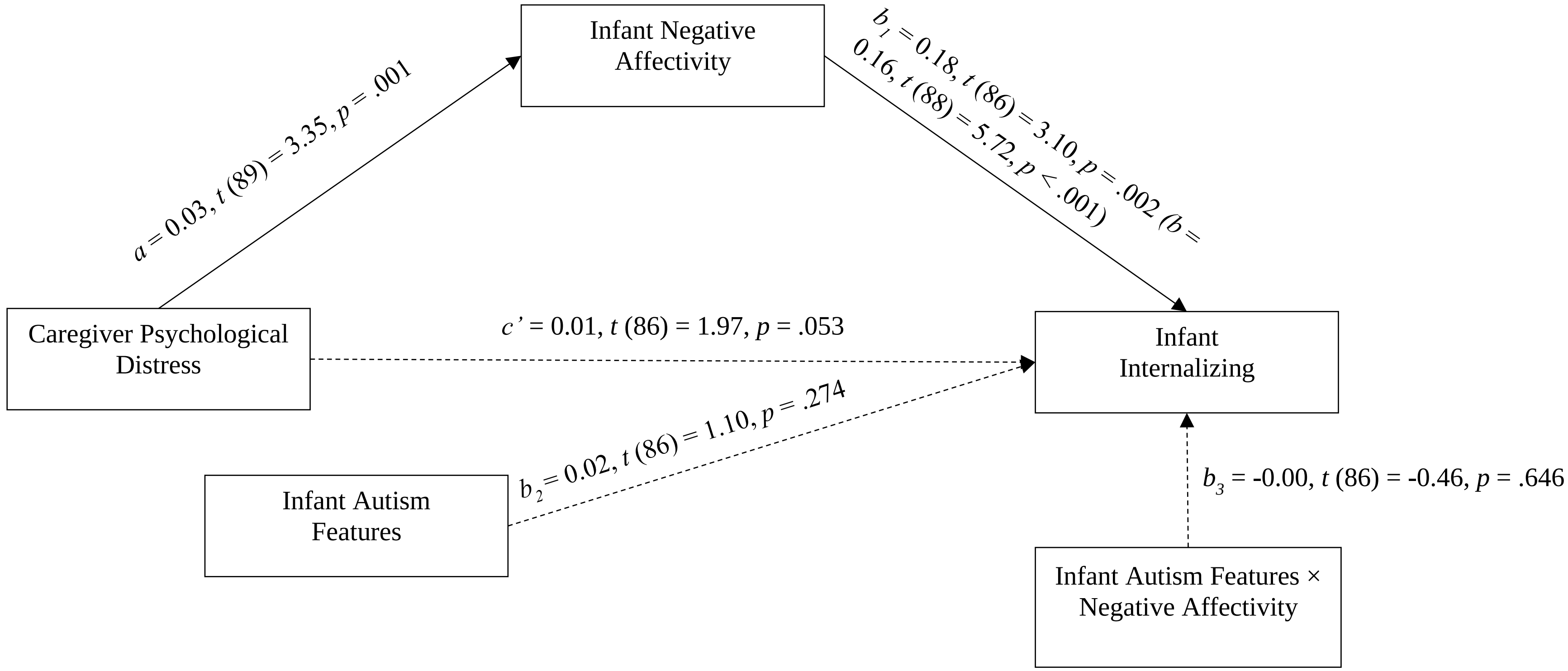
**p* < .05. ***p* < .01.

Analyses were performed using the PROCESS macro for SPSS (Hayes, 2018). Internalizing and externalizing symptoms were examined in separate models as the dependent variable, with caregiver psychological distress as the independent variable and child negative affectivity as the mediator. Listwise deletion of missing values resulted in a sample size of 91 for the internalizing model 88 for the externalizing model. Since significant relations between the proposed mediator(s) and both the dependent and independent variable is a necessary precondition for testing mediation (Hayes, 2018), surgency/extraversion and orienting/regulation were not included in the models.

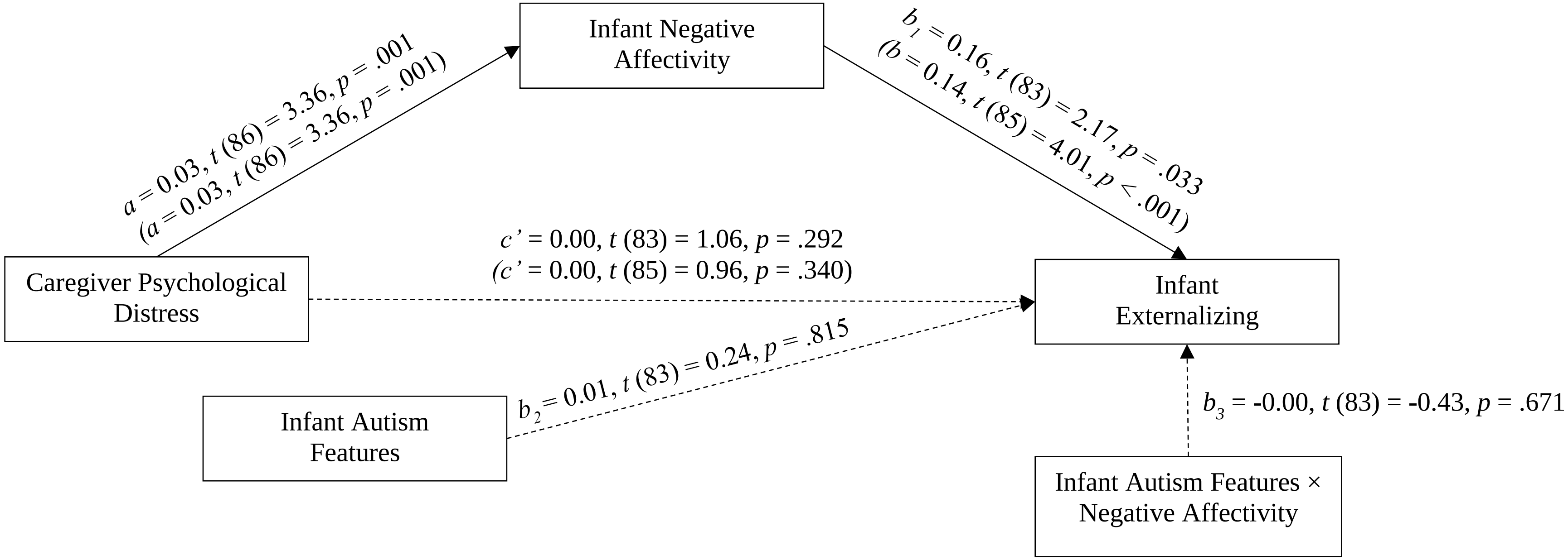
The full model accounted for a significant proportion of the variance in both infant internalizing symptoms, F (2, 88) = 25.30, R^2 = .37, p < .001, and externalizing symptoms, F (2, 85) = 11.11, R^2 = .21, p < .001. There was a significant positive indirect effect ($a \times b$) of caregiver psychological distress on infant internalizing (B = 0.005, 95% bootstrap CI 0.002 to 0.008) and externalizing (B = 0.004, 95% bootstrap CI 0.001 to 0.008) through infant negative affectivity. The direct effect (c') of caregiver psychological distress was significant for infant internalizing (B = 0.005, 95% bootstrap CI 0.002 to 0.011), and non-significant for externalizing (B = 0.003, 95% bootstrap CI -0.003 to 0.010).

Next, AOSI Total score was included in the model as a moderator of the association between negative affectivity and social-emotional difficulties (path b) in order to test the equivalence of temperament pathways across the spectrum of autism expression (i.e., AOSI Total scores ranging from 1, signifying little-to-no autism features, to ≥ 9 predictive of clinical diagnosis; Zwaigenbaum et al., 2005). The mediation effect remained statistically significant in both the internalizing (B = 0.01, 95% bootstrap CI 0.002 to 0.008) and externalizing models (B = 0.004, 95% bootstrap CI 0.001 to 0.009) when AOSI Total score was added as a moderator. However, the direct effect of caregiver psychological distress on infant internalizing was no longer significant. AOSI Total score did not interact with negative affectivity in either model, and there was no direct effect; thus, there was no evidence that the mediating effects of infant negative affectivity – on the relation between caregiver psychological distress and infant social-emotional difficulties – were contingent on infants' autism expression.

Results from these models are depicted in Figure 1.



a) Model predicting infant internalizing symptoms, F (4, 86) = 16.71, R^2 = .44, p < .001



b) Model predicting infant externalizing symptoms, F (4, 83) = 5.75, R^2 = .22, p < .001

Figure 1. Moderated mediation models investigating infant negative affectivity as a mediator of the relation between caregiver psychological distress and infant internalizing (a; n = 91) and externalizing (b; n = 88), including infant autism features as a moderator. Results from the initial mediation model (without the moderator) are also presented within brackets. Regression coefficients are unstandardized, and pathways in bold are significant (p < .05).

7.6. Discussion

This study explored whether the relation of caregiver psychological distress to child social-emotional difficulties through temperament identified previously among neurotypical children extends to young infants with early signs of autism. Consistent with Allen et al. (2018), infant negative affectivity was found to mediate the positive association between caregiver psychological distress and concurrent infant internalizing and externalizing symptoms. There was no moderating effect of AOSI score on these indirect effects; hence, the pathway from caregiver psychological distress to infant negative affectivity to infant social-emotional difficulties may be shared across young children irrespective of whether they have autism features.

Infant orienting/regulation was negatively correlated with internalizing and externalizing symptoms, though unrelated to caregiver psychological distress. This finding contrasts with prior prospective (Hoffman, Crnic, & Baker, 2006) and mediational analyses (Allen et al., 2018; Choe et al., 2014; Suveg et al., 2011) conducted in later childhood, which have shown that caregiver psychological distress predicts children's subsequent emotional dysregulation and, in turn, social-emotional difficulties. The negative impact of caregiver psychological distress on children's self-regulation might thus be dependent on child developmental stage; such that an effect may be apparent for later-developing top-down (deliberate) aspects of self-regulation (e.g., attention switching) but not early-emerging bottom-up (automatic) processes (e.g., attention capture).

Surgency/extraversion was unrelated to caregiver psychological distress and infant social-emotional difficulties in our sample. This is not surprising given previous inconsistencies in the literature linking children's positive affect/sociability to the family environment and developmental outcomes (for reviews, see Putnam, 2012, and Davis & Suveg, 2014). Indeed, Allen et al. (2018) found that positive affect/sociability during childhood did not mediate relations between maternal depression and offspring social-emotional difficulties. Nonetheless, a more nuanced examination of the various facets of positive affect/sociability may help resolve inconsistencies across studies relating these traits to environmental factors and child outcomes.

Level of infant autism features was positively correlated with internalizing symptoms, but unrelated to externalizing symptoms. The latter non-significant association might be due to the young age and limited behavioural repertoire of our sample, as a positive correlation between autism and externalizing symptoms been reported among autistic pre-schoolers (Tureck, Matson, Cervantes, & Turygin, 2015). Further, level of autism features was negatively correlated with temperamental surgency but unrelated to orienting/regulation and negative affectivity; consequently, the nonsignificant interaction of AOSI Total and negative affectivity in the mediation models was not all that surprising.

The results from this study should be interpreted in light of some methodological limitations. First, the cross-sectional design of this study precludes causal inference. We formulated our hypotheses under the assumption that effects flow from caregiver-to-child, although the reverse might also be true. Indeed, Choe et al. (2014) found that toddlers' oppositionality predicted subsequent difficulties with self-regulation and more depressive symptoms for mothers. Studies that have tested bidirectional relations between child temperament and caregiver psychological distress, however, provide more consistent evidence of caregiver evocative effects than vice versa in early childhood (Hanington et al., 2010; Pesonen et al., 2008). The presence and magnitude of caregiver-to-child and child-to-caregiver effects should be elucidated in future studies through use of repeated measures multivariate modelling (e.g., structural equation modelling); specifically, evaluating whether initial child temperament and/or caregiver psychological distress predict subsequent levels of the other construct over and above cross-sectional between-construct associations and within-construct stability over time. Controlling for potential shared genetic influences on child temperament and caregiver psychological distress (e.g., through a genetically informed research design such as illustrated by Micalizzi, Wang, & Saudino, 2017) would further the robustness of this approach.

Next, the use of a single informant and method of assessment may have inflated observed relations between measures. It seems unlikely that the current results were solely due to method variance, however, given associations between caregiver and child outcomes have been observed across different methods of assessment (Goodman et al., 2011). Nonetheless, our results should be interpreted with caution until they are replicated using multiple informants and measurement methods.

Finally, it remains unknown what proportion of infants in our sample will go on to receive an autism diagnosis and/or other clinical diagnoses. The equivalence of the indirect effect of caregiver psychological distress on child social-emotional difficulties (through child temperament) across categorical diagnostic groups should be addressed in future work.

In conclusion, this study is one of few – and, notably, the first in the context of autism – to have explored temperament as a potential mechanism underlying the concurrent relation between caregiver psychological distress and offspring social-emotional difficulties. While preliminary and cross-sectional, these findings suggest the pathway from caregiver psychological distress to child negative affectivity to child internalizing and externalizing identified in neurotypical children might also extend to young infants with early signs of autism. It is hoped that this work will provide impetus for future replications using multiple methods of assessment and longitudinal designs, as the establishment of causal relations would permit clinical translation of these findings. A tentative implication is that child and caregiver affective symptoms should be treated concurrently to promote well-being in the entire family system. Should a caregiver-to-child flow of effects indeed be borne out in longitudinal analyses, the provision of mental health support to caregivers of children with autism symptoms could reduce strain on the caregiver-child relationship and improve children's affective tolerance to, in turn, promote positive social-emotional functioning.

7.7. References

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CHAPTER 8

Study 4

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Child Temperament and Caregiver Psychological Distress Predict the Development of Social-Emotional Difficulties in the Context of Emerging Autism

Lacey Chetcuti[1,2], Mirko Uljarević[3,4], Kandice J. Varcin[5], Maryam Boutrus[2,6], Sarah Pillar[6], Stefanie Dimov[1], Josephine Barbaro[2,7], Cheryl Dissanayake[2,7], Jonathan Green[8,9], Ming Wai Wan[10], Leonie Segal[11], Vicky Slonims[12], Andrew J.O. Whitehouse[2,6], Kristelle Hudry[1], & the AICES Team[13]

[1]Department of Psychology and Counselling, School of Psychology and Public Health, La Trobe University, Australia; [2]Cooperative Research Centre for Living with Autism (Autism CRC), Long Pocket, Brisbane, Queensland, Australia; [3]Stanford Autism Center, Department of Psychiatry and Behavioral Sciences, Child and Adolescent Psychiatry, School of Medicine, Stanford University, USA; [4]Melbourne School of Psychological Sciences, Faculty of Medicine, Dentistry and Health Sciences, The University of Melbourne, Victoria, Australia; [5]School of Allied Health Sciences, Griffith University, Queensland, Australia; [6]Telethon Kids Institute, University of Western Australia; [7]Olga Tennison Autism Research Centre, School of Psychology and Public Health, La Trobe University, Australia; [8]The University of Manchester, Division of Neuroscience and Experimental Psychology, School of Biological Sciences; [9]Manchester Academic Health Science Centre, Manchester University NHS Foundation Trust, Greater Manchester Mental Health NHS Trust; [10]Division of Psychology and Mental Health, School of Health Sciences, University of Manchester; [11]Australian Centre for Precision Health, School of Health Sciences, University of South Australia, Adelaide, South Australia, Australia; [12]Children's Neurosciences, Evelina London Children's Hospital, Institute of Psychiatry, Psychology & Neuroscience, Kings College London, London, UK; [13]the AICES team in alphabetical order: Teresa Iacono, Murray Maybery, Michelle Renton, Nancy Sadka, Leonie Segal, Scott Wakeling, and John Wray.

8.1. Abstract

Child temperament and caregiver psychological distress have been independently associated with social-emotional difficulties among autistic individuals. However, the interrelationship among these risk factors has rarely been investigated. We explored the reciprocal interplay between child temperament (surgency, negative affectivity, and self-regulation) and caregiver psychological distress in the development of child internalizing and externalizing symptoms, drawing on data from a cohort of 103 infants showing early autism traits. Caregivers completed questionnaires when children were aged around 12-months (Time 1 [T1]), 18-months (Time 2 [T2]), and 24-months (Time 3 [T3]). Cross-lagged path models revealed a significant pathway from T1 caregiver psychological distress through lower T2 child self-regulation to subsequently greater T3 child internalizing symptoms. No such caregiver-driven pathway was evident through T2 child negative affectivity or in the prediction of T3 child externalizing symptoms. Further, the pathways from T1 child temperament to T2 caregiver psychological distress to T3 child internalizing or externalizing symptoms were non-significant. Child surgency was mostly unrelated to caregiver psychological distress and social-emotional difficulties. These findings suggest an enduring influence of caregiver psychological distress during infancy on child social-emotional outcomes during toddlerhood, with child emotional dysregulation playing a role in the statistical characterization of this effect.

8.2. Introduction

A diagnosis of autism spectrum disorder (hereafter, *autism*) or the presence of elevated autistic traits is associated with higher severity of internalizing (anxiety and/or depression) and externalizing (inattentive/hyperactive, oppositional, and/or aggressive behaviour) symptoms than observed in the general population (Joshi et al., 2010; Lundström et al., 2011). While the reason for such elevated symptoms has yet to be established, several risk mechanisms and pathways implicated in the typical development of social-emotional difficulties might have similar relevance in the context of autism (Chetcuti, Uljarević, & Hudry, 2019; Mundy et al., 2007). Across populations, a temperamental disposition towards social reticence, and negative and dysregulated emotional responses and experiences have been associated with social-emotional difficulties (for reviews, see Chetcuti, Uljarević, Ellis-Davies, et al., 2020; De Pauw & Mervielde, 2010; Nigg, 2006; Shiner & Caspi, 2003). Further, caregiver psychological distress (anxiety, depression, and/or stress symptoms) has been implicated in the development of internalizing and externalizing symptoms among children with typical development (Goodman et al., 2011; Lawrence, Murayama, & Creswell, 2018) and autism (Yorke et al., 2018).

In a transactional model of child development (Sameroff & Chandler, 1975), mutual influence among these vulnerability factors would be expected. Child temperament and caregiver psychological distress might shape one another over time and, in turn, create a pathway for the development of child internalizing and externalizing symptoms. Relatively few studies have addressed this possibility in typical populations, and even fewer in the context of autism. However, such transactional effects are conceivable given that autism is associated with more challenging temperament characteristics (Chetcuti, Uljarević, Ellis-Davies, et al., 2020) and caregiver psychological distress (Estes et al., 2009, 2013; Green et al., 2020), and with both of these factors independently associated with social-emotional difficulties in this population (Chetcuti, Uljarević, Ellis-Davies, et al., 2020; Yorke et al., 2018). Moreover, vulnerabilities among samples of infants at elevated likelihood for autism suggest the possibility that transactional processes – between child temperament and caregiver psychological distress, leading to the development of social-emotional difficulties – might be underway early in life, when autism is still emerging.

8.2.1. Vulnerability for Social-Emotional Difficulties in Autism

8.2.1.1. Child temperament

Differences in temperament associated with an autism diagnosis are well-documented in the literature, and have been linked with concurrent and prospective social-emotional difficulties (Chetcuti, Uljarević, Ellis-Davies, et al., 2020). The findings are parallel among later-diagnosed infants with a family history of autism: higher negative emotionality-related traits and emotional and behavioural dysregulation is apparent from around the first birthday onward (Clifford et al., 2013; Paterson et al., 2019; Pijl et al., 2019; Zwaigenbaum et al., 2005) and followed by lower levels of sociability/positive affectivity around the second year (Garon et al., 2009; Paterson et al., 2019; Pijl et al., 2019; but see Clifford et al., 2013), compared to undiagnosed low-familial-likelihood controls. These temperament differences are also apparent, albeit to a lesser extent, among high-familial-likelihood infants without autism diagnosis who exhibit subthreshold autistic traits and/or developmental delays (Pijl et al., 2019). Moreover, temperament in elevated likelihood infants has been prospectively associated with social-emotional difficulties. Shephard et al. (2019) found that high shyness and fearfulness in early-life (measured at 7-, 14-, and 24 months) were associated with anxiety symptoms in mid-childhood (at age 7-years), whereas high early-life activity level and poor inhibitory control were associated with mid-childhood inattentive and hyperactive/impulsive symptoms. Correspondingly, Hendry et al. (2020) found that plateaued growth of attentional control between 10 and 25 months of age predicted elevated inattentive and hyperactive/impulsive symptoms among children at elevated autism likelihood at age 3 years.

8.2.1.2. Caregiver psychological distress

Caregivers of children on the autism spectrum encounter many challenges navigating and advocating for their child’s needs and coming to terms with their child’s differences. Compared to caregivers of children with typical development and developmental disorders/delays, caregivers of autistic children report higher parenting-related stress (Estes et al., 2013; Hayes & Watson, 2013) and more depression and anxiety symptoms (Baker et al., 2011; Estes et al., 2009) which, in turn, may increase their child’s social-emotional difficulties. Yorke et al. (2018) conducted a meta-analysis of 61 cross-sectional studies examining associations between caregiver psychological distress and autistic children’s social-emotional difficulties. Pooled concurrent correlations were of small-to-moderate magnitude, and slightly stronger than those found in a comparable meta-analysis of typical population data (i.e., Goodman et al., 2011). The associations for autism appeared similar in strength across child internalizing and externalizing symptoms and for caregivers recruited from clinical vs non-clinical settings and, in most studies, remained significant after adjusting for child age, sex, IQ, and autism severity (Yorke et al., 2018). Longitudinal studies of autistic children and adolescents have reported significant associations of earlier caregiver psychological distress with subsequently higher child social-emotional difficulties (Simonoff et al., 2013), but not with *change* in social-emotional difficulty levels over time (Baker et al., 2011; Peters-Scheffer et al., 2012; Totsika et al., 2013; see Yorke et al., 2018). Yet, caregiver psychological distress may have a distinct impact on social-emotional development during infancy and toddlerhood, when signs of autism are emerging.

8.2.1.3. Child temperament in relation to caregiver psychological distress

Research on autism provides some evidence of association between child temperament characteristics and psychological distress among caregivers. Caregiver psychological distress has been associated with children's concurrent temperamental 'difficulty' (Kasari & Sigman, 1997), lability (Özyurt et al., 2018), and behavioural inflexibility/rhythmicity and low positive emotionality, but not approach/withdrawal (Konstantareas & Papageorgiou, 2006) in middle childhood. Similarly, in a community-referred cohort of 103 infants showing early signs of autism, we recently found caregiver psychological distress to be concurrently associated with infant negative emotionality, but not with infant sociability or self-regulation (Chetcuti, Uljarević, Varcin et al., 2020). This latter finding is contrary to what has been found for autistic children in mid-childhood (Konstantareas & Papageorgiou, 2006) and also among older children with typical development (Hughes et al., 2013), suggesting that an association between caregiver psychological distress and child self-regulation might only become apparent as children age.

Taken together, previous research indicates that autism is associated with a specific pattern of temperament from the first two years of life to the point of diagnosis and beyond – one characterised by high negative emotionality, low sociability/positive affectivity, and low self-regulation (Chetcuti, Uljarević, Varcin et al., 2020). Such differences are also apparent in early life, among infants at elevated likelihood of autism regardless of eventual diagnostic outcome. Further, the degree to which children express these qualities appears to be positively related to concurrent social-emotional difficulties. Longitudinal studies provide some evidence of temperament effects on child social-emotional difficulties over time, particularly for elements of negative emotionality and self-regulation. Furthermore, caregivers of children with autism traits are prone to psychological distress. The extent of such distress relates positively to concurrent, but not to subsequent, social-emotional difficulties (at least during the developmental period of mid-to-late childhood). Finally, evidence of concurrent associations between child temperament and caregiver psychological distress suggests these factors may combine to predict child social-emotional outcomes. Indeed, longitudinal studies of typical development show that child temperament predicts caregiver psychological distress and vice versa (Brooker et al., 2015; Forbes et al., 2008; Sugawara et al., 1999), and that such effects may shape children's social-emotional development (Allen et al., 2018; Behrendt et al., 2019; Choe et al., 2014; Roman et al., 2016), consistent with a transactional model of development.

8.2.2. Caregiver-Driven and Child-Driven Pathways to Child Social-Emotional Difficulties

Despite evidence that child temperament and caregiver psychological distress are influenced by autism, and associated with each other and with children's social-emotional difficulties, only a few studies have explored potential pathways linking these factors. Totsika et al. (2013) explored unidirectional, child-to-caregiver effects in a birth cohort of 132 autistic children and their mothers. There was no evidence suggesting that caregiver psychological distress (at child age 3-years) mediated the path from infant difficult temperament (at child age 9-months) to subsequent child internalizing or externalizing symptoms (at 5-years). Recently, we conducted a cross-sectional investigation – of which the present study is a longitudinal extension – of caregiver-to-child effects in a community-referred cohort of 103 infants showing early signs of autism (Chetcuti, Uljarević, Varcin et al., 2020). Infant negative affectivity was found to statistically mediate positive relations between caregiver psychological distress and concurrent infant internalizing and externalizing symptoms. The cross-sectional design of this study does not permit causal inferences; nevertheless, studies comprising children with typical development evidence this direction of effects.

In a sample of 132 mother-child dyads, Allen et al. (2018) reported an indirect effect from maternal depression (at child age 20-months) to subsequent child internalizing and externalizing symptoms (at 9-years) mediated by child temperament (at 5-years), specifically, high child neuroticism – a personality construct that overlaps conceptually with temperamental negative affectivity (De Pauw & Mervielde, 2010) – and by low conscientiousness, akin to temperamental self-regulation. However, there was no such indirect effect of maternal depression on child internalizing or externalizing symptoms through child extraversion (i.e., akin to temperamental sociability). Similarly, among 143 mother-child dyads, Roman et al. (2016) found an indirect effect of maternal self-reported depression (at child age 2-years) on subsequent teacher-reported child internalizing and externalizing problems (at age 6-years) through children's observed self-regulatory abilities (at age 3-years). Finally, Choe et al. (2014) found an indirect pathway from maternal depression (at child age 2-years) to subsequent child oppositional behaviour (at 4-years), via interim child inhibitory control (at age 3).

Behrendt et al. (2019) incorporated examination of longitudinal effects in the reverse direction, from child temperament through caregiver psychological distress to child social-emotional difficulties. From the simultaneous examination of caregiver-to-child and child-to-caregiver effects it is possible to derive conclusions regarding transactional processes, and compare the relative strength of effects in one vs. the other direction. Behrendt et al. (2019) found that parental postpartum anxiety predicted higher child negative affectivity and lower effortful control (at age 24-months) which, in turn, predicted subsequently higher child social-emotional difficulties (at 36-months). Here too, however – and as with Allen et al.'s (2018) study – there were no such indirect effects mediated through child surgency. Moreover, there was no evidence of an indirect effect driven by infant temperament through caregiver psychological distress to subsequent child social-emotional difficulties (Behrendt et al., 2019).

8.2.3. The Present Study

Building from our previous cross-sectional study (Chetcuti, Uljarević, Varcin et al., 2020), the current study sought to determine whether reciprocal relations among caregiver psychological distress and child temperament might predict the subsequent development of internalizing and externalizing symptoms among children with early autism traits. Based on a transactional model of child development and past findings from typical development, we predicted parallel pathways from (a) earlier child temperament to subsequent child internalizing and externalizing symptoms through caregiver psychological distress and (b) earlier caregiver psychological distress to subsequent child internalizing and externalizing symptoms through child temperament, with effects following the latter pathway stronger than the former. Regarding specific temperament dimensions, we anticipated that greater caregiver psychological distress might be associated with higher child negative affectivity and lower self-regulation at child ages 12- and 18-months, but not related to child surgency. We expected that higher caregiver psychological distress, higher child negative affectivity, and lower child self-regulation at age 18-months would be associated with higher child internalizing and externalizing symptoms at 24-months. Finally, levels of child surgency at 18-months were expected to contribute to the prediction of internalizing and externalizing symptoms at 24-months. We also examined whether longitudinal pathways involving child temperament and caregiver psychological distress varied as a function of children's autism symptoms, but did not expect differential effects.

8.3. Method

8.3.1. Participants and Study Design

Participants were 103 children (68% male, 32% female) and their primary caregiver (96% biological mothers, 3% biological fathers, 1% guardians; mean age 34.28 years at study entry) recruited into a larger study (see Whitehouse et al., 2019 for more details). Referral to the study was by community healthcare providers, for infants showing ≥3 of 5 behavioural markers of autism on the Social Attention and Communication Surveillance-Revised (SACS-R) tool (i.e., atypical/absent pointing, waving, imitation, eye contact, response to name; Barbaro & Dissanayake, 2013; Mozolic-Staunton, Donelly, Yoxall, & Barbaro, 2020). Other inclusion criteria were child chronological age between 9- and 14-months 31 days (corrected for prematurity for infants born <37 weeks) and caregivers having sufficient English language to understand study requirements and participate fully. Exclusion criteria included a diagnosed comorbidity known to affect infant neurological and developmental abilities (including gestation <32 weeks) or family intention to relocate away from study sites within 2 years of enrolment.

Families attended an initial assessment visit (Time 1 [T1]; mean child age 12.39 months, range 9.07 to 16.33) that included child behavioural assessments and caregiver completion of questionnaires. Follow-up assessments were conducted approximately 6-months (Time 2 [T2]; mean child age 18.57 months, range 15.11 to 23.32) and 12-months (Time 3 [T3]; mean child age 24.67 months, range 20.37 to 29.76) after the T1 visit.

8.3.2. Measures

Child temperament was assessed using the caregiver-report Infant Behavior Questionnaire-Revised (IBQ-R; Gartstein & Rothbart, 2003) at T1 and Early Childhood Behavior Questionnaire (ECBQ; Putnam, Gartstein, & Rothbart, 2006) at T2. IBQ-R items (191) and ECBQ items (201) are presented as questions (e.g., "When being dressed or undressed, how often did your child squirm and try to get away?") and caregivers rate the frequency of the behaviour over the preceding one or two weeks (1 = *Never* to 7 = *Always*). To ensure the same temperament constructs were being measured at each timepoint, overarching dimensions were formed from the average of scales that appeared on both the IBQ-R and ECBQ: Surgency (comprising Activity Level, High Intensity Pleasure. and Approach scales), Negative Affectivity (comprising Fear, Frustration, and Sadness scales), and Self-Regulation[8] (comprising Soothability, Cuddliness, Low Intensity Pleasure, and Attention Focusing). Equivalent IBQ-R/ECBQ dimensions were significantly correlated and demonstrated good internal consistency at each timepoint (see Table 2).

Caregiver psychological distress was assessed using a short form of the Depression Anxiety Stress Scales (DASS-21; Lovibond & Lovibond, 1995) at T1 and T2. DASS-21 items (21) are presented as statements (e.g., "I found it hard to wind down") and rated for applicability over the preceding week (0 = *Did not apply to me at all* to 3 = *Applied to me very much or most of the time*). Responses across three subscales (Depression, Anxiety, Stress) were summed to yield an overall score (range 0 to 63). The DASS-21 demonstrated excellent internal consistency at each timepoint (see Table 2).

Child social-emotional functioning was assessed using the caregiver-report Infant-Toddler Social and Emotional Assessment (ITSEA; Carter & Briggs-Gowan, 2006) at all timepoints. ITSEA items (166) are presented as statements (e.g., "Cries or hangs onto you when you try to leave") and caregivers rate the applicability of behavioural descriptions to their child over the preceding month (1 = *Not True/Rarely* to 3 = *Very True/Often*). Raw subscale means were summed to form Internalizing (including Depression/Withdrawal, General Anxiety, Separation Distress, and Inhibition to Novelty) and Externalizing (including Activity/Impulsivity, Aggression/Defiance, and Peer Aggression) domain composite scores. To reduce measurement

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[8] This dimension was labelled 'Self-Regulation' rather than 'Effortful Control' given the omission of most ECBQ subscales indexing *effortful* components of regulation.

confounding, following Chetcuti, Uljarević, Varcin et al. (2020), ITSEA items that were conceptually and semantically similar to IBQ-R and ECBQ items were excluded from the computation of domain composite raw scores, as was the entire subscale assessing Inhibition to Novelty (a temperament-based construct). ITSEA domains have good inter-rater agreement (r=.70 to .78; Carter & Briggs-Gowan, 2006) and the modified domains demonstrated adequate/good internal consistency in the current dataset at all timepoints (see Table 2).

Sample socio-demographic characteristics were ascertained by questionnaire at study entry. Child sex, caregiver education level (Secondary, Tertiary, or University), and annual household income (≤$78k, >$78k and <$104k, or >$104k) were examined as potential covariates (see Table 1).

Child autism symptoms were ascertained at study entry using the Autism Observation Scale for Infants (AOSI; Bryson, Zwaigenbaum, McDermott, Rombough, & Brian, 2008). The AOSI is an examiner-administered, semi-structured observational assessment of behavioural autism traits in infancy, including aspects of visual attention, social communication, play, and sensory-motor development. Target behaviours (19) are rated on a 2- or 3-point scale (where 0 implies typical behaviour and higher values indicate increasing atypicality) and key items (16) are summed to yield a total score (range 0 to 38), which was considered here as a moderator variable.

8.3.3. Statistical Analyses

Cross-lagged path models were used to explore the longitudinal effects of child temperament and caregiver psychological distress on children's social-emotional difficulties. The effects of potential covariates on study variables were explored using ANOVA and *t*-tests with Bonferonni-adjusted post-hoc testing, including child sex, caregiver education level, and annual household income. Zero-order correlations were computed among the DASS-21, IBQ-R/ECBQ dimensions (Surgency, Negative Affectivity, Self-Regulation), and ITSEA domains (Internalizing, Externalizing) within and across timepoints. These analyses were bootstrapped with 2,000 replications to account for positive skew of the DASS-21 and ITSEA.

Cross-lagged path analysis was conducted in M*plus* Version 8 (Muthén & Muthén, 1998-2017) using the robust maximum likelihood estimator appropriate for smaller samples and non-normal data (Muthén & Asparhouhov, 2002). Models were run separately for each IBQ-R/ECBQ dimension and ITSEA domain, with concurrent correlations and longitudinal autoregressive, cross-lagged, and indirect effects estimated simultaneously. When statistically significant indirect effects were found, an interaction term was added to the model (T1 predictor × T1 AOSI) to test the potential moderating role of child AOSI score at T1 on predictive relations between child temperament and caregiver psychological distress. Model fit was assessed with the χ^2 statistic (where p>.05 indicates good fit), root mean square error of approximation (RMSEA; where ≤ 0.06

indicates good fit), Tucker-Lewis index (TLI; where ≥ 0.90 indicates good fit), and standardized root mean square residual (SRMR; where < 0.08 indicates good fit).

8.4. Results

8.4.1. Preliminary Analysis of Potential Covariates

Results from the ANOVA and *t*-tests are presented in Table 1. To summarise, there was no statistically significant effect of child sex or caregiver education level on IBQ-R/ECBQ, DASS-21, or ITSEA scores based on Bonferroni-adjusted p-value of .004. Caregivers from lower income households (<$AUD78,000 per year) had higher DASS-21 and ITSEA scores at each timepoint than those from higher income households (>$AUD104,000).

Table 1

Effects of Participant Demographic Characteristics on Study Variables

	Child Sex					Caregiver Education Level						Annual Household Income					
	Male *n* = 70	Female *n* = 33				Secondary *n* = 25	Tertiary *n* = 16	University *n* = 61				≤$78k *n* = 24	>$78k ≤104k *n* = 19	>$104k *n* = 49			
	M (*SD*)	*M* (*SD*)	*t*	*df*	*p*	*M* (*SD*)	*M* (*SD*)	*M* (*SD*)	*F*	*df*	*p*	*M* (*SD*)	*M* (*SD*)	*M* (*SD*)	*F*	*df*	*p*
Time 1																	
IBQ-R Sur	4.92 (0.67)	4.93 (0.62)	-0.06	94	.954	4.67 (0.69)	4.81 (0.55)	5.05 (0.64)	3.22	2,92	.044	4.84 (0.77)	4.56 (0.67)	5.09 (0.50)	4.71	2,82	.012
IBQ-R Neg	3.36 (0.80)	3.43 (0.76)	-0.40	94	.691	3.24 (0.74)	3.47 (0.85)	3.42 (0.80)	0.50	2,92	.606	3.77 (0.85)	3.31 (0.63)	3.18 (0.72)	4.82	2,82	.010
IBQ-R SReg	4.41 (0.64)	4.48 (0.60)	-0.41	94	.635	4.43 (0.73)	4.25 (0.49)	4.47 (0.61)	0.74	2,92	.481	4.40 (0.60)	4.17 (0.54)	4.54 (0.62)	2.41	2,82	.096
DASS-21	10.00 (7.99)	11.32 (9.63)	-0.71	93	.482	11.04 (7.26)	12.00 (8.79)	10.02 (8.98)	0.34	2,91	.715	16.41^{a} (11.62)	7.71 (5.01)	8.82^{b} (7.31)	7.45	2,81	<.004
ITSEA Int	0.46 (0.22)	0.50 (0.27)	-0.30	89	.768	0.33 (0.23)	0.39 (0.21)	0.41 (0.24)	0.92	2,87	.402	0.53^{a} (0.28)	0.33 (0.21)	0.32^{b} (0.20)	6.34	2,77	.003
ITSEA Ext	0.49 (0.25)	0.33 (0.24)	-0.28	87	.994	0.30 (0.26)	0.29 (0.25)	0.30 (0.24)	0.01	2,85	.991	0.46^{a} (0.31)	0.24 (0.14)	0.23^{b} (0.21)	7.50	2,75	<.004
Time 2																	
ECBQ Sur	4.61 (0.70)	4.30 (0.73)	1.98	89	.051	4.33 (0.84)	4.61 (0.75)	4.55 (0.67)	0.89	2,87	.414	4.45 (0.66)	4.31 (0.86)	4.56 (0.71)	0.78	2,80	.463
ECBQ Neg	2.83 (0.79)	3.03 (0.89)	-1.10	88	.273	2.71 (0.73)	3.42 (1.12)	2.85 (0.76)	3.39	2,86	.038	3.28 (0.99)	3.03 (0.74)	2.71 (0.77)	3.71	2,80	.029
ECBQ SReg	4.58 (0.61)	4.52 (0.77)	0.37	88	.712	4.37 (0.58)	4.49 (0.62)	4.66 (0.71)	1.51	2,86	.227	4.43 (0.67)	4.39 (0.78)	4.65 (0.65)	1.21	2,80	.303
DASS-21	10.58 (8.37)	12.31 (9.85)	-0.87	89	.388	11.82 (10.68)	12.54 (11.52)	10.54 (7.39)	0.35	2,88	.704	19.00^{a} (11.59)	9.44^{b} (7.92)	8.50^{c} (5.71)	12.75	2,79	<.004
ITSEA Int	0.38 (0.23)	0.40 (0.29)	-0.66	86	.509	0.42 (0.21)	0.55 (0.33)	0.48 (0.24)	0.99	2,84	.378	0.61 (0.31)	0.46 (0.26)	0.42 (0.20)	4.22	2,78	.018
ITSEA Ext	0.30	0.30	2.26	86	.027	0.43	0.52	0.42	0.52	2,84	.595	0.62^{a}	0.43	0.34^{b}	6.09	2,78	<.004

	(0.33)	(0.23)				(0.28)	(0.37)	(0.31)				(0.40)	(0.24)	(0.26)			
Time 3																
ITSEA Int	0.47 (0.22)	0.54 (0.28)	-1.25	78	.216	0.47 (0.26)	0.50 (0.26)	0.50 (0.24)	0.13	2,77	.882	0.66^{a} (0.23)	0.57 (0.26)	0.40^{b} (0.22)	8.43	2,69	<.004
ITSEA Ext	0.45 (0.28)	0.41 (0.27)	0.58	78	.562	0.47 (0.21)	0.52 (0.28)	0.41 (0.30)	0.97	2,77	.384	0.50 (0.27)	0.46 (0.30)	0.38 (0.28)	1.25	2,69	.292

Note. Means with different superscripts in the same row/column are significantly different at (Bonferroni-adjusted) $p < .004$. IBQ-R = Infant Behavior Questionnaire – Revised; Sur = Surgency; Neg = Negative Affectivity; SReg = Self-Regulation; DASS-21 = Depression Anxiety Stress Scales; ITSEA = Infant-Toddler Social and Emotional Assessment; Int = Internalizing; Ext = Externalizing; ECBQ = Early Childhood Behavior Questionnaire.

8.4.2. Zero-Order Concurrent and Longitudinal Correlations

Table 2 summarises the correlations between the DASS-21, IBQ-R/ECBQ dimensions, and ITSEA domains within and across timepoints. Significant positive concurrent correlations were apparent among child negative affectivity, caregiver psychological distress, and child internalizing and externalizing symptoms at both T1 and T2. Significant negative correlations were apparent between child self-regulation and concurrent internalizing symptoms at T1, and among concurrent child self-regulation, caregiver psychological distress, and child internalizing and externalizing symptoms at T2. Child surgency was positively correlated with concurrent externalizing symptoms at T2, but not at T1, and unrelated to concurrent caregiver psychological distress and internalizing symptoms at both timepoints.

T1 and T2 surgency were weakly correlated, whereas all other *intra*-construct longitudinal correlations were of moderate-to-strong magnitude. Moderate-to-strong *inter*-construct longitudinal correlations were also apparent. Child negative affectivity and caregiver psychological distress were positively correlated with one another across timepoints, and with children's subsequent internalizing and externalizing symptoms. T1 caregiver psychological distress was correlated with T2 child self-regulation, but not vice versa. T1 and T2 child self-regulation were correlated with T2 and T3 internalizing and externalizing symptoms, respectively. T1 caregiver psychological distress was correlated with T2 child internalizing symptoms, but not T2 externalizing symptoms, whereas caregiver psychological distress at T2 was correlated with both of child internalizing and externalizing symptoms at T3. Finally, surgency at T2 was positively correlated with internalizing at T3, but not associated with subsequent or preceding caregiver psychological distress nor with subsequent externalizing symptoms.

Table 2

Descriptive Statistics, Internal Consistency Coefficients, and Zero-Order Correlations of Study Variables

	***n*[a]**	***M* (*SD*)**	**1.**	**2.**	**3.**	**4.**	**5.**	**6.**	**7.**	**8.**	**9.**	**10.**	**11.**	**12.**	**13.**	**14.**
Time 1																
1. IBQ-R Sur	96	4.95	**.84**	.13	.47***	-.07	-.17	.18	.37**	.03	.40**	-.15	-.16	-.13	-.21	-.09
		(0.66)		-08,.33	.30,.61	-30,.15	-.41,.09	.03,.37	.15,.58	-18,.24	.21,.57	-.38,.10	-.38,.09	-.30,.06	-.40,.02	-.28,.11
2. IBQ-R Neg	96	3.39		**.92**	-.35**	.35**	.56**	.42**	.19	.52**	-.39**	.31**	.44**	.39**	.44**	.32**
		(0.78)			-.50,-.10	.07,.57	.37,.72	.21,.59	-.03,.39	.30,.67	-.58,-.18	.11,.49	.21,.61	.15,.59	.25,.60	.08,.51
3. IBQ-R SReg	96	4.43			**.83**	-.13	-.29*	.11	.16	-.19	.64**	.13	-.26*	-.32**	-.34**	-.24*
		(0.62)				-.34.09	-.51,-.02	-.34,.12	-.12,.39	-.39,.02	.49,.75	-.31,.08	-.49,.02	-.49,-.12	-.54,-.11	-.44,-.02
4. DASS-21	95	9.41				**.92**	.36**	.24*	.03	.28*	-.24*	.73**	.27*	.23	.37**	.13
		(7.85)					.09,.59	-.09,.51	-.19,.27	.05,.49	-.44,-.02	.59,.85	-.02,.54	-.01,.46	.17,.55	-.08,.34
5. ITSEA Int	91	0.39					**.53**	.20	-.03	.41**	-.40**	.32**	.69**	.34**	.53**	.14
		(0.24)						.01,.39	-.29,.26	.23,.58	-.61,-.15	.05,.55	.53,.80	.16,.51	.33,.69	-.10,.40
6. ITSEA Ext	88	0.30						**.78**	.22	.28*	-.24*	.31**	.14	.53**	.31**	.54**
		(0.23)							.06,.39	.02,.52	-.48,-.02	.03,.55	-.12,.41	.28,.75	.10,.49	.31,.74
Time 2																
7. ECBQ Sur	90	4.33							**.83**	.25*	.16	.01	-.10	.31**	-.09	.20
		(0.68)								.03,.46	-.12,.41	-.24,.27	-.33,.19	.15,.45	-.34,.18	-.02,.39
8. ECBQ Neg	90	2.33								**.92**	-.40**	.30*	.60**	.50**	.56**	.41**
		(0.70)									-.58,-.17	.11,.47	.45,.72	.30,.65	.40,.69	.19,.56
9. ECBQ SReg	90	4.56									**.93**	-.25*	-.45**	-.47**	-.51**	-.36**
		(0.67)										-.44,-.05	-.63,-.20	-.64,-.28	-.67,-.31	-.56,-.10
10. DASS-21	91	10.02										**.92**	.28*	.32**	.40**	.29*
		(8.18)											.06,.50	.14,.49	.24,.57	.07,.50

11. ITSEA Int	88	0.48												**.72**	.33**	.70**	.21
		(0.25)													.11,.52	.55,.79	-.03,.43
12. ITSEA Ext	88	0.43													**.92**	.44**	.70**
		(0.29)														.23,.63	.53,.83
Time 3																	
13. ITSEA Int	79	0.51														**.72**	.35**
		(0.50)															.12,.56
14. ITSEA Ext	79	0.45															**.89**
		(0.37)															

Note. Cronbach α values are presented in bold on the diagonal and correlation coefficients above the diagonal. Bias-corrected and accelerated (BCa) confidence intervals are presented below correlation coefficients. [a] Number of participants with available data. IBQ-R = Infant Behavior Questionnaire-Revised; Sur = Surgency; Neg = Negative Affectivity; SReg = Self-Regulation; DASS-21 = Depression Anxiety Stress Scales; ITSEA = Infant-Toddler Social and Emotional Assessment; Int = Internalizing; Ext = Externalizing; ECBQ = Early Childhood Behavior Questionnaire.

*$p < .05$. **$p < .01$. ***$p < .001$.

8.4.3. Cross-Lagged Path Analysis of Independent and Reciprocal Longitudinal Effects

Separate cross-lagged path models were computed for child negative affectivity and self-regulation and for child internalizing and externalizing symptoms (four models in total), though child surgency was not examined further given largely nonsignificant zero-order correlations with other study variables (see Table 2). Annual household income was included as a covariate in each model given the relation with caregiver psychological distress and child social-emotional difficulties (see Table 1).

Model 1 predicting child internalizing symptoms from child negative affectivity and caregiver psychological distress provided a good fit to the data according to all indices, $\chi^2(11) = 9.19$, $p = .604$, RMSEA = 0.00 (90% CI 0.00-0.09), CFI = 1.00, TLI = 1.02, SRMR = 0.05, as did Model 2 predicting child internalizing from child self-regulation and caregiver psychological distress, $\chi^2(11) = 12.72$, $p = .312$, RMSEA = 0.04 (90% CI 0.00-0.11), CFI = 0.99, TLI = 0.98, SRMR = 0.06. Results of Model 1 and 2 are depicted in Figure 1. By contrast, poor fit was apparent for Model 3 predicting child externalizing symptoms from child negative affectivity and caregiver psychological distress, $\chi^2(11) = 21.36$, $p < .05$, RMSEA = 0.10 (90% CI 0.03-0.16), CFI = 0.95, TLI = 0.88, SRMR = 0.09, and Model 4 predicting child externalizing symptoms from child self-regulation and caregiver psychological distress, $\chi^2(11) = 21.74$, $p < .05$, RMSEA = 0.10 (90% CI 0.03-0.16), CFI = 0.94, TLI = 0.87, SRMR = 0.10. Results of Model 3 and 4 are depicted in Figure 2.

The autoregressive paths were positive and significant in all models, indicating that subsequent levels of each construct were predicted by earlier levels of the same construct. In Model 1, caregiver psychological distress was concurrently correlated with child negative affectivity and internalizing symptoms at T1 but not at T2, whereas, at both timepoints, child negative affectivity was correlated with internalizing symptoms. There were no cross-lagged T1 to T2 effects among child negative affectivity and caregiver psychological distress, though both factors at T2 were associated at trend-level with T3 child internalizing symptoms ($p = .056$ and $p = .057$).

In Model 2, child self-regulation was correlated with concurrent internalizing symptoms at both T1 and T2, but unrelated to caregiver psychological distress. Caregiver psychological distress was concurrently associated with child internalizing symptoms at T1, but not at T2. There was a significant indirect, cross-lagged effect from T1 caregiver psychological distress to T2 child self-regulation to subsequent T3 child internalizing symptoms ($\beta = .03$, $p < .05$). However, T2 caregiver psychological distress was not predicted by earlier T1 child self-regulation, or predictive of subsequent T3 child internalizing symptoms.

In Model 3, child negative affectivity was correlated with concurrent externalizing symptoms at both timepoints and T1 caregiver psychological distress, but not T2. Caregiver psychological distress was correlated with concurrent child externalizing symptoms at T2, but not T1. There were no cross-lagged T1 to T2 effects between child negative affectivity and caregiver psychological distress, and neither factor at T2 was associated with T3 child externalizing symptoms.

In Model 4, non-significant concurrent correlations were apparent between child self-regulation and caregiver psychological distress at both T1 and T2, and between caregiver psychological distress and child externalizing symptoms. Child self-regulation was correlated with concurrent externalizing symptoms at T2, but not T1. There was a trend-level association between T1 caregiver psychological distress and subsequent T2 child self-regulation (p = .056), but remaining cross-lagged effects – from T1 self-regulation to subsequent T2 caregiver psychological distress, and from T2 child self-regulation and T2 caregiver psychological distress to subsequent T3 child externalizing symptoms – were non-significant.

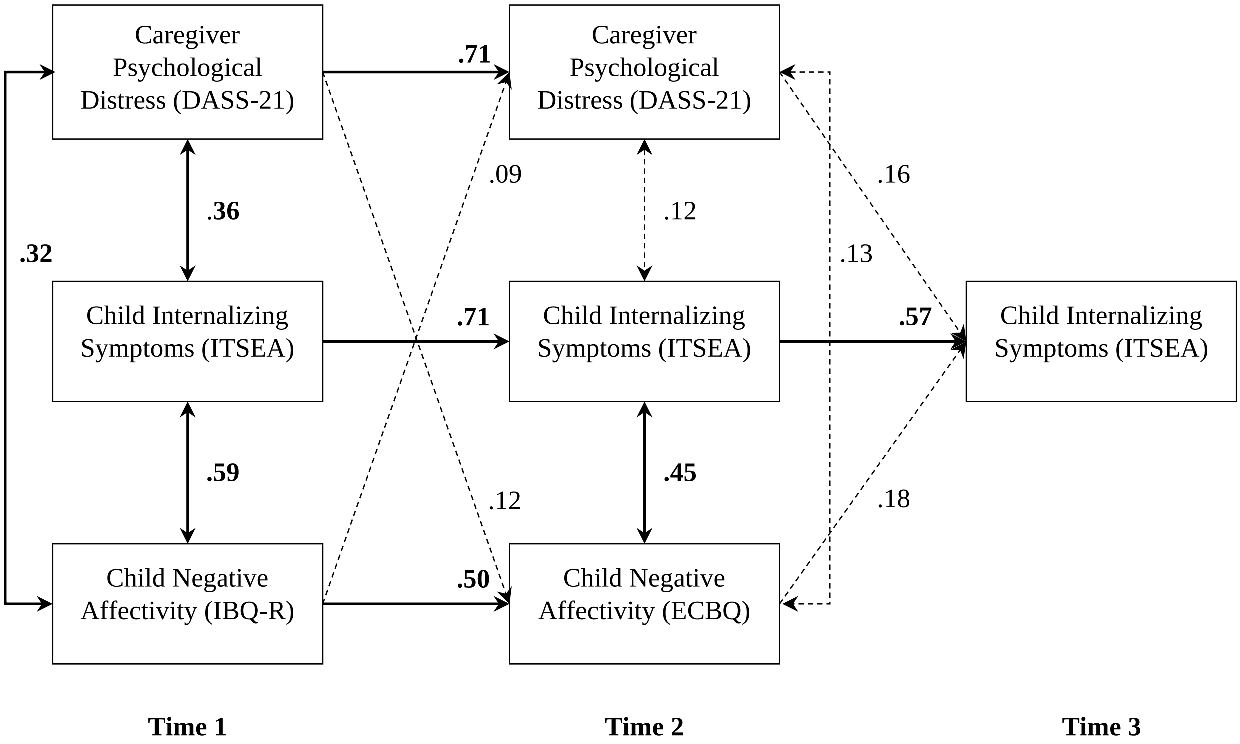

Figure 1a. Model 1 predicting child internalizing symptom outcomes from earlier child negative affectivity and caregiver psychological distress.

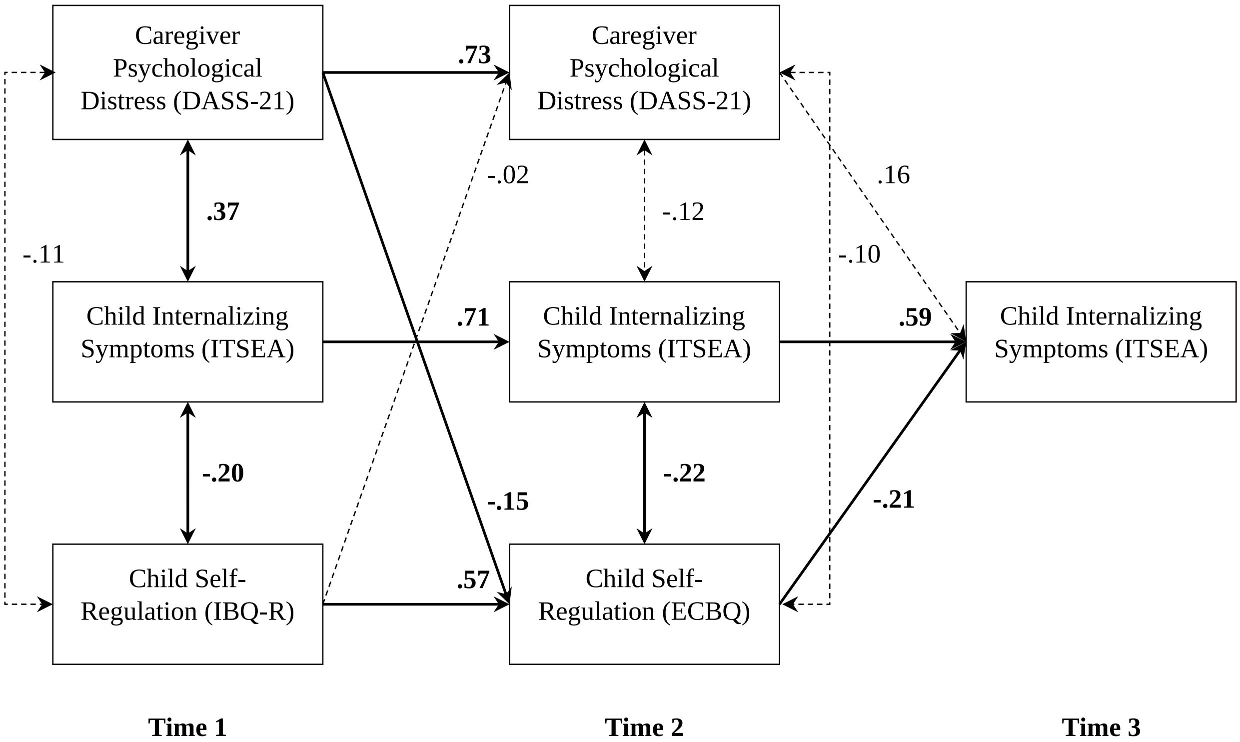

Figure 1b. Model 2 predicting child internalizing symptom outcomes from earlier child self-regulation and caregiver psychological distress.

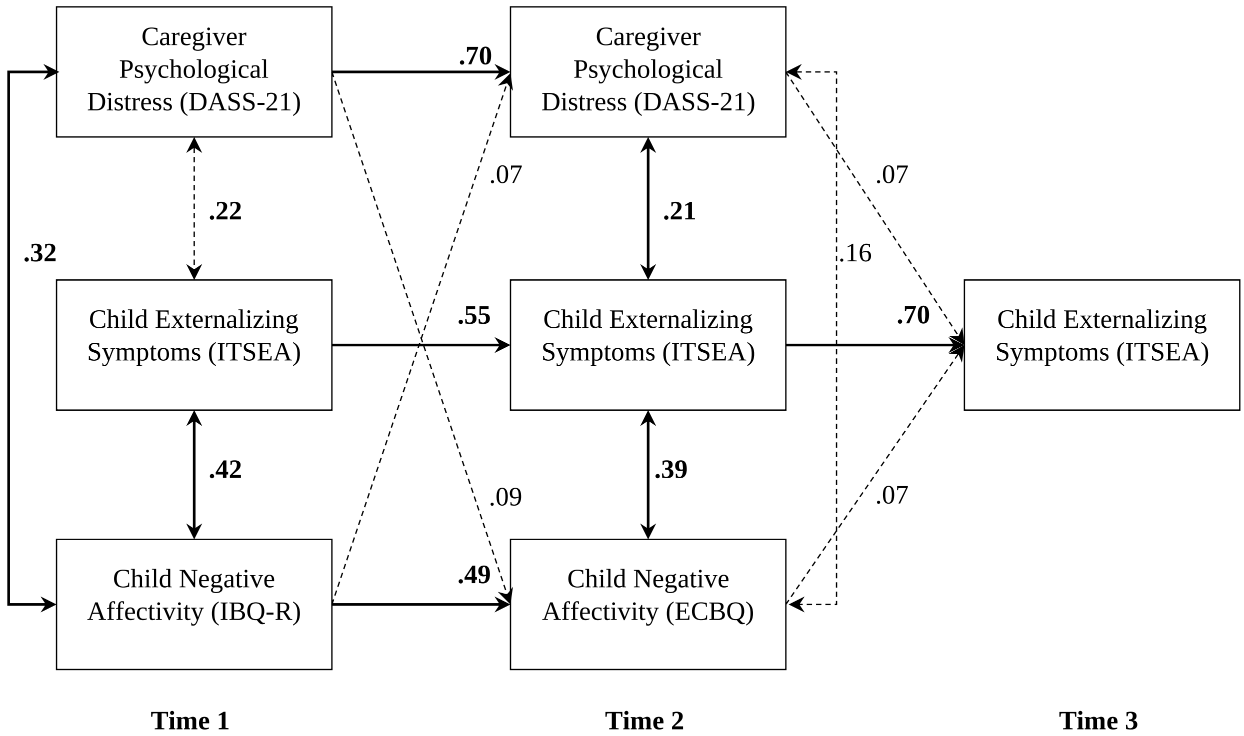

Figure 2a. Model 3 predicting child externalizing symptom outcomes from earlier child negative affectivity and caregiver psychological distress.

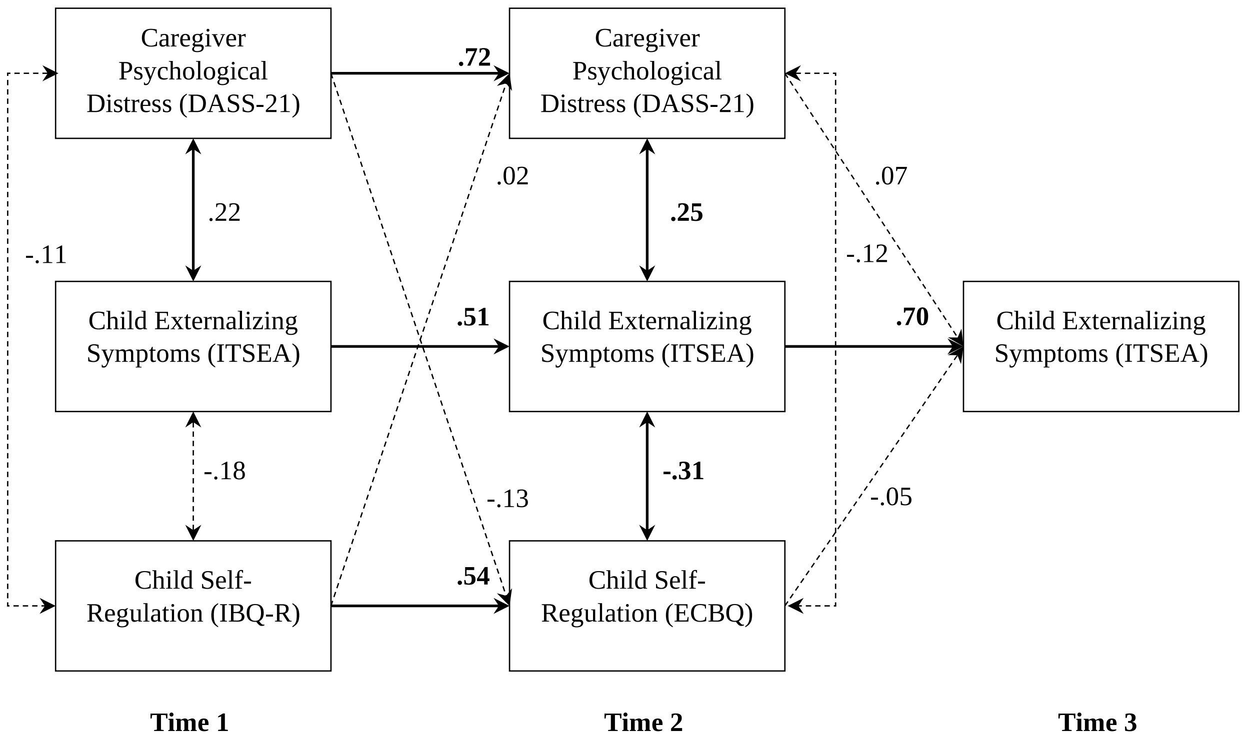

Figure 2b. Model 4 predicting child externalizing symptom outcomes from earlier child self-regulation and caregiver psychological distress.

8.4.4. Moderation Analysis

Moderation analysis was conducted to investigate the potential moderating role of children's T1 autism expression (AOSI) on caregiver-to-child effects identified in the prediction of child internalizing symptoms in Model 2. Child autism expression was significantly positively correlated with concurrent internalizing symptoms, $r = .27$, $p <.01$, but non-significantly correlated with concurrent caregiver psychological distress, $r = .06$, $p = .660$, and child self-regulation, $r = -.06$, $p = .532$. Inclusion of an interaction term between T1 caregiver psychological distress and T1 child autism expression led to poor model fit, $\chi^2(20) = 50.72$, $p = <.001$, RMSEA = 0.12 (90% CI 0.08-0.16), CFI = 0.89, TLI = 0.80, SRMR = 0.16, and the interaction term did not significantly predict child self-regulation at T2, $\beta = 0.10$, $p = 0.38$; thus, there was no evidence that the effect of caregiver psychological distress on subsequent child self-regulation varied according to children's level of autism expression.

8.5. Discussion

Prior research has shown an association between early childhood autism traits and elevated social-emotional difficulties. Child temperament characteristics – namely, high negative emotionality, low sociability/positive affectivity, and low self-regulation – and caregiver symptoms of psychological distress have been implicated independently in children's internalizing and externalizing symptoms, and have evidenced associations with one another. Our study sought to bridge these findings by investigating potential transactional processes by which child temperament and caregiver psychological distress contribute to the development of internalizing and externalizing symptoms in the context of autism. Moreover, by drawing upon data from a cohort of infants at elevated likelihood of autism and their caregivers, this study provides unique insight into the unfolding of these processes before autism is fully apparent. These results demonstrate that – contrary to theoretical predictions (Sameroff & Chandler, 1975) but consistent with evidence from typical development (Behrendt et al., 2019) – there is a *unidirectional* effect of child temperament on caregiver psychological distress predicting subsequent social-emotional difficulties among young children with early autism signs.

Our main finding was that caregiver psychological distress at around child age 12-months (T1) predicted children's subsequent lower self-regulation abilities at around 18-months (T2) which, in turn, predicted later child internalizing symptoms at around 24-months (T3). This result is consistent with studies of typical development (Allen et al., 2018; Roman et al., 2016) and the model was not moderated by children's autism traits as measured by the AOSI at 12-months. This finding suggests a potential common pathway to internalizing symptoms among children with and without autism traits. Contrary to expectation, however, this same pathway – from caregiver psychological distress to subsequent child self-regulation – did not predict the development of children's later externalizing symptoms. This might be because our self-regulation composite score captured only early-emerging, bottom-up (automatic) aspects of self-regulation. Indeed, previous studies implicated this pathway in the prediction of later-emerging, top-down (deliberate) aspects of executive function (Roman et al., 2016), inhibitory control (Choe et al., 2014), effortful control (Behrendt et al., 2019) and conscientiousness (Allen et al., 2018). Moreover, Gartstein et al. (2012) found that preschool externalizing symptoms were not associated with self-regulation in infancy, but positively predicted by self-regulation in the toddler and preschool periods when volitional forms of control emerge.

Caregiver psychological distress at T1 was positively correlated with subsequent child negative affectivity at T2 which, in turn, was positively correlated with later child internalizing and externalizing symptoms at T3. However, this longitudinal pathway was non-significant in cross-lagged path models controlling for within-time covariances and within-construct stability. Allen et al. (2018) and Behrendt et al. (2019) found a significant longitudinal pathway from caregiver psychological distress through child negative affectivity to child internalizing and externalizing symptoms in typical samples. However, neither of these studies had repeated measures of child social-emotional difficulties and it was thus not possible to account for within-time covariance. That is, the temporal effect of child negative affectivity on subsequent internalizing and externalizing symptoms apparent in these studies could have reflected an already-present correlation. Additional work using repeated measures of all constructs is therefore needed to confirm the presence or absence of this longitudinal pathway in the context of autism and typical development.

We found no evidence of a longitudinal path from child temperament through caregiver psychological distress to child social-emotional difficulties, somewhat contrary to predictions. Whereas bidirectional relations between child and caregiver characteristics have been found in some studies (Brooker et al., 2015; Forbes et al., 2008), others have reported less salient (Pesonen et al., 2008; Sugawara et al., 1999) or nonsignificant effects of child temperament on subsequent caregiver psychological distress (Feng et al., 2007; Hanington et al., 2010). Consistent with our results, Behrendt et al. (2019) found that child temperament and caregiver psychological distress were associated with children's later social-emotional difficulties via a caregiver-to-child, and not child-to-caregiver, direction of influence. The perinatal period (pregnancy and the first prenatal year) is a time of increased psychological vulnerability for many caregivers (Vismara et al., 2016). Therefore, it may be that caregivers had pre-existing high levels of psychological distress and thus were less susceptible to change as a result of child temperament. Additionally, it may be that child temperament does not exert an evocative effect on caregiver psychological distress per se, but rather increases the likelihood that caregivers' internal symptoms of distress will play out in their affective tone (Aktar et al., 2017; Aktar & Bögels, 2017) and behaviour (Paulussen-

Hoogeboom et al., 2007) when interacting with their child, with a resultant impact on children's social-emotional outcomes. Consistent with this possiblity, in studies of typical development, infants' high negative emotionality has been shown to predict less optimal parenting behaviours only if mothers were psychologically distressed (Dix & Yan, 2014; Mertesacker et al., 2004; Pauli-Pott et al., 2000). Future work concerning children with early autism traits should seek to establish (a) whether caregiver psychological distress modulates the evocative influence of child temperament on caregiver interaction behaviour, and (b) whether caregiver interactions act as a mechanism through which psychological distress symptoms impact child social-emotional outcomes.

Child surgency was not significantly predicted by or correlated with caregiver psychological distress, and was mostly unrelated to children's social-emotional difficulties at outcome. While some studies indicate lower surgency among children whose caregivers have more symptoms of psychological distress (Bridgett et al., 2013; Olino et al., 2011), this relation has tended to be weaker and less consistent than the relation of caregiver psychological distress with negative and regulatory aspects of child temperament (Goodman et al., 2011). It may be that a more nuanced examination is needed to clarify how these factors contribute, uniquely and reciprocally, to children's social-emotional difficulties. Gartstein and Hancock (2019) reported differential effects of maternal depression, anxiety, and stress symptoms on different fine-grained traits underlying surgency, and Gartstein et al. (2012) found that children's internalizing symptoms were unrelated to overarching surgency but associated with the narrowly-defined aspect of sociability. It may also be that surgency is predictive of social-emotional difficulties at older ages, when social demands and expectations increase and become more complex (Shiner & Caspi, 2003). Consistent with our results, Gartstein et al. (2012) found that externalizing symptoms in toddlerhood were associated with concurrent but not preceding levels of surgency. Existing literature has supported an association between surgency and social-emotional difficulties in older autistic children and adolescents (Burrows et al., 2016; De Pauw et al., 2011).

8.5.1. Study Limitations and Future Directions

The reliance of this study on caregiver-report measures is a limitation given the possibility of respondent bias and shared method variance (Chetcuti et al., 2019); hence, it will be important to further replicate and extend our findings in the context of comprehensive multi-modal assessments. Nonetheless, the pathway from caregiver psychological distress to child social-emotional difficulties through child self-regulation was also identified by Roman et al. (2016) who used different measurement modalities to assess each construct, lending confidence to the present results. This study might also have been underpowered to detect significant relations between caregiver psychological distress and child negative affectivity, and between child negative affectivity and subsequent internalizing and externalizing symptoms. These findings should thus be replicated in larger samples, including cohorts comprising individuals both with and without an autism diagnosis and other diagnoses to permit direct comparison of causal pathways. Further, the ITSEA Internalizing domain yielded low internal consistency at Time 1 ($\alpha = 0.53$). It may be that there is a less reliable distinction between internalizing symptoms and the developmentally-appropriate use of emotions (e.g., crying) in infancy to signal needs and desires; yet, ITSEA scores were significantly and positively associated across the three timepoints, suggesting that internalizing and externalizing symptoms were likely to remain elevated across infancy and toddlerhood (also see Briggs-Gowan et al., 2006).

The focus of this study on infants with emerging traits of autism permitted insights into internalizing and externalizing pathways at an earlier stage in child development than would have been the case if an autism-diagnosed sample were investigated (i.e., given 49-months is the average age of autism diagnosis in Australia; Bent, Dissanayake, & Barbaro, 2015) and it remains to be determined which of these infants will go on to receive a clinical diagnosis. There was no moderation effect of AOSI scores on the relation between caregiver psychological distress and child self-regulation, suggesting this pathway leading to child internalizing symptoms is similar across children with varying levels of autism traits. A further examination of transdiagnostic processes might include testing the equivalence of caregiver-to-child and child-to-caregiver effects in samples with and without different forms of neurodevelopmental disorders.

Finally, future studies might also consider exploration of alternative directional pathways. Indeed, children's social-emotional difficulties have been shown to influence the expression of temperament in typical populations (De Bolle et al., 2012, 2016; Feng et al., 2007) and predict psychological distress among caregivers of autistic children (Neece et al., 2012; Zaidman-Zait et al., 2014). Moreover, Choe et al. (2014) tested the reverse pathway in a typical sample and found that child inhibitory control mediated the effects of early oppositional behaviour on subsequent maternal depressive symptoms. The significant zero-order correlations among the IBQ-R/ECBQ scales (see Table 1) suggests there may also be value in exploring how temperament traits shape one another, to predict social-emotional outcomes. Indeed, some evidence suggests that the effect of child surgency on internalizing and externalizing symptoms might operate indirectly through negative affectivity (Behrendt et al., 2019).

8.5.2. Conclusions

This is the first study to examine the unique and reciprocal effects of child temperament and caregiver psychological distress in the development of social-emotional difficulties among children with early autism traits. The results suggest that children's self-regulation may play a role in the association between caregivers' heightened psychological distress and children's internalizing symptoms from infancy through toddlerhood. Intervention efforts aimed at supporting the mental health of caregivers of children with autism traits during the pre-diagnosis period might thus be effective in reducing the downstream impact of caregiver psychological distress symptoms on child social-emotional difficulties. A number of factors have been identified as predictive of well-being in this caregiver population – including social and economic support (e.g., Bromley et al., 2004), parenting perceptions (e.g., locus of control; Falk et al., 2014), and coping styles and strategies (e.g., Vernhet et al., 2019) – that may be useful targets. It might also be important to create and foster a child rearing environment that promotes adaptive expression and modulation of emotions. Intervention programs targeting caregiver understanding of temperament (e.g., unique profiles, goodness-of-fit), behavioural-management skills, and temperament-contingent responding have shown positive effects on caregiver mental health and child social-emotional outcomes in typical populations (Iverson & Gartstein, 2018), and may also be effective among caregivers of children with early autism traits. Research should thus be undertaken to determine the efficacy of such interventions in the context of autism.

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8.7. Appendices

Table A1

Cross-Lagged Panel Analysis Results for Annual Household Income in Models 1-4

	T1 Caregiver Psychological Distress		T1 Child Internalizing		T1 Child Externalizing		T3 Child Internalizing		T3 Child Externalizing	
	β	*p*	β	*p*	β	*p*	*r*	*p*	*r*	*p*
Model 1	-.23	<.05	-.27	<.05			-.23	.067		
Model 2	-.23	<.05	-.27	<.05			-.27	<.05		
Model 3	-.23	<.05			-.37	<.001			.21	.094
Model 4	-.24	<.05			-.35	<.001			.19	.124

CHAPTER 9

General Discussion

The overarching aim of this thesis was to examine the nature of individual temperament differences and role of these in predicting social-emotional outcomes in the context of autism in early-life. A systematic literature review and meta-analysis (Chapter 1) revealed a growing body of existing work on temperament in the context of autism. However, despite a considerable number of published studies (N = 64), the majority of work thus far was determined to have focused almost exclusively on describing group-level differences across samples of participants with and without an ASD diagnosis. In addition, with few exceptions, prior studies that had investigated temperament in relation to autism-associated individual differences were limited by a cross-sectional research design and examined traits separately from one another and in isolation from the environmental context. Consequently, an editorial perspective (Chapter 2) advocated the need to reorient research efforts towards examining temperament and the clinical phenotype of autism within an individual differences framework, while accounting for environmental factors. The methodological insights gained through work on this editorial perspective informed the theoretical and analytical framework employed in subsequent empirical work (Chapters 5-8), to attain a richer understanding of the role of temperament in social-emotional outcomes in the context of autism.

This concluding chapter synthesises findings from the four empirical chapters/articles presented in this thesis. As the results of each empirical study have been appraised in detail within each given chapter/article – in relation to specific hypotheses, previous empirical research and relevant theory – a broader overarching discussion is presented here. The following sections summarize and interpret the findings, reflect on the general strengths and limitations of the research methodology, and consider the empirical and clinical implications of the findings.

9.1. Temperament Differences among Infants with Early Autism Signs

In Studies 1 and 2 (Chapters 5 and 6, respectively), latent profile analysis (LPA) was used to characterize temperament differences within the cohort of children with early signs of autism (N = 103). Subgroups were delineated according to different constellations of temperament traits on the basis of the Infant Behavior Questionnaire-Revised (IBQ-R; Gartstein & Rothbart, 2003) in infancy (Time 1), and Early Childhood Behavior Questionnaire (ECBQ; Putnam, Gartstein, & Rothbart, 2006) in toddlerhood (Time 2-3). In this statistical technique, each individual child is viewed as a holistic ‘system’ made up of components that function interactively with one another. The suitability of these techniques for studying temperament has been recognized (Cloninger & Zwir, 2018) and demonstrated (Thomas & Chess, 1977) in the context of typical child development. Further, studies that focus on the within-person configuration of traits are likely of more relevance to clinical practice than studies on individual traits, as treatment decisions are often guided by clinicians’ holistic impression of each child and their needs. Yet, prior to publication of the current research, these techniques had not been used to study temperament in the context of autism (but see a recent study by Lee et al., 2020).

The results from the LPA supported a foundational assumption of this thesis, that children with autism features differ from one another in their temperamental profiles. At Time 1, infants were separable into three subgroups characterized by specific constellations of temperament traits: *inhibited/low positive* infants, who were less cheerful and more subdued in their reactions to new people and/or situations, *active/negative reactive* infants, who were highly active and emotionally labile, and *well-regulated* infants, who were emotionally balanced and easily soothed. The qualitative nature of temperament differences remained generally consistent as the children grew older, with inhibited/low positive, active/negative reactive, and sociable/well-regulated subgroups identified through separate LPAs conducted on temperament data collected again at each of Time 2 and 3. Yet, the distance between mean IBQ-R/ECBQ subscale scores for each subgroup appeared wider at later timepoints, and an additional *reactive/regulated* subgroup of toddlers – differentiated by middle-range reactivity and self-regulation traits – emerged uniquely at Time 3. It thus appeared that the children with autism features in this cohort became increasingly different from one another with age. Next, having found that the nature of temperament differences was largely time-invariant, it was of interest to see whether temperamental continuity was mirrored at level of the individual child.

Of the existing research on temperament in the context of autism, a handful of investigations had explored the consistency of dimension/trait levels over time using cross-time correlations, regressions, or repeated measures analysis of variance (ANOVA; Bieberich & Morgan, 2004; Del Rosario et al., 2014; Garon et al., 2015; Macari et al., 2017; Pijl et al., 2019; Reyes et al., 2019). These analyses produce an 'average estimate' of trends across each individual within a research sample. However, the LPA results discussed above suggest there might be different subpopulations within the broader cohort of children with autism features, among whom the form and temporal course of temperament trait development might differ. Another possibility, not addressed in prior investigations, is that discrete traits interact with and modulate one another's expression over time, and do so differently for different subgroups of children (Rothbart & Bates, 2006). With these shortcomings in mind, Study 2 adopted an alternative approach to investigate temperament continuity in the sample of children with autism features.

Cross-tabulation analysis was used to explore children's movement between temperament subgroups identified through LPA from infancy (Time 1) to toddlerhood (Times 2 and 3). While stable for a significant proportion of children, temperament subgroup classification shifted for others. Specifically, temporal discontinuity of classification was found for one-third of infants from Time 1 to 2 and for around one-half of toddlers from Time 2 to 3, with sociable/well-regulated, active/negative reactive, and inhibited/low positive toddlers at Time 2 all having equal likelihood of subsequent reactive/regulated classification at Time 3. These results fit with the theoretical conception of temperament as a complex dynamic system of interrelated traits that is shaped, to varying degrees and in different ways, across individuals and over developmental time (Shiner et al., 2012). Studies of typically developing children suggest that temperament change – while genetically influenced – is largely attributable to properties of the environment (Saudino & Wang, 2012). This research thus proceeded to investigate whether change in the temperament characteristics of children with autism features was associated with caregiver psychological distress.

9.2. Caregiver Psychological Distress as a Temperament-Shaping Influence

Prior to the current research, links between caregiver symptoms of psychological distress and child temperament – while widely studied in typically developing samples (e.g., Goodman et al., 2011) – had only been investigated several times in autistic samples (Kasari & Sigman, 1997; Konstantareas & Papageorgiou, 2006; Özyurt, Eliküçük, Tufan, & Baykara, 2018), with only one identified prior study using a longitudinal design (Totsika et al., 2013). Contributing to this scant literature, Studies 3 and 4 (Chapters 7 and 8) respectively explored concurrent (Time 1) and longitudinal (Time 1 to 2) relations between caregiver psychological distress – as measured by the Depression, Anxiety, and Stress Scales (DASS-21; Lovibond & Lovibond, 1995) – and child temperament characteristics. Based on the limited existing research, caregiver psychological distress was expected to relate to child negative affectivity and to lower surgency and self-regulation. Results from the current research partially supported these predictions.

Caregivers of children with higher negative affectivity reported higher levels of contemporaneous psychological distress at both Time 1 and Time 2, with moderate effect size. Caregiver psychological distress was also negatively associated with self-regulation at Time 2, with small effect size, but was not associated with this temperamental feature at Time 1 and, furthermore, was unrelated to child surgency at either timepoint. Moreover, significant cross-time correlations were apparent between caregiver psychological distress at Time 1 and both child negative affectivity and lower self-regulation at Time 2, in both cases with a weak effect size; however, the cross-time correlation was non-significant for Time 2 child surgency. To yield a more robust estimation of causal effects, cross-time relations were estimated while simultaneously controlling for within-time covariances and within-construct stability. Caregiver psychological distress at Time 1 remained associated with child lower self-regulation at Time 2, but was not associated with Time 2 child negative affectivity. Caregiver's heightened psychological distress might thus shape the contemporaneous expression of children's negative affectivity and developmental trajectory of self-regulation during very early childhood, in the context of emerging autism.

In addition to being shaped by the environment, children's temperament may also have an eliciting effect on others' responses (Scarr & McCartney, 1983) and serve to shape caregiver characteristics such as psychological distress (Brooker et al., 2015; Forbes et al., 2008; Pesonen et al., 2008; Sugawara, Kitamura, Toda, & Shima, 1999). Having found a causal connection between caregiver psychological distress and subsequent child temperament (self-regulation), it was of interest to explore whether these factors might evidence mutual reinforcement in a transactional feedback loop (Sameroff, 1975, 2009); that is, to model whether infant temperament characteristics might have a parallel effect of shaping caregiver psychological distress symptoms. However, only Time 1 negative affectivity was correlated with subsequent caregiver psychological distress (at Time 2) with moderate effect size, and this relation did not survive when within-time covariances and within-construct stability were controlled. These results suggest that longitudinal relations between child temperament and caregiver psychological distress do not operate in bidirectional manner. Rather, evidence of a causal relation was apparent only in the direction of high caregiver psychological distress predicting subsequent low child self-regulation.

9.3. Connections between Temperament and Social-Emotional Outcomes

At the time this program of research was conceived, research on the relation of temperament to social-emotional functioning had relied on cross-sectional research design and focused only on older autistic children and adolescents. Only a few studies published after commencement of this thesis research have explored these associations among very young children with autism features, and using longitudinal design (Hendry et al., 2020; Shephard et al., 2019). Here, this question was addressed – in the cohort of children at elevated autism likelihood – from two different perspectives: Studies 1 and 2 involved drawing comparisons between concurrently-identified categorical subgroups of children with autism features identified on the basis of different constellations of fine-grained temperament traits (person-centered analysis), whereas Studies 3 and 4 involved the examination of continuous associations with overarching temperament dimensions (variable-centered analysis). Across studies, it was hypothesized that children's internalizing and externalizing symptoms would be concurrently associated with (and predicted by, in the case of Study 4) temperamental negative affectivity, low surgency, and low self-regulation. Partial support for these hypotheses was obtained.

Studies 1 and 2 revealed a rather consistent pattern of differences in social-emotional functioning between temperamental subgroups of children with autism features at around 12-months (Time 1), 18-months (Time 2), and 24-months (Time 3) of age. Broadly, active/negative reactive and inhibited/low positive children had the highest reported social-emotional functioning difficulties on the Infant-Toddler Social and Emotional Assessment (ITSEA; Carter & Briggs-Gowan, 2006) whereas sociable/well-regulated children had the lowest reported difficulties.

Internalizing symptom levels and social-emotional competence were mostly equivalent for active/negative reactive and inhibited/low positive children at each timepoint. Consistent with the principle of equifinality (Cicchetti & Rogosch, 1996), this suggests that different temperamental risk factors may relate to the same form of social-emotional difficulties among children with autism features. By contrast, active/negative reactive children had higher reported externalizing symptom levels than did inhibited/low positive children at each timepoint (although not always statistically significantly so), suggesting some degree of specificity. Lastly, children with a consistent active/negative reactive or inhibited/low positive temperament classification at each of Time 2 and Time 3 had higher internalizing symptoms and lower competence, while children with a consistent sociable/well-regulated classification had lower externalizing symptoms and higher competence (relative to the unique Time 3 subgroup of children classified reactive/regulated). This finding suggests there may be corresponding changes in temperament and social-emotional functioning over time in the context of emergent autism.

Linear analysis conducted as part of Studies 3 and 4 revealed significant relations between children's continuously-measured temperament and social-emotional functioning. Negative affectivity was correlated (zero-order) with both internalizing and externalizing symptoms, both concurrently at each of Time 1 and Time 2 (with moderate-to-strong effect size) and prospectively over time (with weak-to-moderate effect size). However, Time 2 negative affectivity was associated at trend-level only with Time 3 internalizing in cross-lagged path models where stability of constructs and concurrent associations were statistically controlled. Surgency was correlated only with concurrent externalizing symptoms at Time 2, in a positive direction (weak effect size). Lastly, self-regulation was concurrently correlated with internalizing (but not externalizing) symptoms at Time 1 (weak effect size) and both internalizing and externalizing symptoms at Time 2 (weak-to-moderate effect size), in a negative direction. Correlations in the same direction were also found prospectively over time – respectively, from Time 1 or Time 2 self-regulation to Time 2 or Time 3 internalizing and externalizing symptoms – and results from cross-lagged path analyses suggested that Time 2 low self-regulation positively predicted Time 3 increased internalizing symptoms. This latter result suggests a causal relation between low self-regulation and internalizing symptoms in the context of autism.

This program of research explored relations among temperament and social-emotional functioning using both person-centered (categorical subgroups) and variable-centered (continuous dimensions/traits) analytic methods. Prior research on this topic – in both typical and atypical development – has tended to use one approach or the other; hence, comparing results from these different approaches in the same dataset is a relatively novel undertaking. Both approaches provided convergent evidence for the role of negative affectivity and low self-regulation in the occurrence of social-emotional difficulties in children with autism features. The results were less congruous for surgency, however, whereby social-emotional difficulties were associated with an inhibited/low positive subgroup characterized by low surgency-related traits (combined with low self-regulation), but mostly unrelated to surgency when measured dimensionally.

The apparent dissociation of results for temperamental surgency yielded by person-centered and variable-centered analyses raises the interesting question of interplay between regulatory and reactive components of temperament. This topic has been discussed (Muris & Ollendick, 2005; Nigg 2017; Rothbart & Bates, 2006) and tested (e.g., Jonas & Kochanska 2018; Moran, Lengua, & Maureen, 2013) in the context of typical child development, but largely overlooked in the context of autism. That is to suggest there may be an interactive effect between children's surgency and self-regulation in the prediction of social-emotional difficulties. For those children with autism features and low surgency, low self-regulation might increase susceptibility to internalizing and/or externalizing symptoms while high self-regulation might serve as a protective factor against these.

An alternative possibility is that each temperament dimension makes a unique, additive contribution to the likelihood of social-emotional difficulties in children with autism features. As concurrent and cross-time correlations were mostly non-significant between surgency and internalizing and externalizing symptoms, this would imply that the relation of inhibited/low positive temperament to heightened social-emotional difficulties was predominantly driven by the low self-regulation-, rather than low surgency-related traits, of this subgroup. Indeed, the same argument could be posited for the active/negative reactive temperament classification since correlations between negative affectivity and internalizing and externalizing symptoms – while statistically significant – were not ascertained while controlling for any covariance with self-regulation. Further research is thus necessary to determine the *unique predictive contribution* of each temperament dimension for social-emotional functioning outcomes in the context of autism.

9.4. Study Strengths and Limitations

The generalizability of the present findings is strengthened by the recruitment of infants with autism *features*, rather than a clinical ASD diagnosis. AOSI and ADOS-2 scores spanning the full range of possible values, and centered around instrument cut-offs for clinical ASD, suggest that subclinical and clinical presentations were represented equally in this cohort. Such variability was a strength, insofar that it permitted exploration of temperament at an earlier stage of child development – than likely would have been possible with an ASD-diagnosed sample, given the average age of diagnosis in Australia is around 4 years (e.g., Bent, Dissanayake, & Barbaro, 2015) – and the generalizability of temperament processes across the subclinical-to-clinical continuum of autism expression (Studies 3 and 4). Such insight has not been afforded within previous investigations where there has been restricted focus on children with a clinical

ASD diagnosis. Nevertheless, *all* of the infants recruited to this research had atypical social-communication features at study entry, as indicated by ≥3 of 5 SACS-R key autism markers; hence, the true non-clinical end of the autism spectrum – defined strictly as children with no autism symptoms at any stage of development – might not have been truly represented in this cohort.

The use of a longitudinal design with repeated measurement is a strength of this research; this provided the opportunity to explore and shed important new light on the patterns and predictors of temperament change, and links between temperament and later social-emotional functioning outcomes. Nevertheless, child ages ranged widely within timepoints and overlapped across timepoints – 9-16 months at Time 1, 15-23 months at Time 2, and 20-30 months at Time 3 – making it difficult to draw robust conclusions about the nature of temperament differences and associated processes during specific developmental stages. Moreover, the age-bands of participants within the current study did not always align with the stipulated age ranges of the questionnaire measures. For example, the IBQ-R (Gartstein & Rothbart, 2003) – administered here at Time 1 with infants aged as old as 16-months – intended for infants aged 3- to 12-months, while the ECBQ (Putnam et al., 2006) – administered here at Time 2 and Time 3 when infants were aged upward of 15-months – is intended for toddlers aged 18 to 36 months. Nonetheless, the items that made up the IBQ-R and ECBQ were judged to be age-relevant at face value, and checks on concurrent correlations between child age and IBQ-R/ECBQ scores at a given timepoint were mostly non-significant (except for Time 2 Distress to Limitations, Soothability, and Surgency, and Time 3 Motor Activation).

Similarly, the ITSEA (Carter & Briggs-Gowan, 2006) is intended for children aged 12- to 35-months but was administered at Time 1 when some infants were aged as young as 9-months. One of the six sections of the ITSEA (Section C) was largely not applicable to infants at Time 1 given the language skill requirement (i.e., must be combining words). Nevertheless, only three items from this section counted towards ITSEA domain scores utilized in the present research – namely, one item (of 37 total) for Competence (i.e., *"Talks about other people's feelings*"), one item (of 32 total) for Internalizing (i.e., *"Takes a while to speak in unfamiliar situations"*), and one item (of 24 total) for Externalizing (i.e., *"Swears"*) – and null responses to these items did not preclude computation of these summary scores (Carter & Briggs-Gowan, 2006). Moreover, the positive and significant autoregressive paths between Internalizing and Externalizing domain scores (found in Study 4) indicated continuity of scores from Time 1 to Time 3 even though the sample was initially younger than the ITSEA lower age limit.

A related potential limitation is that the factor structures of the IBQ-R (Gartstein & Rothbart, 2003), ECBQ (Putnam et al., 2006), and ITSEA (Carter & Briggs-Gowan, 2006) were ascertained in typically developing samples and might not hold in other samples. The mostly acceptable internal consistency estimates observed in the current data (i.e., $\alpha > .60$) provided further post-hoc support for the use of the IBQ-R/ECBQ and ITSEA in the current sample of children with autism features. Yet, low and unacceptable internal consistency estimates were obtained for the ITSEA Internalizing domain, as reported in Study 4 (Time 1 $\alpha_{t1} = .53$) and ECBQ Impulsivity ($\alpha_{t2} = .46$) and Discomfort ($\alpha_{t2} = .58$) scales. To our knowledge, there have been no investigations of the factor structure of these questionnaires in atypical samples. Until this occurs, the current and others' (previous and future) results from the use of these instruments with children with autism features should be interpreted with caution as they might not accurately capture the constructs they purport to measure.

Related to the previous point, ITSEA items were developed and refined in typically developing samples (Briggs-Gowan & Carter, 1998; Carter, Briggs-Gowan, Jones, & Little, 2003) and might have thus not adequately captured the unique experiences of children with autism features. Little is known regarding the specific presentation of social-emotional difficulties in children with autism features, though similarities and differences in presentation have been found among older children with and without autism (for reviews, see Kerns & Kendall 2012; Stewart et al., 2006). For example, Ozsivadjian, Knott, and Magiati (2012) explored perspectives on the presentation of anxiety in children with autism (aged 7 to 18 years) using a focus group methodology. Changes and disruptions to routines, sensory sensitivities, and social difficulties emerged as autism-specific anxiety triggers. Moreover, parents reported that their autistic children used more behavioural than verbal means to express anxiety, such as increased sensory and restricted/repetitive behaviour. Qualitative evaluation of the applicability of ITSEA items in typically developing samples could be a valuable means of further refining this measure.

The removal of ITSEA items that overlapped in content with IBQ-R/ECBQ items adds strength to the present findings; this procedure reduced the possibility of inflated associations between temperament- and social-emotional functioning constructs through measurement confounding. Though a joint confirmatory factor analysis of ITSEA and IBQ-R/ECBQ items would have been a more robust procedure for detecting measurement confounding, this was not possible in the current research given the participant sample size. However, studies that have used both conceptual (i.e., expert ratings of similarity) and empirical (i.e., factor analysis) methods to detect confounding of temperament and social-emotional functioning measures have found that the two approaches identify different specific items (Lemery, Essex, & Smider, 2002; Lengua, West, & Sandler, 1998). These approaches thus appear to capture unique information and should be used together to identify and eliminate overlapping items within existing measures to yield more 'pure' measures of these constructs.

Caregiver-report questionnaires are beneficial insofar that they provide a window into child behaviour across a variety of different contexts. This is a fundamental shortcoming of observational measures where child behaviour is captured and quantified at a single point in time – often in a novel laboratory setting with unfamiliar researchers – thereby limiting ecological validity. Nonetheless, questionnaire measures are more susceptible to respondent bias that can threaten the validity of results. Studies have explored sources of bias in the IBQ-R by comparing caregiver ratings with those derived from observational indices (Bayly & Gartstein, 2013; Gartstein & Marmion, 2008; Parade & Leerkes, 2008). Despite generally good agreement, some discrepancies have been found due to caregivers' own temperament traits and mental health status. However, disparities between ratings were neither related to infant or caregiver age or sex, nor to family socioeconomic status, suggesting that caregiver perceptions of child temperament are not influenced by demographic/background characteristics. It may also be that differences in caregivers' frame of reference – used to make judgments about child behaviour – contribute to inflated item ratings (in either direction). For instance, caregivers have been shown to exaggerate temperament differences and similarities between siblings by evaluating them relative to one another (Majdandzic, van den Boom, & Heesbeen, 2008; Saudino, Wertz, Gagne, & Chawla, 2004). Similar forms of respondent bias likely operate across the ECBQ, ITSEA, and DASS-21 and, since these were completed by the same caregiver informant, this 'common method variance' may have inflated/deflated the observed relations between constructs. As suggested in Chapter 2, future related studies should adopt a multi-method/multi-informant measurement approach that combines self/other reports and behavioural observations.

9.5. Future Clinical and Empirical Directions

9.5.1. The Role of Temperament in Social-Emotional Difficulties

Though it was not a specific objective of this work to clarify *how* temperament and social-emotional difficulties are connected, some causal inferences can be drawn from the longitudinal results. In Study 2, children with autism features who shifted out of the Time 2 inhibited/low positive or active negative reactive subgroups, and into the Time 3 regulated/reactive or sociable/well-regulated subgroups, had fewer Time 3 social-emotional difficulties than did those who retained their inhibited/low positive or active negative reactive classification over time. More robust evidence of a causal connection was obtained in Study 4, whereby Time 2 low self-regulation predicted subsequently increased internalizing symptoms at Time 3 (as did Time 2 negative affectivity, albeit at trend-level significance), above and beyond the variance explained by within-time covariances and within-construct stability. Of note, these relations were apparent when the confounding effect of item-content overlap was minimized (i.e., by excluding ITSEA items that overlapped with the IBQ-R/ECBQ). Taken together, these results suggest that the temperament characteristics of children with autism features may play a role in the development (vulnerability association) and/or maintenance (pathoplastic association) of social-emotional difficulties (e.g., see Shiner & Caspi, 2003). This insight has important clinical implications; consideration of temperament may allow the proactive identification of those particular children susceptible to future social-emotional difficulties and also inform the individualization of support strategies. This topic warrants further dedicated research, including the examination of whether social-emotional difficulties shape temperament expression (complication/scar association) or share etiological origins with temperament (continuum/spectrum association). In particular, larger studies using a genetically informed design (e.g., comprising twin pairs) would allow for distinguishing the unique influence of genetic (e.g., heritability), shared familial/environmental (e.g., caregiver characteristics), and non-shared environmental factors (e.g., life experiences) on the covariance between temperament and social-emotional difficulties.

9.5.2. Continuities with Typical Child Development

Despite a preponderance of literature on temperament in autism there has been relatively little exploration of inter-individual differences to date (see Chapter 1). This research program was thus guided by and interpreted alongside literature from the general population. Consistent with transdiagnostic theory (e.g., Insel et al., 2010; Mundy et al., 2007), temperament variability was expected to have the same ‘meaning’ in the present context of emerging autism as in the context of typical development. It is acknowledged that such a conclusion cannot be definitively drawn from this study due to lack of a non-autistic comparison group. Nevertheless, similarities are apparent in the nature of the temperament subgroups, characteristics, and processes involved in children’s social-emotional development that have arisen from the current results, compared to those from published studies of typically developing samples (see preceding empirical chapters for a full discussion of this point). Support for this conjecture also comes from studies that have adopted the framework proposed Van Leeuwen et al., (2007) to probe the generalizability of temperament across clinical and non-clinical samples. This method involves testing three successive levels of differences between samples: means and variances (Level 1), psychometric properties (Level 2), and covariation patterns (Level 3) of temperament measures and traits. De Pauw et al. (2011) and Burrows et al. (2016) used this method to compare autistic and typically developing children and adolescents and found differences in terms of reported dimension/trait levels, but similar internal consistencies and patterns of covariation between identified temperament dimensions/traits with internalizing and externalizing symptoms. These findings support the suggestion that autism alters the expression of temperament traits but not the form or function of temperament per se. The intriguing implication is that existing temperament-based supports that have grown out of the empirical literature on non-autistic children could have relevance to those on the autism spectrum. Nonetheless, comparative analyses similar to those of De Pauw et al. (2011) and Burrows et al. (2016) should be undertaken among datasets from samples of younger autistic and non-autistic children to determine the generality of this inference across all of childhood.

9.5.3. Temperament-Based Support for Social-Emotional Functioning

The patchy effectiveness of ‘one-size-fits-all’ approaches to clinical care has spurred the broader fields of psychology and psychiatry (e.g., Cuthbert & Insel, 2013), and the specific area of early childhood autism support (e.g., Vivanti et al., 2014), toward the use of strategies that meet individuals’ specific needs. These results suggest that child temperament could serve as the basis of individualized supports for social-emotional functioning. Though this possibility has not been explored in the context of autism, temperament-based programs have been formulated and shown to be effective for enhancing the social-emotional functioning of typically developing children (for reviews, see Iverson & Gartstein, 2018; McClowry, Rodriguez, & Koslowitz, 2008). Two of the most widely implemented and studied programs – *INSIGHTS into Children’s Temperament* (McClowry, 2003) and *Cool Little Kids* (Rapee, Lyneham, & Scniering, 2006) – draw on child temperament in distinct yet similarly advantageous ways, and may provide a framework for the development of support strategies for children with autism features. These programs are described below, with a specific focus on aspects that may be applicable to the autism population.

9.5.3.1. Temperament-targeted (indicated) support.

A key insight from this work is that individual temperament differences relate to differences in social-emotional functioning. In particular, children with autism features and a temperament high in negative affectivity and/or low in self-regulation were especially likely to exhibit high concurrent social-emotional difficulties, and to experience an exacerbation of internalizing symptoms over time. The implication is that the presence of these temperament traits among children with autism features might indicate a heightened propensity for social-emotional difficulties. Therefore, it may be valuable to use measures of negative affectivity and self-regulation to screen children with autism features for propensity toward social-emotional difficulties, thereby identifying those who may benefit from therapeutic support to optimize outcomes.

Temperament screening has been employed in the context of Cool Little Kids (Rapee et al., 2006) to identify pre-schoolers from the general population who have high levels of inhibition/withdrawal and thereby considered to be at-risk for the later development of anxiety disorders. A combination of caregiver-report questionnaires and observational methods has been used to select children for inclusion in Cool Little Kids. The procedures for screening and enrolment into Cool Little Kids have been shown to be acceptable to caregivers (Beatson et al., 2014) and cost-effective to implement (Chatterton et al., 2020), with a recent online adaptation offering additional efficiency over paper-and-pen versions of screening questionnaires (Morgan et al., 2017; Morgan, Rapee, & Bayer, 2016). Further, in an initial efficacy study of Cool Little Kids, 90% of pre-school children enrolled on the basis of inhibited/shy temperament were found to already met criteria for an anxiety disorder at baseline (Rapee, Kennedy, Ingram, Edwards, & Sweeney, 2005). This result supports temperament screening as a valid means of identifying children at-risk for social-emotional difficulties. The program itself – which consists of six group sessions (90 minutes each) of caregiver psychoeducation and skills training – has also been shown efficacious for reducing later anxiety disorders and internalizing symptoms compared to a waitlist control (Rapee & Jacobs, 2002; Rapee et al., 2005) including amongst a subset of autistic children comprised within a larger population-based cohort (Bischof, Rapee, Hudry, & Bayer, 2018).

Procedures for screening temperament – such as those used within Cool Little Kids (Rapee et al., 2006) – could potentially be incorporated into the routine clinical assessment of children with autism features. Given the time-consuming nature of observational measures and high level of expertise required, caregiver-report questionnaires could represent a more cost- and time-effective option for determining children's suitability for programs to support social-emotional development, particularly when delivered online (Chatterton et al., 2020). Importantly, the accurate identification of temperamental risk factors necessitates measurement tools that are reliable, valid and resistant to bias.

9.5.3.2. Temperament-tailored (universal) support.

Targeting therapeutic supports to certain temperamental types of children with autism features would ensure that clinical resources are directed to those who need them most. However, there is also potential for children at-risk of social-emotional difficulties to be overlooked in the screening process and denied placement in prevention programs. This would be of particular concern if temperament screening occurs at a single time point – and given the potential for change over time demonstrated in the current Studies 2 and 4 – and is limited to only certain traits or trait combinations (whereas children with different temperaments may plausibly benefit from the same supports). This problem may be overcome by integrating social-emotional supports within existing clinical services delivered to *all* children with autism features, such as within early intensive behavioural intervention. However, this work has shown that temperament varies among children with autism features, and that such temperament differences relate to different profiles of social-emotional functioning. It might thus be important to select and implement strategies aligned to the unique temperament and needs of each child.

INSIGHTS into Children's Temperament (hereafter, INSIGHTS; McClowry, 2003) is a preventative program aimed at enhancing the social-emotional functioning outcomes of school-aged children in the general population. INSIGHTS is implemented over a 10-week period and includes curricula for caregivers (both parents and teachers) and children that is relevant to a range of different child temperaments. The caregiver curriculum is focused on understanding and recognizing the unique temperament qualities and needs of each child and responding with contingent behaviour management strategies. Meanwhile, children are introduced to puppets that represent different temperament types – labelled *high maintenance, cautious/slow-to-warm-up, industrious,* and *social/eager-to-try* (McClowry, 2002a, 2002b) – and use these to act out problem-solving scenarios and build empathy. Using puppets provides children with a safe vehicle to express emotions and recreate challenging situations without the fear of embarrassment or rejection from peers, and also allows children to become more attuned to their own and others' temperament (Hatamiya, 2011). Efficacy trials of INSIGHTS have revealed positive effects on caregiver sense of efficacy in managing child behaviour (O'Connor, Rodriguez, Cappella, Morris, & McClowry, 2012), and in teacher classroom management (McClowry, Snow, Tamis-LeMonda, & Rodriguez, 2010) and classroom engagement (Cappella et al., 2015). Moreover, compared to children enrolled in an attention-control reading program, children enrolled in INSIGHTS have shown significant reductions in attentional difficulties, oppositional behaviour, and covert disruptive behaviour (McClowry et al., 2010; McClowry, Snow, & Tamis-LeMonda 2005; O'Connor et al., 2012).

Though INSIGHTS was formulated for school-aged children with typical development, similar therapeutic support strategies may be useful for improving social-emotional development in the context of emerging autism. It may be appropriate to direct supports for young children's social-emotional development chiefly or solely at caregivers, as infant/toddler cognitive resources are still developing and there is a strong reliance on caregivers to get their needs met. In both Cool Little Kids (Rapee et al., 2006) and INSIGHTS (McClowry, 2003), caregivers are encouraged to appreciate their child's temperament characteristics and respond in ways that enhance social-emotional functioning outcomes. Central to this approach is the theoretical notion that optimal social-emotional development arises from a match between child temperament and environment conditions, referred to as 'goodness-of-fit' (Thomas & Chess, 1977). Future investigations of goodness-of-fit in the context of autism will be critical to elucidating which combinations of child temperament and caregiver behaviour should be promoted through temperament-tailored intervention. With respect to analysis, this might entail testing the moderation effects of caregiver behaviour on relations between children's temperament – either in terms of discrete traits or trait combinations – and their social-emotional outcomes.

9.5.3.3. Providing additional support for caregivers.

Extensive literature on typical child development indicates the pertinent role of environmental experiences in shaping temperament expression and associated outcomes (Rothbart & Bates, 2006). Environmental factors, such as caregiver characteristics and behaviour, can exacerbate (or mitigate) the effects of children's temperament on social-emotional functioning consistent with the notion of goodness-of-fit (Thomas & Chess 1977; for a review, see Slagt et al., 2016), and/or can reinforce (or discourage) the expression of temperament characteristics that promote children's susceptibility to social-emotional difficulties. Consistent with the latter suggestion, Study 4 found that heightened caregiver psychological distress predicted subsequent lower infant self-regulation and, in turn, elevated later internalizing symptoms. Caregiver psychological distress might thus be an important additional factor to address in temperament-based supports for children with autism features. There are at least two ways this could be achieved.

First, caregiver psychological distress levels could be regarded as a second indicator of children's susceptibility to social-emotional difficulties (alongside temperament) and incorporated into screening instruments to determine intake into support programs. These results suggest that, among children with autism features, those infants who have a distressed caregiver *and* a reactive and/or dysregulated temperament may be especially good candidates for programs aimed at enhancing social-emotional functioning. Second, temperament-based programs could incorporate content for *both* children and caregivers, such as strategies to manage the challenging thoughts and emotions of both parties. These supplementary components seeking to address caregiver psychological distress may indeed be feasibly incorporated into temperament-based programs together – as shown by Kennedy, Rapee, and Edwards (2009) who conducted an efficacy trial of Cool Little Kids specifically targeting caregivers of temperamentally inhibited/withdrawn pre-schoolers who themselves had a history of anxiety, reported during screening. Among 71 participating caregivers, 76% of mothers and 42% of fathers met DSM criteria for a current primary anxiety disorder, and the standard six-session Cool Little Kids program was augmented with an additional two sessions especially targeting caregivers' own anxiety management. Children whose parents participated in the program showed a significant reduction in anxiety diagnoses and temperamental inhibition at 6-month follow-up, relative to waitlist controls. Interestingly, however, caregiver post-intervention anxiety levels were not significantly different between the Cool Little Kids and waitlist control groups. Therefore, temperament-based programs that place a stronger emphasis on reducing caregiver psychological distress could produce greater efficacy.

Another promising approach to supporting caregiver psychological well-being is mindfulness training, broadly aimed at strengthening meta-cognitive awareness of present-moment experiences (Grabovac, Lau, & Willett, 2011). Such programs have been shown to reduce psychological distress among caregivers of children on the autism spectrum (Cachia, Anderson, & Moore, 2016; Hartley, Dorstyn, & Due, 2019) and may be of particular value early in a child's life (Taylor, Cavanagh, & Strauss, 2016) for facilitating positive reappraisal and acceptance of children's emerging developmental differences (Rayan & Ahmad, 2016). In support of feasibility, research suggests that mindfulness-based training programs need not be intensive or prolonged to confer benefits for caregivers of children on the spectrum (Rayan & Ahmad, 2016, 2017) and can be implemented as an adjunct to child-focused programs delivered at a young age (Weitlauf et al., 2020).

9.6. Conclusion

This thesis presents the findings from a cohesive program of related research studies, with the overarching aim of examining the nature of individual temperament differences and role of these in predicting autism-related social-emotional outcomes. This work has shown that children with emerging autism traits differ from one another in their temperament characteristics, and that these differences are meaningful for the prediction of social-emotional functioning. The configural nature of trait differences showed relative continuity from infancy to toddlerhood, but temperament differences between children became more pronounced as the participants in this research grew older. Nonetheless, the expression of temperament may change across the life-span at the individual-level; some children with autism traits retained the same trait patterns from infancy to toddlerhood, while for others there were changes. The presence of psychological distress among caregivers related to children's contemporaneous and later expression of traits – to self-regulation in particular – and might thus contribute to the development of social-emotional difficulties in the autism population. Notwithstanding the limitations discussed above, the insights gained from this research provide the foundation for the development of temperament-based supports to improve the social-emotional functioning outcomes of children on the autism spectrum.

9.7. References

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Appendices

Appendix A - Autism Observation Scale for Infants (AOSI) Items

†Visual Tracking
†Disengagement of Attention
†Orientation to Name
†Differential Response to Facial Emotion
†Anticipatory Responses
†Imitation of Actions
†Social Babbling
†Eye Contact
†Reciprocal Social Smile
†Coordination of Eye Gaze and Action
†Reactivity
†Social Interest and Shared Affect
†Transitions
†Motor Control and Behaviour
†Atypical Motor Behaviours
†Atypical Sensory Behaviours
Engagement of Attention
Insistence on Having or Playing with Particular Objects or Specific Activities
Sharing Interest

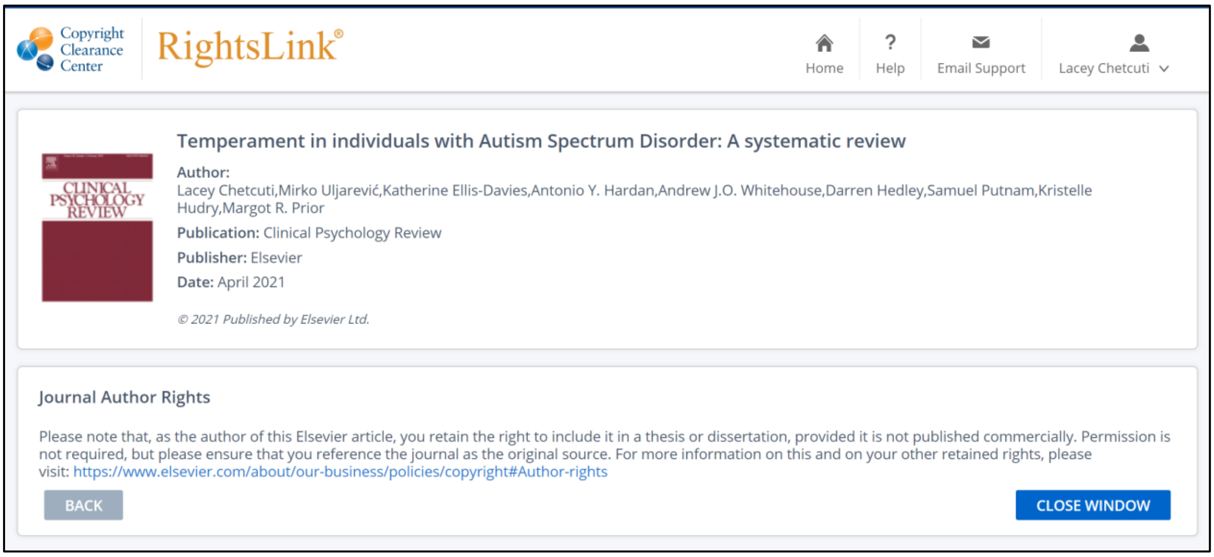
Note. †Item counts towards marker count and total score.

Appendix B - Autism Diagnostic Observation Schedule – 2nd Edition, Toddler Module (ADOS-T) Items

Overall Level of Non-Echoed Spoken Language	[†]Showing
Frequency of Babbling	[†‡]Spontaneous Initiation of Joint Attention
[†]Frequency of Spontaneous Vocalization Directed to Others	[†]Response to Joint Attention
[†]Intonation of Vocalizations or Verbalizations	[†‡]Quality of Social Overtures
Immediate Echolalia	Amount of Social Overtures/Maintenance of Attention: Examiner
Stereotyped/Idiosyncratic Use of Words or Phrases	[‡]Amount of Social Overtures/Maintenance of Attention: Parent/Caregiver
Use of Another's Body	Level of Engagement
[‡]Pointing	[‡]Overall Quality of Rapport
[†]Gestures	Functional Play with Objects
Frequency of Undirected Vocalization	Imagination/Creativity
[†‡]Unusual Eye Contact	Functional and Symbolic Imitation
Teasing Toy Play	[†‡]Unusual Sensory Interest in Play Material/Person
Unable Toy Play	[†‡]Hand and Finger Movements/Posturing
[†‡]Facial Expressions Directed to Others	Other Complex Mannerisms
[†‡]Integration of Gaze and Other Behaviors During Social Overtures	Self-Injurious Behavior
[†]Shared Enjoyment in Interaction	[†‡]Unusually Repetitive Interests or Stereotyped Behaviors
[‡]Response to Name	Overactivity
[‡]Ignore	Fussiness/Irritability
[‡]Requesting	Aggression and Disruptive Behavior
Amount of Requesting	Anxiety
Giving	

Note. [†]Item counts towards score if child is aged between 12 and 20 months *or* if child is aged between 21 and 30 months and used fewer than five words during assessment. [‡]Item counts towards score if child is aged between 21 and 30 months and used at least five words during assessment.

Appendix C - Published Manuscript (Chapter 1)



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Author:
Lacey Chetcuti,Mirko Uljarević,Katherine Ellis-Davies,Antonio Y. Hardan,Andrew J.O. Whitehouse,Darren Hedley,Samuel Putnam,Kristelle Hudry,Margot R. Prior

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Review

Temperament in individuals with Autism Spectrum Disorder: A systematic review

Lacey Chetcuti [a,1], Mirko Uljarević [b,c,*,1], Katherine Ellis-Davies [d], Antonio Y. Hardan [c], Andrew J.O. Whitehouse [e], Darren Hedley [a], Samuel Putnam [f], Kristelle Hudry [a], Margot R. Prior [b]

[a] Olga Tennison Autism Research Centre, School of Psychology and Public Health, La Trobe University, Melbourne, Australia
[b] Melbourne School of Psychological Sciences, University of Melbourne, Melbourne, Australia
[c] Department of Psychiatry and Behavioral Sciences, Child and Adolescent Psychiatry, Stanford Autism Center, School of Medicine, Stanford University, USA
[d] Department of Psychology, Swansea University, Wales, United Kingdom
[e] Telethon Kids Institute, University of Western Australia, Australia
[f] Department of Psychology, Bowdoin College, United States

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ABSTRACT

The study of temperament in Autism Spectrum Disorder (ASD) has the potential to provide insight regarding variability in the onset, nature, and course of both core and co-morbid symptoms. The aim of this systematic review was to integrate existing findings concerning temperament in the context of ASD. Searches of Medline, PsychInfo and Scopus databases identified 64 relevant studies. As a group, children and adolescents with ASD appear to be temperamentally different from both typically developing and other clinical non-ASD groups, characterized by higher negative affectivity, lower surgency, and lower effortful control at a higher-order level. Consistent with research on typically developing children, correlational findings and emerging longitudinal evidence suggests that lower effortful control and higher negative affect are associated with increased internalizing and externalizing problems in ASD samples. Longitudinal studies suggest there may be temperamental differences between high familial risk infants who do and do not develop ASD from as early as 6-months of age. Limitations of existing research are highlighted, and possible directions for future research to capitalize on the potential afforded through the study of temperament in relation to ASD are discussed.

1. Introduction

Autism Spectrum Disorder (ASD) is characterized by social-communication impairments – such as deficits in social-emotional reciprocity and in developing, maintaining, and understanding relationships – alongside restricted/repetitive patterns of behavior/interest and/or atypical responses to sensory input. The model of ASD symptom expression proposed within the 5th edition of the Diagnostic and Statistical Manual of Mental Disorders (DSM-5; American Psychiatric Association, 2013) goes some way in terms of alignment with the current dimensional conceptualization of this cluster of neurodevelopmental conditions than was true for the categorical model adopted within the previous edition (see Vivanti et al., 2013). However, neither the former nor the current classification system successfully capture the heterogeneity observed among individuals with ASD, nor adequately explain the sources of individual difference in presentation and outcome.

Alongside the varying manifestations of the core symptom profile, significant heterogeneity is apparent across every facet of ASD, including the timing of onset and course of symptom emergence, developmental outcomes in terms of cognitive/language impairment, and the presence of comorbidities including behavioral problems and mental health difficulties (Bryson et al., 2007; Prior et al., 1998). Such variation in phenotypic expression and associated outcomes beckons a need to provide support and treatment that is appropriately tailored to the individual needs of each person. Nevertheless, an inadequate understanding of the underlying processes and mechanisms that give rise to heterogeneity in ASD is a major impediment to this objective;

* Corresponding author at: Melbourne School of Psychological Sciences, University of Melbourne, Melbourne, Australia.
E-mail address: mirko.uljarevic@unimelb.edu.au (M. Uljarević).
[1] Authors contributed equally to the production of this manuscript

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precluding the refinement of intervention protocols and targets and making it difficult to predict longer-term outcomes on the basis of early presentation.

Although symptom severity and level of associated cognitive/language impairments are important prognostic indicators – such that individuals with milder symptom severity, greater functional abilities, and better verbal skills during childhood appear more likely to have optimal adult outcomes (Magiati, Tay, & Howlin, 2014) – heterogeneity in ASD is not fully attributable to disorder-specific characteristics. Rather, it has been suggested (Insel, Landis, & Collins, 2013; Mundy, Henderson, Inge, & Coman, 2007) that factors that are not specific to particular categorical diagnoses, but rather vary among all individuals regardless of diagnostic label, may provide important prognostic value over and above core symptom severity and level of cognitive functioning. Temperament is one such factor of potential importance for explaining the heterogeneity of ASD (Chetcuti, Uljarević, & Hudry, 2019).

Temperament is the term used to characterize biologically-based, individual differences in affectivity, reactivity, and regulation, particularly within the childhood years (McAdams, 1995; Revelle, 1995). A 40-year research base supports the conceptualization of temperament as a central organizer of development (Marshall, Fox, & Henderson, 2000); demonstrating the importance of temperament in understanding childhood developmental differences and later life outcomes. In this regard, research on temperament in the context of ASD could hold significant potential for furthering our understanding of the variability inherent to this cluster of conditions.

Therefore, the current review was conducted with the aim of providing a snapshot of existing literature on the topic of temperament and ASD. A brief overview of temperament concepts is provided, so as to identify the common tenets and reconcile a taxonomy of higher-order dimensions. This unified taxonomy is adopted to systematically integrate findings obtained via different measures representing distinct theoretical traditions. Next, we consider the influence of temperament on developmental outcomes and manifestations of psychopathology in typically developing/non-ASD populations, to provide a premise for comparison to individuals with ASD. We conclude this review by offering future directions and suggestions for how research in this area may be strengthened.

1.1. Overview of conceptualizations of temperament

In a seminal roundtable discussion and publication, Goldsmith et al. (1987) brought together researchers representing prominent temperament theories galvanizing the field. These models are described below.

A pioneering influence on the study of temperament came from the work of Thomas and Chess (1968) who delineated the following nine temperament dimensions: *activity*, *approach-withdrawal* (to/from new stimuli), *rhythmicity* (regularity of biological functions), *mood* (positive or negative), *distractibility* (ease of soothing), *threshold* (to respond), *intensity* (of response), *persistence*, and *adaptability* (to new experiences). Thomas and Chess's conceptualized temperament as the *style* rather than the content of behavior and emphasized the transactional relations between children's temperamental characteristics environmental influences, such as family dynamics. Hence, they stressed the influence of "goodness of fit" or the compatibility between a child's temperament and his/her environment. In addition to the nine dimensions, Thomas and Chess also introduced a typology of child temperaments – *easy*, *difficult*, and *slow-to-warm-up* temperament types – each with clear clinical implications (McClowry, Rodriguez, & Koslowitz, 2008). From within the Thomas and Chess model, Kyrios and Prior (1990) identified a higher-order temperament factor among pre-schoolers – that of self-regulation – which was derived from a cluster of dimensions including distractibility, persistence and rhythmicity related behaviors.

Buss and Plomin (1975, 1984) proposed that the dimensions of *emotionality*, *activity*, and *sociability* were stable over time and showed considerable generality across different temperament theories. An impulsivity dimension, originally included in Buss and Plomin's model of temperament, was later removed because it was considered not to have genetic/biological influence. However, more recent work has suggested that impulsivity (or components thereof) is heritable and relevant in the clinical domain (Gagne & Saudino, 2010).

Goldsmith (1987; 1982) conceptualized temperament as individual differences in the tendency to experience and express emotional behavior, with a focus on dimensions such as *positive affectivity*, *fear*, *anger*, and *psychobiological reactivity*. Emotion and emotion regulation were also central to the conceptualization of temperament proposed by Rothbart (in Goldsmith et al., 1987) who placed increased emphasis on underlying psychobiological processes. Within what can be considered a neurobiological approach, Rothbart proposed numerous temperament domains which were later integrated into the following higher-order factors: *surgency* (including activity level, sociability, and pleasure expressed in anticipation of reward or during high-intensity activities); *negative affectivity* (including anger, sadness, fear, physical discomfort, and recovery from distress); and a factor labelled *regulatory capacity* in infants and *effortful control* in older individuals (including the ability to focus attention, demonstrate satisfaction during low-intensity activities and, among older children, the capacity to exercise inhibitory control). These factors were subsequently integrated into more comprehensive biological and environmental themes relevant to personality models for adults (Putnam, Ellis, & Rothbart, 2001; Rothbart, Ahadi, & Hershey, 1994).

A neurobiological approach also underlies a conception of temperament proposed by Cloninger (1986) who originally argued for *novelty seeking*, *harm avoidance* and *reward dependence* as basic dimensions and proposed these to be associated with the monoaminergic activity (Cloninger, 1987). *Persistence* was later introduced as a fourth basic temperament dimension (Cloninger, Przybeck, Svrakic, & Wetzel, 1994). Cloninger's conceptualization differs from the aforementioned theories in that it was originally developed as a theory of adult personality, and later expanded to describe temperament in childhood. However, psychometric limitations have been noted in several versions of inventories based on Cloninger's model, calling into question his hypothesized structure of temperament traits (Farmer & Goldberg, 2008).

As can be seen, individual variability is the norm across all facets of temperament theory. While different theoretical approaches have offered various definitions of temperament, common to most is the understanding that individual differences in temperament are identifiable from early in life, persist over time, and show cross-contextual stability. Most conceptualizations also consider temperament to be heritable, although the extent to which this is a definitional criterion is debated (see Shiner et al., 2012).

1.2. Reconciling a higher-order framework for temperament traits

Although consensus on the dimensional structure of temperament has not been reached, several narrative reviews (Shiner et al., 2012; Zentner & Bates, 2008) and structural analyses of temperament measures (Mervielde & De Pauw, 2012) suggest that different conceptual models may converge on a set of overarching traits; potentially identified as affectivity/emotionality, sociability, and self-regulation. The unified taxonomy of overarching temperament traits (described below) is useful, as it facilitates the systematic integration of findings obtained via different measures representing different theoretical traditions.

An *affectivity/emotionality* trait describes an individual's tendency to experience negative emotions. This trait is clearly captured within each theoretical model; emerging from the mood and adaptability dimensions of Thomas and Chess, Buss and Plomin's emotionality, Rothbart's negative affectivity, and Cloninger's harm avoidance factors. A *sociability* trait refers to the tendency to actively engage with others, which is represented by sociability and shyness in Buss and Plomin's model, captured by Rothbart's surgency dimension, and Cloninger's reward dependence. Although Thomas and Chess's model lacks a clear sociability component, persistence, intensity, and approach-withdrawal are empirically related to sociability/shyness and surgency at certain ages (Mervielde & De Pauw, 2012). While sometimes viewed as a basic or independent dimension of temperament, activity level is viewed as an expression of behavioral activation and thus subsumed in this taxonomy within the dimension of sociability. This is consistent with Rothbart's model wherein the activity is subsumed within surgency, and with adult personality taxonomies where energy/activity level is conceived as a facet of extraversion. Finally, a factor that can be broadly termed *self-regulation* refers to the capacity to regulate emotions and action, which captures Thomas and Chess's and Cloninger's persistence dimensions, and Rothbart's effortful control.

1.3. Temperament as a predictor of developmental outcomes

A major research focus of temperament research has concerned the ways in which temperament affects health, emotional adjustment, and social outcomes, both directly and indirectly through reciprocal interaction with parenting practices (Belsky & Pluess, 2009; Sanson, Hemphill, & Smart, 2004). For instance, persistence and effortful control have been shown to have a positive influence on social competence, self-esteem, and educational outcomes (Keogh, 2003; Spinrad et al., 2007). Child temperament is also known to have a reciprocal influence on parenting behaviors as well as on relationships with siblings and peers. For example, within the domain of social development, temperamental traits have been associated with mother-infant interaction elicitation of particular types of parental response (McClowry et al., 2008). Furthermore, Kim and Kochanska (2012) found that infants' negative affectivity at 7 months moderated the impact of parent-child mutuality on later child self-regulation at 15 months. More specifically, infants high in negative emotionality showed lower levels of self-regulation when in a less responsive parent-child relationship but better self-regulation when in a responsive relationship.

Importantly, different domains of temperament interact with one another when predicting behavioral outcomes. The interactions between reactivity and regulatory dimensions of temperament are particularly relevant; such that regulatory capacities buffer against the potential adverse impact of negative emotionality (Kim & Kochanska, 2012).

1.4. Temperament in relation to psychopathological symptoms and disorders

In addition to developmental outcomes, extensive research has explored whether individual temperament characteristics relate to differences in psychopathology. While some studies have focused exclusively on the prediction of discrete clinical symptoms and disorders (e.g., ADHD), many have investigated links between temperament and common psychopathological symptoms hierarchically organized into broad-band internalizing and externalizing dimensions (Achenbach, 1966). Temperamental inhibition/social withdrawal has been shown to be a risk factor for the development of anxiety and other internalizing problems (Kagan & Snidman, 2004; Prior, Sanson, Smart, & Oberklaid, 1999; Putnam & Stifter, 2005) while positive emotionality/sociability has been found to contribute to externalizing problems (Kochanska & Kim, 2013). Similarly, irritability/negative emotionality and low self-regulation have been associated with both internalizing and externalizing (Eisenberg et al., 2001).

In recent years, researchers have moved toward exploring the nature of relations among temperament traits and psychopathological symptoms. Four explanatory models have been explicated (Watson, Clark, & Harkness, 1994); the *predisposition/vulnerability* model states that certain temperamental characteristics increase the probability of developing psychopathology, while the *continuity/spectrum* model posits that temperament and psychopathology share etiological underpinnings and represent opposite ends of the same underlying continuum. Other models suggest there may be an etiological distinction between temperament and psychopathology and posit that temperament may exacerbate (*pathoplasty/exacerbation* model) or be exacerbated by psychopathology (*complication/scar* model) after onset.

These explanatory models are not mutually exclusive, and all have received at least some empirical support. Nevertheless, studies that have tested competing models simultaneously through statistical modelling provide strong support for a continuity/spectrum association, as opposed to predisposition/vulnerability (De Bolle, Beyers, De Clercq, & De Fruyt, 2012; De Bolle, De Clercq, Caluwé, & Verbeke, 2016; Martel, Gremillion, Roberts, Zastrow, & Tackett, 2014). Likewise, twin studies show that a substantial proportion of the genetic influences underlying temperament are shared with psychopathology (Gjone & Stevenson, 1997).

In summary, a large body of research in non-ASD populations has demonstrated that particular dimensions of temperament can have both direct and indirect positive and negative influences on development across the lifespan and across a broad range of domains including social-emotional, behavioral, and psychopathology outcomes. In view of this evidence, we propose that research on temperament in the context of ASD could hold significant potential for furthering our understanding of the variability inherent in the developmental trajectories and outcomes for individuals with this cluster of conditions (for a discussion, see Chetcuti et al., 2019). Indeed, researchers have been exploring temperament in the context of ASD for around 30 years, and this is a timely opportunity to systematically integrate the findings across existing work to ascertain how temperament has been conceptualized and measured in this particular clinical field, to identify consistencies in the evidence base and gaps that still require attention and importantly, to propose a roadmap for future research in this area.

2. Methods

2.1. Databases and search terms

Medline, PsychInfo and Scopus databases were searched for published articles available through March 11th, 2020. Combinations (including truncated versions) of terms related to ASD and temperament were searched across all available fields: autism, asperger(s), pervasive developmental disorder, ASD, temperament, behavioral inhibition, negative affect, positive affect, surgency, extraversion, effortful control, reactivity, regulation, self-regulation, behavioral style, approach, avoidance, persistence, activity, rhythmicity. Terms within each subset were entered with the Boolean operation 'OR', and then aggregated using the operator 'AND'. Database searches were supplemented by a review of the reference sections of identified empirical and review papers involving temperament studies.

Both the first and second author independently screened articles for inclusion and articles were included based on consensus decision. Several inclusion and exclusion criteria were set for the retention of papers. First, papers were included if the target population comprised individuals diagnosed with an ASD (inclusive of autism, ASD, Autistic Disorder, Asperger's Disorder, Asperger Syndrome, atypical autism, or PDD-NOS). Studies that explored the association between temperament and *ASD traits* – either in the general population or among samples of individuals with other conditions (e.g., Anorexia Nervosa, ADHD etc.) – were excluded from this review. Within retained publications, no restrictions were imposed in terms of whether exploration of temperament was the primary study goal or whether temperament was included as one among a number of constructs of interest. Where temperament was not the primary focus, however, only the study section relevant to temperament was summarized for this review. Studies that did not use questionnaire or observational measures that specifically captured temperament in a quantitative manner were not eligible for inclusion; for instance, studies that only explored neurobiological systems linked to temperament (e.g., right/left lateralization), studies on executive functioning, studies looking at qualitative temperament behavior. No restrictions were imposed regarding the ages of individuals with ASD, nor regarding sample size, though single case studies and case series were not included. Non-empirical papers and unpublished studies were not included, nor were those published in languages other than English. These eligibility criteria were applied to database searches where possible through use of limits and filters, and during article screening.

2.2. *Search results and coding procedures*

The search process is depicted in Fig. 1. After removing duplicates and obviously non-relevant papers, initial searches yielded 789 studies, 629 of which were excluded following the reading of the abstract, resulting in 160 studies potentially retained for analysis. Following a full review, a further 101 studies were excluded due to (i) being irrelevant or (ii) not meeting the aforementioned criteria. Review of reference lists yielded another 5 studies, for a total of 64 studies included in this analysis.

Retained studies were coded for: (a) full description of the ASD group in terms of chronological age (CA) and sex composition and other control group/s; (b) design (cross-sectional vs. longitudinal); (d) features of temperament measures adopted, including name, type (i.e., questionnaire/interview/observational study), informant (i.e., parent- or self-report). Background information is summarized in Table 1. Studies were then coded in terms of the results obtained, summarized across Tables 2 and 4 (cross-sectional and longitudinal studies) and Table 5 (prospective studies of ASD).

2.3. *Statistical analysis*

A meta-analysis was performed to consolidate studies (i) comparing level of specific temperament dimensions between ASD and non-ASD (normative and/or clinical) groups and (ii) exploring association between temperament dimensions and other factors. Where measures were comparable but not identical, the reported statistics were standardised to facilitate combination and comparing of the effect estimates. For studies that reported comparisons or correlations across several time points, findings reported here refer to the baseline data, however, supplemental analyses were conducted to investigate potential different effects at later time points. The mean correlations between temperament dimensions and other factors and comparisons between ASD and non-ASD groups were aggregated using a random-effects model.

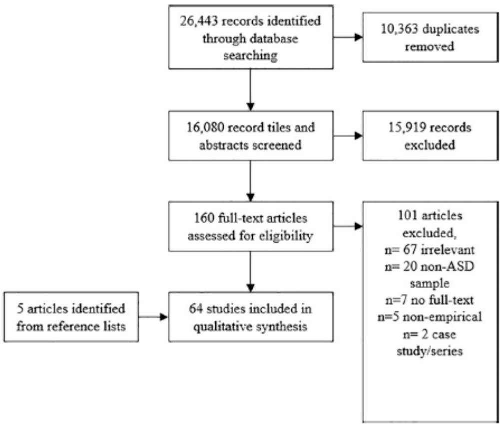

Fig. 1. PRISMA flow diagram.

3. Results

3.1. *Overview of studies*

Among the 64 studies retained for review, 45 were cross-sectional, one was a long-term follow-up study, and 18 were prospective longitudinal. The majority of studies focused on very young children and younger adolescents. Twenty-nine studies provided a comparison of ASD to TD individuals only, and 18 studies provided a comparison to individuals with some other clinical condition – most frequently, individuals with ADHD (6 studies) or with developmental delay/Down syndrome (10 studies)– alongside a TD group, in most cases.

Most studies matched individuals in groups on at least one variable – most commonly chronological age (CA) – either exclusively (7 studies) or in combination with other parameters (12 studies). In three studies, ASD and comparison groups differed in terms of mental age/IQ (Glaser & Shaw, 2011; Gottlieb & Bortner, 1984; Ratekin, 1993). Thus, there was substantial variability across studies in the sampling of target and comparison groups as well as in methods of group matching.

3.2. *Measuring temperament*

Fifty four studies used questionnaire measures of temperament, while eight reported on observational measurement and two combined both of these methods (i.e., Macari et al., 2018; Ratekin, 1993). The most frequently used questionnaire measures were based on the work of Rothbart and colleagues, with 27 studies using age-appropriate versions of their measures. Thirteen studies used measures based on the conceptualization proposed by Thomas and Chess (1968). Nine studies used a questionnaire measure based on Cloninger's model (1986; 1987) while only one study used a measure based on Buss and Plomin's model (Buss & Plomin, 1975, 1984). Six remaining studies used questionnaire measures not clearly aligned with any of the dominant models of temperament (see Table 1.).

In terms of informants, 13 studies relied on self-report, while two included both self- and other-report measures, and 39 relied on other-report alone. The choice of informant seemed dependent on participants' age and developmental stage; such that research with younger children predominantly relied on parent-report, and self-report measures were more frequently utilized in later childhood/adolescence. Only one study had both mothers and fathers provide independent reports on the temperament of each child participant (i.e., Boström, Broberg, & Hwang, 2010).

Among the 54 questionnaire-based studies, only ten examined the psychometric properties of the temperament measure adopted with the ASD participant sample in question. Five studies explored the psychometric properties of measures derived from the conceptual approach of Thomas and Chess. Konstantareas and Papageorgiou (2006) computed Cronbach's α on the overall Dimensions of Temperament Scale–Revised (DOTS–R–Child: Windle & Lerner, 1986), finding $\alpha = 0.62$, but did not report data for individual DOTS-R subscales. Internal consistency >0.70 was also reported by Rivers and Stoneman (2008) for activity level, persistence, behavior inhibition, and negative emotionality scales of the Temperament Assessment Battery-Revised (TAB-R). Del Rosario, Gillespie-Lynch, Johnson, Signman, and Hutman (2014) found that among 6-month-old infants with later diagnosed ASD, only one of the nine scales of the Revised Infant Temperament Questionnaire (RITQ) – the activity scale – had adequate internal consistency (Cronbach's $\alpha = 0.74$), though this situation improved such that by 36 months of participant age, only three of the Behavior Style Questionnaire (BSQ) scales (i.e., persistence, sensory reactivity and rhythmicity) had internal consistency coefficients <0.70.

Hepburn and Stone (2006) reported test-retest reliability scores (mean = 26 days between assessments) >0.68 for all of the BSQ subscales, and internal consistency >0.70 for all apart from rhythmicity ($\alpha = 0.48$), mood ($\alpha = 0.51$) and threshold ($\alpha = 0.40$). Similarly, Barger

Table 1
Overview of the studies.

Study	Subject characteristics					Design	Temperament measure			
	ASD			Other						
	n	Age[a]	% male	Type	n		Name	Type	Format[b]	Alignment
Adamek et al. (2011)	111	M = 4.2 yrs (SD = 1.5)	82	Reference TD	517	CS	CBQ-Short Form	Q	PR (87% Mo)	Ro
Anckarsäter et al. (2006)	66	Mdn = 31 yrs (Range = 19-60)[c]	55[c]	1) ADHD 2) ADHD + ASD	1) 100 2) 47	CS	TCI	Q	SR	Cl
Baker, Fenning, and Moffitt (2019)	46	M = 81.51 mths (SD = 24.18)	80	–	–	CS	Dysregulation Coding System	O	–	–
Bailey et al. (2000)	31	M = 64.1 mths (Range = 36-84)[c]	100	1) FXS 2) Reference TD	1) 31 2) 350	CS	BSQ	Q	SR	T&C
Barger et al. (2019)	649	M = 4.9 yrs (SD = 0.6)	82	TD	866	CS	BSQ	Q	PR (Mo)	T&C
Berkovits et al. (2017)	108	M = 5.7 yrs (SD = 1.1)	82.4	–	–	L	ERC	Q	PR (Mo)	–
Bieberich and Morgan (2004)	14	M = 8.37 yrs (SD = 2.46)	86	DS	15	L	MN-PARS	O	–	–
Bieberich and Morgan (1998)	18	M = 8.23 yrs (SD = 2.53)	78	DS	18	CS	MN-PARS	O	–	–
Bölte et al. (2008)	49	M = 10.3 yrs (SD = 3.8)	72[c]	–	–	CS	JTCI	Q	PR (Mo)	Cl
Bolton et al. (2012)	86	6 mths	NR	–	–	L	CTQ	Q	PR (Mo)	T&C
Bos et al. (2018)	66	M = 11.65 yrs (SD = 1.27)	100	TD	89	L	Mood Questionnaire	Q	SR	–
Boström et al. (2010)	12	M = 37.42 (SD = 24.15)[c]	61.8[c]	1) DS 2) ID/DD 3) CP/MI 4) Other diagnoses 5) TD	1) 9 2) 14 3) 5 4) 15 5) 178	CS	EASI Temperament Survey	Q	PR (Mo & Fa)	B&P
Brock et al. (2012)	54	M = 56.17 mths (SD = 13.67)	83	1) DD 2) Reference TD	1) 33 2) 350	CS	BSQ	Q	PR (NR)	T&C
Bryson et al. (2018)	16	6 mths	44	1) HR-No ASD 2) LR	1) 67 2) 53	L	IBQ	Q	PR (NR)	Ro
Burrows et al. (2016)	104	M = 13.31 yrs (SD = 2.06)	87	TD	94	CS	EATQ-R	Q	SR	Ro
Chuang, Tseng, Lu, and Shieh (2012)	67	M = 64.21 mths (SD = 9.01)	85	TD	44	CS	BSQ Chinese version	Q	PR (NR)	T&C
Chuang et al. (2014)	106	M = 54.4 mths (SD = 9.6)	85	–	–	CS	BSQ Chinese version	Q	PR (NR)	T&C
Clifford et al. (2013)	17	M = 7.2 mths (SD = 1.1)[c]	65	1) LR 2) HR-TD 3) HR-Atypical	1) 48 2) 24 3) 12	L	IBQ-R, ECBQ	Q	PR (NR)	Ro
De Pauw et al. (2011)	175	M = 10.28 yrs (SD = 2.4)	85	TD	500	CS	CBQ Dutch very short form, EATQ-R	Q	PR (50% Mo)	Ro
Del Rosario et al. (2014)	10–16	M = 6.5 mths (SD = 0.9)	86	HR-TD	7–27	L	CTS	Q	PR (NR)	T&C
Faja and Dawson (2015)	21	M = 82.0 mths (SD = 7.1)	71	TD	21	CS	CBQ	Q	PR (NR)	Ro
Fenning et al. (2018)	46	M = 6.39 yrs (SD = 1.95)	80	–	–	CS	Dysregulation Coding System	O	–	–
Garon et al. (2009)	34	6–12 mths	65	1) LR 2) HR-No ASD	1) 73 2) 104	L	TBAQ-R	Q	PR (NR)	Ro
Garon et al. (2016)	98	6–12 mths	NR	1) LR 2) HR-No ASD	1) 162 2) 285	L	IBQ, TBAQ-R	Q	PR (NR)	Ro
Glaser and Shaw (2011)	19	M = 9.48 yrs (SD = 3.81)	63	22q13 DS	18	CS	TABS	Q	PR (NR)	–
Gomez and Baird (2005)	65	M = 8.3 yrs	89	Reference TD	120	CS	TABS	Q	PR (94% Mo)	–
Gottlieb and Bortner (1984)	12	M = 5.2 yrs (SD = 7.2 mths)	NR	1) DD/ID 2) Reference TD	1) 12 2) 350	CS	BSQ	Q	PR (NR)	T&C
Helles et al. (2016)	40	M = 11.5 yrs (SD = 4.8)	100	Reference TD	NR	L	TCI	Q	SR	Cl
Hendry et al. (2018)	16	M = 8.80 mths (SD = 0.83)	89		1) 23 2) 75	L	CBQ-Short Form	Q	PR (NR)	Ro

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Table 1 (*continued*)

Study	Subject characteristics					Design	Temperament measure			
	ASD			Other						
	n	Age[a]	% male	Type	n		Name	Type	Format[b]	Alignment
				1) LR 2) HR-No ASD						
Hepburn and Stone (2006)	110	M = 57.3 mths (SD = 15.4)	86	Reference TD	350	CS	BSQ	Q	PR (Mo)	T&C
Hirschler-Guttenberg, Golan, et al. (2015)	40	M = 63.38 mths (SD = 12.35)	87	TD	40	CS	Modified Lab-TAB	O	–	Ro
Hirschler-Guttenberg, Feldman, et al. (2015)	40	M = 63.38 mths (SD = 12.35)	87	TD	40	CS	Modified Lab-TAB	O	–	Ro
Hooijer and Sizoo (2020)	74	Mdn = 28.5 yrs (IQR 23–42.3)	61	–	–	CS	TCI Dutch abbreviated version	Q	SR	Cl
Jahromi, Meek, and Ober-Reynolds (2012)	20	M = 58.95 mths (SD = 11.50)	NR	TD	20	CS	Lab-TAB, Unsolvable puzzles task	O	–	Ro, –
Kasari and Sigman (1997)	28	M = 42.39 mths (SD = 11.61)	93	1) DD/DS 2) TD	1) 26 2) 28	CS	BSQ	Q	PR (NR)	T&C
Kerekes et al. (2013)	1886	9 and 12 yrs	55	–	–	CS	JTCI	Q	PR (89% Mo)	Cl
Konstantareas and Stewart (2006)	19	M = 6.16 yrs	63	TD	23	CS	CBQ	Q	PR (Mo)	Ro
Konstantareas and Papageorgiou (2006)	43	M = 122.6 mths (SD = 71.8)	84	–	–	CS	DOTS-R-Child	Q	PR (Mo)	T&C
Korbut et al. (2020)	26	M = 3.30 yrs (SD = 0.68)	73	–	–	L	ECBQ	Q	PR (NR)	Ro
Macari et al. (2017)	165	M = 26.46 mths (SD = 5.77)	82	1) DD 2) TD	1) 58 2) 92	L	TBAQ-S	Q	PR (74.5% Mo)	Ro
Macari et al. (2018)	43	M = 21.9 mths (SD = 3.0)	88	1) DD 2) TD	1) 16 2) 40	CS	Modified Lab-TAB, ECBQ	Q, O	PR (NR)	Ro
Millea et al. (2013)	28	M = 12.34 yrs (SD = 1.93)	89	–	–	CS	EATQ-R Short Form	Q	SR	Ro
Myles et al. (2007)	156	M = 14.97 yrs	79	Reference TD	NR	CS	EATQ-R	Q	PR (NR)	Ro
Nazim and Khalid (2019)	92	M = 8.62 yrs (± 1.87)	66	–	–	CS	CBQ Urdu version, TMCQ Urdu version	Q	PR (NR)	Ro
Ostfeld-Etzion et al. (2016)	40	M = 63.38 mths (SD = 12.35)	88	TD	40	CS	CBQ	Q	PR (Mo)	Ro
Özyurt et al. (2018)	31	Mdn = 44 mths (IQR = 12)	61[c]	1) DLD 2) TD	1) 45 2) 52	CS	ERC	Q	PR (Mo)	–
Paterson et al. (2019)	61	M = 6.45 mths (SD = 0.59)	79	1) HR-No ASD 2) LR	1) 221 2) 114	L	IBQ-R	Q	PR (NR)	Ro
Pijl et al. (2020)	75	M = 8.3 mths (SD = 1.4)	75	1) HR-Atypical 2) HR-Typical 3) LR	1) 34 2) 75 3) 66	L	IBQ-R, ECBQ	Q	PR (NR)	Ro
Ratekin (1993)	30	M = 42.53 mths (SD = 11.28)	90	1) DD 2) TD	1) 30 2) 30	CS	PTQ, NR	Q, O	–	–
Reyes et al. (2019)	37	M = 34.11 mths	78	1) DD 2) TD	1) 29 2) 27	L	CTS	Q	PR (NR)	T&C
*Rivers and Stoneman (2008)	50	M = 7.6 yrs	84	TD Siblings	50	CS	TAB-R, SATI	Q	PR (98% Mo)	T&C
Samyn et al. (2011)	27	M = 12.73 yrs (SD = 1.46)	100	1) ADHD 2) TD	1) 27 2) 27	CS	ECS, ACS, EATQ-R	Q	PR (NR), SR	Ro
Samyn et al. (2015)	31	M = 12.83 yrs (SD = 1.41)	100	1) ADHD 2) TD	1) 30 2) 148	CS	ECS, ACS, EATQ-R	Q	PR (NR), SR	Ro
Samyn et al. (2017)	25	M = 12.94 yrs (SD = 1.45)	100	1) ADHD 2) TD	1) 25 2) 25	CS	ECS, ACS, EATQ-R	Q	SR	Ro
Schwartz et al. (2009)	44	M = 155.34 mths (SD = 28.08)	84	TD	38	CS	EATQ-R	Q	SR	Ro
*Shephard et al. (2019)	15	M = 7.31 mths (SD = 1.19)[c]	48[c]	1) HR-No ASD 2) LR	1) 27 2) 37	L	IBQ-R, ECBQ	Q	PR (NR)	Ro
Sizoo et al. (2009)	75	M = 33.6–36.9 yrs (SD = 10.6–13.8)	80	1) ADHD 2) Reference TD	1) 53 2) NR	CS	VTCI	Q	SR	Cl
Sizoo et al. (2014)	75	M = 34.3 yrs. (SD = 11.87)	81	ADHD	53	CS	VTCI	Q	SR	Cl
Soderstrom et al., 2002	31	Mdn = 23 yrs (Range = 17–55)	90	Reference TD	NR	CS	TCI	Q	SR	Cl
Uljarević et al. (2017)	71	M = 18.71 yrs (SD = 2.51)	69	–	–	CS	ATQ	Q	SR	Ro
Vuijk et al. (2018)	66	M = 38 yrs (SD = 12.5)	100	Reference TD	66	CS	TCI	Q	SR	Cl

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Table 1 (*continued*)

Study	Subject characteristics					Design	Temperament measure			
	ASD			Other						
	n	Age[a]	% male	Type	n		Name	Type	Format[b]	Alignment
Yirmiya et al. (2006)	21–30	M = 20.23 wks (SD = 3.24)	37–62	HR-TD	21–31	L	ICQ	Q	PR (Mo)	–
Zantinge et al. (2019)	21	M = 60 mths (SD = 9.33)	95	TD	45	CS	Lab-TAB	O	–	Ro
Zwaigenbaum et al. (2005)	12–19	M = 6.44 mths (SD = 12.50)[c]	NR	1) HR-No ASD 2) LR	1) 32 2) 15–23	L	IBQ, TBAQ	Q	PR (Mo)	Ro

Note.
[a] Age is chronological, at the first timepoint for longitudinal studies.
[b] Parent respondent(% mother or father) is in parentheses.
[c] Characteristics not reported separately for ASD. PR = parent report; SR = self-report; NR = not reported. ASD = Autism Spectrum Disorder; TD = Typically Development; ADHD = Attention Deficit Hyperactivity Disorder; FXS = Fragile X Syndrome; DLD = Developmental Language Delay; DS = Down Syndrome; ID = Intellectual Disability; CP/MI = Cerebral Palsy/Motor Impairment; DD = Developmental Delay; LR = Low Risk; 22q13 DS = 22q13 Deletion Syndrome; HR = High Risk; L = Longitudinal; CS = Cross-sectional; CBQ = Children's Behavior Questionnaire; TCI = Temperament and Character Inventory; BSQ = Behavioral Style Questionnaire; ERC = Emotion Regulation Checklist; MN-PARS = Minnesota Preschool Affect Rating Scales; JTCI = Junior Temperament and Character Inventory; CTQ = Carey Temperament Questionnaires; EASI = Emotionality Activity Sociability and Impulsivity; EATQ-R = Early Adolescent Temperament Questionnaire-Revised; IBQ = Infant Behavior Questionnaire-Revised; ECBQ = Early Childhood Behavior Questionnaire; SIB-R = Scales of Independent Behavior-Revised; TBAQ = Toddler Behavior Assessment Questionnaire; TABS = Temperament and Atypical Behavior Scale; DOTS-R-Child = Dimensions of Temperament Scale–Revised; TBAQ-R = Toddler Behavior Assessment Questionnaire-Revised; Lab-TAB = Laboratory Temperament Assessment Battery; PTQ = Preschool Temperament Questionnaire; TAB-R = Temperament Assessment Battery-Revised; SATI = School-Aged Temperament Inventory; ECS = Effortful Control Scale; ACS = Attentional Control Scale; VTCI = Dutch Temperament and Character Inventory; ATQ = Adult Temperament Questionnaire; ICQ = Infant Characteristics Questionnaire; Ro = Rothbart; Cl = Cloninger; T&C = Thomas and Chess; B&P = Buss and Plomin.

et al. (2019) reported internal consistency estimates >0.70 for all subscales apart from mood ($\alpha = 0.67$), persistence ($\alpha = 0.60$), rhythmicity ($\alpha = 0.59$), and threshold ($\alpha = 0.52$). Of note, the CTS also do not tend to have strong internal consistency in non-ASD populations (Windle & Lerner, 1986).

Five studies explored the psychometric properties of measures derived from the conceptual approach of Rothbart. Konstantareas and Stewart (2006) found that, with the exception of the smiling and laughter scale ($\alpha \leq 0.53$), internal consistency values for the Children's Behavior Questionnaire (CBQ) fine-grained scales were > 0.63, with most being above 0.75. Internal consistency estimates >0.60 were reported for all fine-grained scales of the Toddler Behavior Assessment Questionnaire-Revised (TBAQ-R) (Garon et al., 2009), but only four (of 12) scales comprised in the Early Adolescent Temperament Questionnaire-Revised (EATQ-R) (Burrows, Usher, Schwartz, Mundy, & Henderson, 2016). Nonetheless, Burrows et al. (2016) reported acceptable internal consistency for the EATQ-R dimensions (surgency [$\alpha = 0.72$], negative affect [$\alpha = 0.76$], effortful control [$\alpha = 0.74$], and affilation [$\alpha = 0.64$]), as did Uljarević, Richdale, Evans, Cai, and Leekam (2017) for the effortful control dimension of the Adolescent/Adult Temperament Questionnaire (ATQ; $\alpha = 0.84$) and Korbut, Hedley, Chetcuti, Sahin, and Nuske (2020) for Early Childhood Behavior Questionnaire (ECBQ) dimensions apart from surgency-extraversion ($\alpha = 0.36$).

Two studies examined the factor structure of temperament questionnaires in the context of ASD. Barger et al. (2019) derived factors corresponding to the original BSQ maladaptability, activity, and rhythmicity scales were in children with ASD and a population comparison group. However, several novel factors emerged across both groups blending BSQ items from different scales – labelled environmental sensitivity, quiet persistence, food openness, social inattention, social approach, and crying – and the ASD group showed evidence of a unique negative social interactions factor. Further, Garon et al. (2016) found the same higher-order factors and factor loadings could be specified for the Infant Behavior Questionnaire (IBQ) and Toddler Behavior Assessment Questionnaire-Revised (TBAQ-R) among high and low familial ASD risk infants. However, differences in factor intercepts indicated non-invariance of the IBQ and TBAQ-R across groups.

In summary, the majority of studies of temperament in ASD have used only one method of assessing temperament, most frequently questionnaire. From the psychometric evidence reported, it seems reasonable to utilize measures of temperament developed for use with TD populations among ASD samples. Measures based on the temperament models put forward by Thomas and Chess and Rothbart have garnered the most psychometric support in samples with ASD; however, two studies (i.e., Barger et al., 2019; Garon et al., 2016) suggest there may be differences in instrument factor structure. Furthermore, very few studies have used both self- and informant-reports of temperament and only one study has used both maternal and paternal reports (Boström et al., 2010).

Finally, although several studies have explored the relationship between temperament and both the core and associated/co-morbid problems experienced by people with ASD, only one study adopted the conservative method of removing items from temperament measures in an attempt to avoid overlap with other related constructs. Specifically, Adamek et al. (2011) removed two and reworded three CBQ items from the anger/frustration subscale in order to avoid overlap between temperamental negative affectivity and problem behaviors, as measured by the Aberrant Behavior Checklist. We return to consider this point further, below.

3.3. *Summary of empirical results*

A detailed summary of results from each study is presented in Tables 2, 4 and 5. Here, we first consider the findings of studies that have compared temperament trait levels between samples of individuals with ASD and TD individuals, before turning to those that have compared individuals with ASD to those with other clinical conditions. To facilitate interpretation we synthesize the findings using the higher-order framework presented above and focus our narrative on those studies that have used assessments based on the dominant models of temperament (i.e., those of Rothbart, Thomas and Chess, Buss and Plomin, and Cloninger) in examining between-group similarities and differences. Nevertheless, Table 2 presents results for all studies, including those that have adopted questionnaire measures not clearly aligned with any of the dominant frameworks. Finally, we consider findings regarding

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Table 2
Summary of between-group differences.

Study	Affectivity/Emotionality		Sociability		Self-regulation	
	ASD vs TD	ASD vs	ASD vs TD	ASD vs	ASD vs TD	ASD vs
Adamek et al. (2011)	>anger/frustration <discomfort ≈soothability ≈sadness		>high intensity pleasure ≈activity level ≈impulsivity ≈shyness		<inhibitory control <attentional focusing >low intensity pleasure	
Anckarsäter et al. (2006)	>harm avoidance	ADHD: ≈harm avoidance	<reward dependence	ADHD: <reward dependence	<novelty seeking ≈persistence	ADHD: <novelty seeking ≈persistence
Bailey et al. (2000)	<adaptability ≈mood	FXS: >mood ≈adaptability	<intensity <approach ≈activity	FXS: <activity <intensity ≈approach	<persistence <distractibility <threshold >rhythmicity	FXS: <distractibility <threshold ≈rhythmicity ≈persistence
Barger et al. (2019)	>maladaptability >crying		<social approach >social inattention ≈activity		<rhythmicity <quiet persistence <food openness <environmental sensitivity	
Bieberich and Morgan (2004)		DS: ≈negative affect (irritability, hostility, compliance; T1/2)		DS: <positive affect (affective sharing; T1/2)		DS: <self-regulation (attention, object orienting, persistence; T1/2)
Bieberich and Morgan (1998)		DS: >negative affect		DS: <positive affect ≈activity level		DS: <self-regulation
Boström et al. (2010)		DS: >emotionality CP/MI: >emotionality ID: ≈emotionality OD: ≈emotionality		DS: <sociability >shyness ≈impulsivity ≈activity CP/MI: <sociability ≈impulsivity ≈shyness ≈activity ID: <sociability >impulsivity ≈shyness ≈activity OD: <sociability ≈impulsivity ≈shyness ≈activity		
Brock et al. (2012)	<adaptability ≈mood	DD: ≈adaptability ≈mood	>activity <approach <intensity	DD: <approach ≈activity ≈intensity	<rhythmicity <persistence <distractibility <threshold	DD: <distractibility ≈rhythmicity ≈persistence ≈threshold
Burrows et al. (2016)	>negative affect (aggression, depressive mood) ≈frustration		<surgency (high intensity pleasure, fear, shyness) ≈affiliation (affiliation, pleasure sensitivity, perceptual sensitivity)		<attention ≈effortful control (activation control, inhibitory control)	
Chuang et al. (2012)	<adaptability >mood		>activity <approach ≈intensity		<persistence <distractibility <threshold ≈rhythmicity	
De Pauw et al. (2011)	>negative affect		<surgency		<effortful control	
Faja & Dawson (2013)			≈approach ≈impulsivity		<effortful control (attention focusing, inhibitory control, low intensity pleasure) ≈perceptual sensitivity	
Glaser and Shaw (2011)						22q13 DS: >self-regulatory difficulties (detached) ≈hypersensitive ≈underreactive ≈dysregulated

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Table 2 (*continued*)

Study	Affectivity/Emotionality		Sociability		Self-regulation	
	ASD vs TD	ASD vs	ASD vs TD	ASD vs	ASD vs TD	ASD vs
Gomez and Baird (2005)					>self-regulatory difficulties (detached, hypersensitive, underreactive, dysregulated)	
Helles et al. (2016)		No longer ASD: ≈harm avoidance ASD with comorbidity: <hard avoidance		No longer ASD: >reward dependence ASD with comorbidity: ≈reward dependence		No longer ASD: <novelty seeking ASD with comorbidity: ≈novelty seeking
Hendry et al. (2018)					<effortful control	HR-No ASD: <effortful control
Hepburn and Stone (2006)	<adaptability ≈mood		≈activity ≈approach ≈intensity		<threshold of responsiveness <persistence ≈distractibility ≈rhythmicity	
Hirschler-Guttenberg, Feldman, et al. (2015)					≈emotion regulation	
Hirschler-Guttenberg, Golan, et al. (2015)	>negative emotionality with father (but ≈ with mother)		<positive emotionality		>self-regulatory behavior	
Hooijer and Sizoo (2020)		ASD with suicidal ideation: <harm avoidance ASD with suicidal attempt(s): ≈harm avoidance		ASD with suicidal ideation: ≈reward dependence ASD with suicidal attempt (s): ≈reward dependence		ASD with suicidal ideation: >novelty seeking ≈persistence ASD with suicidal attempt (s): ≈novelty seeking ≈persistence
Jahromi et al. (2012)					<persistence	
Kasari and Sigman (1997)	>difficult temperament	DD/DS: >difficult temperament				
Konstantareas and Stewart (2006)	<soothability ≈discomfort		≈shyness ≈smiling and laughter		<attention focusing <attention shifting <inhibitory control ≈perceptual sensitivity	
Macari et al. (2017)	>negative emotionality (soothability) ≈anger ≈discomfort ≈sadness ≈social fear	DD: ≈negative emotionality ≈soothability ≈anger ≈discomfort ≈sadness ≈social fear	<surgency (positive anticipation) ≈activity ≈high intensity pleasure	DD: <surgency (positive anticipation) ≈activity ≈high intensity pleasure	<effortful control (attention shifting, inhibitory control, low intensity pleasure, perceptual sensitivity) ≈attention focusing	DD: <effortful control (attention shifting, inhibitory control, low intensity pleasure, perceptual sensitivity) ≈attention focusing
Macari et al. (2018)	<fear intensity ≈anger intensity ≈ incongruent negative emotions	DD: <fear intensity >anger intensity ≈incongruent negative emotions	≈joy intensity	DD: ≈joy intensity		
Myles et al. (2007)	>fear >frustration >aggression >depressed mood		>affiliation >shyness ≈surgency/high intensity pleasure		<activation control	
Ostfeld-Etzion et al. (2016)	≈anger frustration ≈discomfort ≈soothability ≈fear ≈sadness		≈activity level ≈approach ≈high intensity pleasure ≈impulsivity ≈shyness ≈smiling and laughter		<attention focusing <inhibitory control <perceptual sensitivity ≈attention shifting ≈low intensity pleasure	
Özyurt et al. (2018)		DLD: >emotional lability				DLD: <emotion regulation
Ratekin (1993)		DD: >sensitivity	<approach >intensity			DD: >distractibility

(*continued on next page*)

Table 2 (*continued*)

Study	Affectivity/Emotionality		Sociability		Self-regulation	
	ASD vs TD	ASD vs	ASD vs TD	ASD vs	ASD vs TD	ASD vs
	>sensitivity <mood <adaptability	<mood <adaptability		DD: <approach >intensity	>distractibility <task orientation <personal social flexibility	<task orientation <personal social flexibility
Reyes et al. (2019)	>mood (T1/2) <adaptability (T2)	DD: >mood (T1/2) <adaptability (T1/2)	<approach (T1/2) >intensity (T1) ≈activity	DD: >activity (T2) <approach (T1/2) ≈intensity	<distractibility (T1/2) <rhythmicity (T2) <persistence (T2) ≈threshold	DD: <distractibility (T1/2) <rhythmicity (T2) <persistence (T2) ≈threshold
Samyn et al. (2011)					<inhibitory control (PR/SR) <activation control (PR) <attention control (PR/SR) <attention focusing <attention shifting ≈persistence/low distractibility ≈impulsivity	ADHD: >activation control (SR) >persistence/low distractibility >impulsivity ≈attention focusing ≈attention shifting ≈inhibitory control ≈attention control
Samyn et al. (2015)					<attention control (PR) <activation control (PR) <inhibitory control (PR) <persistence/low distractibility <attention focusing <attention shifting ≈impulsivity	ADHD: >attention control (PR/SR) >activation control (SR) >impulsivity (SR) >persistence/low distractibility ≈attention focusing ≈attention shifting ≈inhibitory control
Schwartz et al. (2009)	>negative affectivity		<surgency ≈affiliativeness		≈effortful control	
Sizoo et al. (2009)	>hard avoidance		<reward dependence		≈novelty seeking ≈persistence	
Sizoo et al. (2014)	>harm avoidance	ADHD: >harm avoidance	≈reward dependence	ADHD: ≈reward dependence	≈novelty seeking ≈persistence	ADHD: <novelty seeking ≈persistence
Soderstrom et al. (2002)	>harm avoidance		<reward dependence		<novelty seeking ≈persistence	
Vuijk et al. (2018)	>harm avoidance		<reward dependence		<novelty seeking ≈persistence	
Zantinge et al. (2019)	≈fear expression					

Note. “<” and “>” are signs used to denote that one group shows either higher or lower level of behaviors/traits/problems in question. ASD = Autism Spectrum Disorder; TD = Typically Development; ADHD = Attention Deficit Hyperactivity Disorder; FXS = Fragile X Syndrome; DLD = Developmental Language Delay; DS = Down Syndrome; ID = Intellectual Disability; CP/MI = Cerebral Palsy/Motor Impairment; DD = Developmental Delay; 22q13 DS = 22q13 Deletion Syndrome; T = timepoint; PR = parent report; SR = self-report.

associations among measures of temperament and other factors examined within studies (Table 4), before summarising the findings of prospective longitudinal investigations of temperament and ASD diagnosis (Table 5). Although there was a wide variability across studies in terms of temperament assessments and characteristics of ASD and comparison groups, it was possible to aggregate data for the broad temperamental dimensions of affectivity/emotionality, self-regulation and sociability. Similar measurement and design issues were present with regards to studies exploring association among temperament dimensions and other factors, and it was therefore possible to synthesize some of this evidence using the meta-analytic approach but only with regards to the noted broad temperamental dimensions. Quantitative findings for the comparisons between ASD and non-ASD groups are presented in Table 3. Quantitative findings for the correlational studies are presented in Table 6.

3.4. *Temperamental differences between ASD and TD samples*

Studies using questionnaire measures based on Rothbart's conceptualization of temperament have shown that, when compared to TD children/adolescents, those with ASD tend to show a characteristic pattern of scores across the broad factors/constructs assessed; lower effortful control, lower surgency and affiliativeness, and higher negative affect (Adamek et al., 2011; De Pauw, Mervielde, Van Leeuwen, & De

Table 3
Meta-analysis of studies exploring temperamental differences between ASD, typical development and other clinical samples.

	N studies	Mean ES	se	95% CI	*p*	Q	I^2	*p*
ASD vs TD								
Affectivity/Emotionality	8	2.34	0.659	[1.059, 3.636]	<0.001	369.269	98.64%	<0.001
Self-regulation	7	−2.10	0.707	[−3.485, −0.712]	0.003	358.731	98.85%	<0.001
Sociability	7	−1.12	0.509	[−2.115, −0.121]	0.028	244.042	97.95%	<0.001
ASD vs other clinical samples								
Affectivity/Emotionality	7	0.46	0.142	[0.186, 0.741]	0.001	17.11	59.61%	0.009
Self-regulation	6	−0.51	0.995	[−2.463, 1.436]	0.61	331.71	98.89%	< 0.001
Sociability	6	−0.47	0.70	[−1.854, 0.909]	0.502	245.96	97.91%	< 0.001

Clercq, 2011; Garon et al., 2009; Glaser & Shaw, 2011; Macari, Koller, Campbell, & Chawarska, 2017; Myles et al., 2007; Ostfeld-Etzion, Feldman, Hirschler-Guttenberg, Laor, & Golan, 2016; Samyn, Roeyers, & Bijttebier, 2011; Samyn, Roeyers, Bijttebier, Rosseel, & Wiersema, 2015; Uljarević et al., 2017).; Schwartz et al., 2009).

This profile appears to hold irrespective of the specific age of participant samples (though see Schwartz et al., 2009, for an exception). However, findings from a recent study (i.e., Macari et al., 2018) suggest that the *specific* profile of temperament differences between individuals with and without ASD might depend on the context of temperament assessment. Macari et al. (2018) assessed the peak intensity of emotion expressed in response to a modified set of induction probes derived from the Laboratory Temperament Assessment Battery (Lab-TAB; Goldsmith & Rothbart, 1993). Unlike questionnaire-based studies, they found that toddlers with ASD expressed similar intensity, joy and anger but less intense fear than age-matched TD controls. This result has yet to be replicated, though it is interesting to note that Zantinge, van Rijn, Stockmann, and Swaab (2019) found a positive correlation between rate arousal and fearful expression among TD controls but no such correlation among children with ASD.

Studies using measures based on Thomas and Chess's model of temperament tend to report consistent findings in terms of lower adaptability, distractibility and persistence among individuals with ASD compared to TD controls (Bailey, Hatton, Mesibov, Ament, & Skinner, 2000; Brock et al., 2012; Chuang, Tseng, Lu, Shieh, & Cermak, 2014; Hepburn & Stone, 2006), consistent with higher negative affectivity and lower effortful control reported in studies using measures based on Rothbart's model of temperament. Several studies report lower intensity among individuals with ASD (Bailey et al., 2000; Brock et al., 2012) though others report no such significant between-group differences (Chuang et al., 2014), and one study (Reyes, Walsh, Soke, & Hepburn, 2019) reported higher intensity among children with ASD in the toddler years but non-significant differences at a subsequent timepoint. Two studies have classified children into difficult and easy temperament subtypes, with Kasari and Sigman (1997) reporting that children with ASD had more difficult temperament compared to TD peers, and Chuang et al. (2014) finding that 34.3% of children with ASD were classified as having difficult temperament (compared to 10% in TD samples; Thomas, 1968) and only 34.5% having easy temperament characteristics. Since difficult temperament primarily comprises lower adaptability and negative mood, these findings are consistent with higher negative affectivity reported in studies using Rothbart's scales.

Studies using the Temperament and Character Inventory (Cloninger et al., 1994) have almost consistently reported increased harm avoidance (consistent with higher negative affectivity in Rothbart's scales) and reduced reward dependence in ASD compared to TD samples (Anckarsäter et al., 2006; Sizoo, van den Brink, van Eenige, & van der Gaag, 2009; Vuijk et al., 2018; Soderstrom, Rastam, & Gillberg, 2002; although see *Sizoo et al., 2015), whereas reduced novelty seeking was reported in some studies (Anckarsäter et al., 2006; Soderstrom et al., 2002; Vuijk et al., 2018) but not all (Sizoo et al., 2009, 2014). A study by Helles, Gillberg, Gillberg, Billstedt, and Wallinius (2016) compared temperament profiles among the following 3 subgroups of adults who had been diagnosed with ASD in childhood: a) those who no longer met ASD criteria, b) those with ASD plus psychiatric comorbidity, and c) those with ASD only (without comorbidity). When compared to a reference sample, both the ASD plus comorbidity and ASD only groups had higher harm avoidance, while the ASD only group had lower novelty seeking and the ASD plus comorbidity group had lower self-directedness and cooperativeness. Individuals who no longer met ASD criteria had higher reward dependence.

Effect sizes and heterogeneity statistics for the comparisons of temperamental differences between ASD and TD samples are shown in Table 3. It was possible to synthesize evidence for broad temperamental dimensions of affectivity/emotionality (8 studies; Burrows et al., 2016; Clifford et al., 2013; De Pauw et al., 2011; Kasari & Sigman, 1997; Macari et al., 2017; Paterson et al., 2019; Schwartz et al., 2009; Vuijk et al., 2018), self-regulation (7 studies; Burrows et al., 2016; Clifford et al., 2013; De Pauw et al., 2011; Macari et al., 2017; Paterson et al., 2019; Schwartz et al., 2009; Vuijk et al., 2018) and sociability (7 studies; Burrows et al., 2016; Clifford et al., 2013; De Pauw et al., 2011; Macari et al., 2017; Paterson et al., 2019; Schwartz et al., 2009; Vuijk et al., 2018). It was not possible to analyse results for several studies that utilized general population norms rather than comparison group (e.g., Anckarsäter et al., 2006; Sizoo et al., 2009; *Sizoo et al., 2015; Soderstrom et al., 2002). As can be seen from Table 3, there were significant effects across all three temperament dimensions, with ASD group showing significantly higher levels of affectivity/emotionality (2.34, $p < .001$, 95% CI = 1.06, 3.64) and significantly lower levels of self-regulation (−2.10, $p = .003$, 95% CI = −3.48, −0.71) and sociability (−1.12, $p = .028$, 95% CI = −2.15, −0.12). All mean effects were highly heterogeneous.

In summary, while methodological differences make it difficult to conclusively identify patterns of lower-order temperament traits in relation to ASD, there does appear to be some convergence of findings at a higher-order level. Higher negative affect, adaptability, and harm avoidance, and higher rates of broadly difficult temperament appear to converge to suggest that children and adolescents with ASD can be distinguished from TD controls by a profile of higher affectivity/emotionality. Similarly, lower surgency, affiliativeness, persistence, reward dependence, and effortful control indicate a profile of lower sociability and self-regulation in ASD. Findings of lower distractibility might also be related to difficulties with self-regulation, such that individuals with ASD tend to show abnormal disengagement of visual attention and perseverative interests (Landry & Bryson, 2004). While yet to be replicated, evidence of an attenuated fear response in ASD a laboratory setting (e.g., Macari et al., 2018) raises the question of whether context plays a role in the pattern of findings of across studies.

3.5. *Temperamental differences between ASD and other clinical samples*

Studies that have compared temperamental trait levels between individuals with ASD and ADHD have found higher activation control and persistence (Samyn et al., 2011, 2015) and harm avoidance (Sizoo, van der Gaag, & van den Brink, 2015), but lower impulsivity (Samyn et al., 2011, 2015) and sensory seeking (Sizoo et al., 2014) among individuals with ASD. Anckarsäter et al. (2006) found that individuals with dual diagnoses of ASD and ADHD have higher novelty seeking than those diagnosed with ASD alone.

Studies comparing temperament between samples of individuals with ASD and those without ASD but with developmental delay found that ASD group had lower self-regulation, positive affect, and surgency (Macari et al., 2017), lower approach and distractibility (Brock et al., 2012; Reyes et al., 2019) (but Ratekin, 1993, identified higher distractibility), as well as more difficult temperament (Kasari & Sigman, 1997). Interestingly studies by Boström et al. (2010) and Macari et al. (2017) reported no differences between ASD and developmentally delayed groups in terms of negative affect, and Macari et al. (2018) observed less intense fear in toddlers with ASD compared to developmentally delayed controls.

Two studies have compared temperament between groups of individuals with ASD and individuals with known genetic syndromes, finding higher threshold for change, lower activity and intensity, and more negative mood and greater distractibility in ASD when compared to individuals with Fragile X syndrome (Bailey et al., 2000), and lower intensity when compared to individuals with 22q13 Deletion Syndrome (Glaser & Shaw, 2011).

Effect sizes and heterogeneity statistics for the comparsions of temperamental differences between ASD and other clinical samples are shown in Table 3. It was possible to synthesize evidence for broad temperamental dimensions of negative affectivity (7 studies; Anckarsäter et al., 2006; Bieberich & Morgan, 1998, 2004; Clifford et al.,

Table 4
Summary of correlational findings.

Study	Construct(s) of interest (Measure)	Correlational results
Adamek et al. (2011)	Irritability (ABC).	Irritability + correlated with negative affectivity (and sadness, anger/frustration, discomfort, and soothability [−] subscales) and surgency (and activity level and high intensity pleasure subscales), and – correlated with effortful control (and inhibitory control subscale).
Baker et al. (2019)	Chronological age.	Older age associated with a stronger + association between child independent and dyadic dysregulation, and stronger − association between parental scaffolding and child independent dysregulation.
Barger et al. (2019)	Chronological age; Gender; Cognitive level (MSEL); ASD symptoms (SCQ); Maternal race; Maternal education.	Chronological age + correlated with negative social, only; Gender NS correlated with any temperament factor; Cognitive level + correlated with quiet persistence, activity rhythmicity, and negative social; ASD severity + correlated with maladaptivity, social inattention, and crying, and − correlated with environmental sensitivity, quiet persistence, social approach, rhythmicity, food openness, and negative social; Maternal race differences found for maladaptivity, social inattention, crying, and food openness; Maternal education differences found for quiet perseverance and crying.
Berkovits et al. (2017)	Time; Cognitive level (WPPSI-III); Language (CASL-2); Problem behavior (CBCL); Social skills (SSIS); ASD symptoms (SRS, ADOS-2).	Emotion regulation and lability/negativity stable from T1 to T2; Cognitive level NS correlated with emotion regulation or lability/negativity; Language NS correlated with emotion regulation or lability/negativity; Problem behavior – correlated with emotion regulation and + correlated with lability/negativity; Change (at T2) in externalizing predicted by emotion regulation; Change (at T2) in internalizing predicted by lability/negativity; Social skills + correlated with emotion regulation and – correlated with lability/negativity; ASD symptoms (per SRS) – correlated with emotion regulation and + correlated with lability/negativity (but NS correlated per ADOS-2).
Bieberich and Morgan (2004)	Time.	T1 self-regulation + correlated with T2 self-regulation; Positive affect and negative affect NS correlated at T1 and T2.
Bölte et al. (2008)	ASD symptoms (SRS).	ASD symptoms + correlated with novelty seeking and harm avoidance, − correlated with reward dependence, self-directedness, and cooperativeness.
Bos et al. (2018)	Disruptive behavior (CSI); Anxiety symptoms (CSI); Depression symptoms (CDI); Somatic complaints (SCL).	Disruptive behavior (at T3) + predicted by worry/rumination (at T1); Anxiety symptoms + predicted by negative emotionality; Depression symptoms + predicted by worry/rumination; Somatic complaints + predicted by worry/rumination and negative emotionality.
Boström et al. (2010)	Informant (mother vs father).	Mother report of child temperament + correlated with father report of child temperament across all scales (activity, shyness, sociability, emotionality, and impulsivity).
Brock et al. (2012)	Sensory features (SP, SEQ, TDDT-R, SPA).	Sensory features + associated with withdrawal and negative mood; Sensory hyporesponsiveness – associated with adaptability, threshold, and distractibility.
Bryson et al. (2018)	Visual attention (gap-overlap task).	Left-directed disengage latencies associated with activity, soothability, fear, and + associated with distress to limitations at 12 mths (NS correlated with temperament at 6 mths); Right-directed disengage latencies – associated with fear and + associated with distress to limitations at 12 mths (NS correlated with temperament at 6 mths).
Burrows et al. (2016)	Problem behavior (BASC-2).	Internalizing + associated with negative affect and – associated with surgency and effortful control; Externalizing + associated with negative affect and – associated with effortful control.
Chuang et al. (2012)	Sensory features (SP-C).	Sensory seeking – associated with activity level and adaptability, and + associated with distractibility; Sensory avoidance – associated with adaptability and + associated with persistence; Sensory hypersensitivity –associated with intensity; Sensory hyposensitivity – associated with mood and persistence.
Chuang et al. (2014)	Health-related quality of life (TAPQOL-C).	Social functioning – associated with intensity and + associated with threshold; Cognitive functioning – associated with distractibility; Emotional functioning – associated with intensity and distractibility and + associated with rhythmicity.
De Pauw et al. (2011)	Problem behavior (CBCL).	Internalizing – associated with surgency and effortful control, and + associated with negative affect; Externalizing – associated with effortful control and + associated with surgency and negative affect.
Del Rosario et al. (2014)	Time.	T1 to T5 decreases in activity level and adaptability.
Faja & Dawson (2013)	Chronological age; Cognitive level (DAS-2); Attention problems (BASC-2); Hyperactivity (BASC-2); Social skills (SSRS, VABS-2); ASD symptoms (ADOS-SA).	Age, cognitive level, attention problems, hyperactivity, and social skills NS associated with effortful control; ASD symptoms – correlated with effortful control.
Garon et al. (2009)	ASD symptoms (ADOS-SA).	ASD symptoms – associated with behavioral approach (after cognitive level controlled)
Garon et al. (2016)	Time. ASD symptoms (ADOS, ADI-R).	T1 positive/negative affect + associated with T2 positive/negative affect. T3 ASD symptoms – associated with T2 effortful control.
Helles et al. (2016)	General functioning (GAF); Cognitive level (WAIS-III); ADHD symptoms (ASRS); Depression symptoms (BDI); ASD symptoms (ASDI).	General functioning – correlated with harm avoidance, and + correlated with reward dependence and persistence; Cognitive level and ADHD symptoms NS correlated with temperament; Depression symptoms + correlated with harm avoidance; ASD symptoms – correlated with novelty seeking.
Hendry et al. (2018)	Visual attention (eye-tracking)	Change in look duration to faces (from 9 to 15 mths) – associated with effortful control; Change in look duration to non-social scrambled face stimuli NS associated with effortful control.
Hirschler-Guttenberg, Feldman, et al. (2015)	Maternal regulation facilitation (observed); Maternal temperament (ATQ); Maternal parenting style (PSDQ).	Maternal regulation facilitation – associated with child self-regulation of anger, and + associated with child co-regulation of anger and fear; Maternal temperament NS associated with child temperament; Authoritarian parenting + associated with child self-regulation of anger, and – associated with child co-regulation of anger; Authoritative parenting + associated with child self-regulation of fear.
Hirschler-Guttenberg, Golan, et al., 2015	Dyadic reciprocity (observed); Cognitive level (SB).	

(continued on next page)

Table 4 (*continued*)

Study	Construct(s) of interest (Measure)	Correlational results
		Mother-child and father-child reciprocity – correlated with child self-regulation; Mother-child reciprocity – correlated with child negative emotionality; Cognitive level + correlated with self-regulation (interaction with father, only).
Kasari and Sigman (1997)	Parent stress (PSI); Social engagement and responsiveness (observed): Cognitive level (Cattell, SB); Language (RDLS); ASD symptoms (ABC).	Parent stress (related to child characteristics) + correlated with difficult temperament; Time engaged with parent (but not examiner) – correlated with difficult temperament; Responsiveness to examiner (but not parent) – correlated with difficult temperament; Cognitive level – correlated with difficult temperament; Expressive and receptive language – correlated with difficult temperament; ASD symptoms + correlated with difficult temperament.
Konstantareas and Papageorgiou (2006)	Maternal stress (QRS).	Maternal stress + correlated with activity level (general), task orientation and rhythmicity (daily habits, and – correlated with flexibility/rigidity, mood, and rhythmicity (sleep).
Konstantareas and Stewart (2006)	Chronological age; Cognitive level (DPII); ASD symptoms (CARS).	Chronological age NS associated with temperament; Cognitive level + associated with negative affectivity; ASD symptoms – associated with effortful control.
Korbut et al. (2020)	Challenging behavior (HSQ-PDD).	Challenging behavior frequency/severity (T2) + correlated with (T1) negative affectivity, and – correlated with (T1) effortful control (but NS after cognitive level controlled); Challenging behavior severity (T2) – correlated with (T1) surgency (but NS after cognitive level controlled).
Macari et al. (2017)	Time; Cognitive level (MSEL); ASD symptoms (ADOS-G).	T1 effortful control, surgency, and negative emotionality + correlated, respectively, with T2 effortful control, surgency, and negative emotionality; Non-verbal cognitive level + correlated with surgency (positive anticipation scale), verbal cognitive level NS correlated with temperament; ASD symptoms NS correlated with temperament; ASD symptoms at T2 associated with minimal improvement in perceptual sensitivity from T1 to T2.
Macari et al. (2018)	Informant (observed vs parent-report); ASD symptoms (ADOS-2).	Observed fear intensity + correlated with parent-reported fear, and observed joy intensity + correlated with parent-reported positive anticipation; ASD symptoms (social affect domain) – correlated with intensity of joy;
Millea et al. (2013)	Social anxiety (SASC-R).	Social anxiety + associated with negative affectivity; Social anxiety-socialization association moderated by negative affectivity,
Nazim and Khalid (2019)	Cognitive level (NR); Problem behavior (NR); ASD symptoms (CARS).	Cognitive level + correlated with effortful control and – correlated with negative affectivity; Problem behavior + correlated with negative affectivity and – correlated with surgency and effortful control; ASD symptoms + correlated with negative affectivity and – correlated with effortful control.
Ostfeld-Etzion et al. (2016)	Self-regulated compliance (observed).	Self-regulated compliance + associated with attention focusing.
Özyurt et al. (2018)	Language (TELD-3); Maternal depression (BDI); Cognitive level (DDST).	Receptive language + correlated with emotion regulation and – correlated with emotional lability; Expressive language + correlated with emotion regulation; Maternal depression + correlated with emotional lability; Cognitive level + correlated with emotion regulation.
Paterson et al. (2019)	Cognitive level (MSEL); ASD symptoms (AOSI).	Verbal and non-verbal cognitive level NS correlated with temperament (after correction); ASD symptoms NS associated with temperament.
Pijl et al. (2019)	Time.	T1 to T2 decreases in surgency and effortful control.
Reyes et al. (2019)	Time.	T1 activity and approach + correlated, respectively, with T2 activity and approach; T1 to T2 decreases in rhythmicity, persistence, and threshold of responsiveness.
Rivers and Stoneman (2008)	Sibling relationship (SIB, SSRS)	Sibling relationship NS correlated with temperament of child with ASD; Positive sibling relationship – associated with persistence of both siblings (TD and ASD).
Samyn et al. (2011)	ADHD symptoms (DBD); ASD symptoms (SRS).	PR inattention and hyperactivity/impulsivity – correlated with inhibitory control (PR/SR), activation control (PR/SR), attention control (PR/SR), persistence/low distractibility (SR), impulsivity (SR), attention focusing (SR), and attention shifting (SR); TR inattention – correlated with inhibitory control (PR/SR), activation control (PR/SR), attention control (PR/SR), persistence/low distractibility (SR), impulsivity (SR), attention focusing (SR), and attention shifting (SR); TR hyperactivity/impulsivity – correlated with inhibitory control (PR/SR), activation control (PR/SR), attention control (PR/SR), persistence/low distractibility (SR), impulsivity (SR), and attention focusing (SR); ASD symptoms – correlated with inhibitory control (PR/SR), activation control (PR), attention control (PR/SR), attention focusing (SR), and attention shifting (SR).
Samyn et al. (2017)	Executive attention (ANT).	Executive attention NS correlated with effortful control.
Schwartz et al. (2009)	Problem behavior (BASC-2); ASD symptoms (ASSQ, SCQ).	Internalizing + correlated with negative affectivity and – correlated with surgency; Externalizing, social skills, atypicality, and withdrawal NS correlated with temperament; ASD symptoms NS correlated with temperament.
Shephard et al. (2019)	ADHD symptoms (Conners 3); Anxiety symptoms (SCAS); ASD symptoms (SRS-2).	Mid-childhood ADHD symptoms + associated with toddlerhood activity level, inhibitory control, and fear (after ASD symptoms controlled); Mid-childhood anxiety and ASD symptoms + associated with toddlerhood shyness and fear;
(*Sizoo et al., 2015)	ASD symptoms (AQ).	ASD symptoms + correlated with harm avoidance and – correlated with reward dependence; Social interaction + correlated with arm avoidance and – correlated with reward dependence; Attention to details NS correlated with temperament.
Zantinge et al. (2019)	Physiological arousal (heart rate).	Physiological arousal NS correlated with expression of fear.

Note. "+" and "–" denote positive and negative correlations/associations. NS = non-significant; ASD = Autism Spectrum Disorder; ADHD = Attention Deficit Hyperactivity Disorder; T = time; PR = parent-report; SR = self-report; TR = teacher-report; ABC = Aberrant Behavior Checklist; MSEL = Mullen Scales of Early Learning; SCQ = Social Communication Questionnaire; WPPSI-III = Wechsler Preschool and Primary Scale of Intelligence–Third *Edition;* CASL-2 = Comprehensive Assessment of Spoken Language–Second Edition; SSIS-SS = Social Skills Improvement System; SRS = Social Responsiveness Scale; ADOS-2 = Autism Diagnostic Observation Schedule–Second Edition; CSI = Child Symptom Inventory; CDI = Children's Depression Inventory; SCL = Somatic Complaints List; SP = Sensory Profile; SEQ = Sensory Experiences Questionnaire; TDDT-R = Tactile Defensiveness and Discrimination Test; SPA = Sensory Processing Assessment for Young Children; BASC-2 = Behavior Assessment System for Children–Second Edition; SP-C = Sensory Profile, Chinese; TAPQOL-C = Preschool Children Quality of Life, Chinese; CBCL = Child Behavior Checklist; DAS-2 = Differential Ability Scales–Second Edition; SSRS = Social Skills Rating System; ADI-R = Autism Diagnostic Interview-Revised; ADOS-SA = Autism Diagnostic Observation Schedule, Social Affect; VABS-2 = Vineland Adaptive Behavior Scales–Second Edition; GAF = Global Assessment of Functioning; WAIS-III=Wechsler Adult Intelligence Scale–Third Edition; ASRS = Adult ADHD Self-Report Scale; BDI = Beck Depression Inventory; ASDI = Asperger Syndrome

Diagnostic Interview; ATQ = Adult Temperament Questionnaire; PSDQ = Parenting Styles and Dimensions Questionnaire; SB = Stanford-Binet Intelligence Scale; PSI = Parenting Stress Index; RDLS = Reynell Developmental Language Scales; ABC = Autism Behavior Checklist; QRS = Questionnaire on Resources and Stress; DPII = Developmental Profile–Second Edition; HSQ-PDD = Home Situations Questionnaire–Pervasive Developmental Delays; ADOS-G = Autism Diagnostic Observation Schedule–Generic; SACS-R = Social Anxiety Scale for Children–Revised; CARS = Childhood Autism Rating Scale; TELD-3 = Test of Early Language Development–Third Edition; DDST = Denver II Developmental Screening Test; AOSI = Autism Observation Scale for Infants; SIB = Sibling Inventory of Behavior; SSRS = Satisfaction with the Sibling Relationship Scale; DBD = Disruptive Behavior Disorder Rating Scale; ANT = Attention Network Test; ASSQ = Autism Spectrum Screening Questionnaire; SCAS = Spence Children's Anxiety Scale; AQ = Autism Quotient.

2013; Kasari & Sigman, 1997; Macari et al., 2017; Sizoo et al., 2014), self-regulation (6 studies; Anckarsäter et al., 2006; Bieberich & Morgan, 1998, 2004; Clifford et al., 2013; Macari et al., 2017; Sizoo et al., 2014) and sociability (6 studies; Anckarsäter et al., 2006; Bieberich & Morgan, 1998, 2004; Clifford et al., 2013; Macari et al., 2017; Sizoo et al., 2014). As can be seen from Table 3, ASD group had significantly higher levels of negative affectivity (0.46, $p = .001$, 95% CI = 0.19, 0.74) but there were no significant differences for self-regulation and sociability. All mean effects were highly heterogeneous.

In summary, similar to studies comparing samples of individuals with ASD to TD controls, studies that have drawn a comparison to individuals with other clinical/developmental conditions suggest the possibility of certain group-level temperamental differences. Again, the variety of temperament instruments, along with the variety in comparison groups, used in these studies precludes the systematic integration of findings concerning lower-order temperament dimensions. Nonetheless, individuals with ASD can be distinguished from other clinical samples by higher affectivity/emotionality (higher harm avoidance, more negative mood), low sociability (lower impulsivity, activity, approach, intensity, positive affect), and low self-regulation (greater distractibility), just as when compared to TD individuals.

3.6. Longitudinal investigations into temperament and ASD

Compared to the relatively large number of cross-sectional studies, synthesized above, longitudinal studies on temperament and ASD have emerged only recently in the literature. Table 5 summarises findings from 19 studies, three of which used assessments based on Thomas and Chess's model of temperament, another 11 drawing upon Rothbart's assessments and one following Cloninger's model. The remaining four used measures not clearly aligned with a dominant theoretical model.

One study reviewed above (Helles et al., 2016) compared current temperament profiles of adults diagnosed with ASD in childhood who had participated in a long-term follow-up study. Eight studies examined the longitudinal stability of child temperament in ASD and reported significant cross-time correlations (Berkovits, Eisenhower, & Blacher, 2017; Bieberich & Morgan, 2004; Garon et al., 2016; Macari et al., 2017; Reyes et al., 2019) and a trajectory of decreasing activity level, adaptability, and self-regulation (Del Rosario, Gillespie-Lynch, Johnson, Sigman, & Hutman, 2014; *Pijl et al., 2019; Reyes et al., 2019) and increasing surgency (Paterson et al., 2019) in early-life. Two studies (i. e., Berkovits et al., 2017; Bos, Diamantopoulou, Stockmann, Begeer, & Rieffe, 2018) explored the longitudinal relation between temperament and aspects of child functioning and found that emotion dysregulation was predictive of increased behavioral difficulties in school-aged children with ASD. Finally, Macari et al. (2017) explored how changes in particular aspects of temperament across a 12-month period predicted outcomes in various aspects of the ASD clinical phenotype. Lower change scores suggesting less improvement or decline in perceptual sensitivity predicted more severe later ASD symptoms, while improvements in inhibitory control and low-intensity pleasure predicted gains in level of adaptive social skills over the same time period.

Ten studies have taken the approach of tracking the early development of infants with an older sibling with ASD, thereby considered to be at higher-than-usual risk for also being diagnosed with the condition (see Zwaigenbaum et al., 2005, for a review) and able to be followed prospectively from early infancy until late toddlerhood/early childhood when diagnostic outcome status could be determined. These are summarized in Tables 4 and 5.

Del Rosario et al. (2014) found that infants who developed ASD showed higher activity and lower approach and adaptability across infancy, and as early as 6 months, compared to TD infants. Unlike Del Rosario et al., Zwaigenbaum et al. (2005) found *decreased* activity at 6 months among high-risk siblings later diagnosed with ASD, relative to non-ASD-diagnosed and low-risk comparison infants. Although a comparative pattern of extreme distress reactions, longer durations of orienting to objects, and decreased expression of positive affect was evident by 12 months in siblings later diagnosed with ASD. Four studies (Garon et al., 2009, 2016; Clifford et al., 2013; *Paterson et al., 2019) using Rothbart's temperament measures found that higher negative affect and lower effortful control (and lower positive affect/surgency, only for Garon et al., 2016 and Paterson et al., 2019) distinguished 24-month-olds who later received an ASD diagnosis from those who had a more typical developmental outcome. Furthermore, Garon et al. (2016) found that lower effortful control at 24 months was associated with more severe ASD symptoms at 36 months. Finally, one study examined temperament as an early predictor of ASD outcome in a general population sample. Bolton, Golding, Emond, and Steer (2012) found no temperament dimension at 6-months to be predictive of later ASD traits or diagnosis (after controlling for gender and IQ). However, by 24 months of age, adaptability, persistence and threshold were all significant predictors of later ASD diagnosis.

Two recent prospective studies examined the *specific* predictive value of temperament for later ASD diagnosis. Through use of a novel machine-learning algorithm method, Pijl et al. (2020) found that temperament trait combinations at 24 months had low positive predictive value and specificity for ASD diagnostic outcome at 36 months among infants at higher familial likelihood. Nevertheless, effortful control and its combination with surgency and negative affect had a high negative predictive value for ruling out ASD diagnosis. Shephard et al. (2019) investigated the specificity of associations between infant temperament traits and childhood symptoms of ADHD and anxiety, as compared to ASD. Higher activity and low inhibitory control were specifically associated with ADHD and not ASD or anxiety, whereas higher fearfulness and shyness predicted both anxiety and ASD symptoms.

Notwithstanding significant methodological heterogeneity within this small number of studies – in terms of assessment time-points, measures used, and statistical approach – it seems possible that temperament differences between individuals with and without ASD may be observed from as early as 6-months of age. This type of research, while still in its early days, presents promising potential for the field.

3.7. Concurrent associations among temperament and other factors

As can be seen in Table 4, studies have also explored associations between temperament and a wide range of other core and co-morbid symptoms among individuals with ASD. In general – and as reported for non-ASD populations – lower levels of temperamental effortful control and/or higher levels of negative affect have been associated with more behavioral problems (Adamek et al., 2011; Berkovits et al., 2017), internalizing and externalizing symptoms (De Pauw et al., 2011; Burrows et al., 2016; Korbut et al., 2020; Nazim & Khalid, 2019; Schwartz et al., 2009), anxiety (Uljarević et al., 2017), and social anxiety (Millea, Shea, & Diehl, 2013) among individuals with ASD. By contrast, studies looking at the association between temperament and core ASD symptoms (e.g., Bölte, Poustka, & Constantino, 2008; Fenning, Baker, & Moffitt, 2018; Kerekes et al., 2013), cognitive level (e.g., Faja & Dawson, 2015; Kasari & Sigman, 1997), language (e.g., Berkovits et al., 2017; Özyurt, Dinsever Eliküçük, Tufan, & Baykara, 2018), and sensory features (e.g., Brock et al., 2012; Chuang et al., 2014) have all yielded inconsistent results (please refer to Table 2. for more detail). Finally, recent studies using more experimental approaches reported associations between childhood temperament traits and eye-tracking measures of visual-spatial attention (Bryson et al., 2018) and social attention (Hendry et al., 2018) in ASD, but non-signifcant relations between temperament and heart rate (Zantinge et al., 2019) or performance on a neuropsychological task assessing executive attention (Samyn, Roeyers, Bijttebier, & Wiersema, 2017).

Other studies have explored associations between temperament and familial characteristics, including parental stress levels and sibling relationship quality. For example, Konstantareas and Papageorgiou (2006) found that increased level of stress in mothers was associated with lower infant flexibility, mood, and regular sleep, and higher levels of activity and general rhythmicity. There are also findings suggesting heightened negative emotionality and self-regulatory difficulties in children with ASD may be associated with parenting that is less synchronous and responsive (Hirschler-Guttenberg, Golan, Ostfeld-Etzion, & Feldman, 2015; Kasari & Sigman, 1997).

Effect sizes and heterogeneity statistics for the association of temperamental dimensions of affectivity/emotionality, self-regulation and sociability with other factors are shown in Table 6. It was possible to synthesize evidence for IQ (7 studies; Barger et al., 2019; Berkovits et al., 2017; Kasari & Sigman, 1997; Korbut et al., 2020; Macari et al., 2017; Nazim & Khalid, 2019; Paterson et al., 2019), behavioral problems (5 studies; Adamek et al., 2011; De Pauw et al., 2011; Korbut et al., 2020; Nazim & Khalid, 2019; Schwartz et al., 2009), overal ASD social and communication symptoms (8 studies; Barger et al., 2019; Berkovits et al., 2017; Bölte et al., 2008; Kasari & Sigman, 1997; Korbut et al., 2020; Nazim & Khalid, 2019; Schwartz et al., 2009; Sizoo et al., 2014) and social and communication impairments (4 studies; Macari et al., 2017; Macari et al., 2018; Schwartz et al., 2009; *Sizoo et al., 2015). We were not able to include a number studies due to the following reasons (i) not reporting correlational findings but rather regression/SEM analysis (e.g., Garon et al., 2009; Garon et al., 2016; Konstantareas & Stewart, 2006; Paterson et al., 2019), (ii) correlations reported only for combined sample that in addition to ASD, also included TD and/or clinical comparison group (e.g., Bos et al., 2018; Hirschler-Guttenberg, Golan, et al., 2015; Özyurt et al., 2018; Samyn et al., 2011; Shephard et al., 2019), (iii) reported only correlations that were significant (e.g., Helles et al., 2016), or (iv) only reported a range of correlational coefficients, rather than separate values (e.g., *Faja and Dawson, 2015). For association with IQ, mean effect size r was significant for sociability ($r = 0.12$, $p < .001$, 95% CI = 0.055, 0.180) and self-regulation ($r = 0.17$, $p = .003$, 95% CI = 0.057, 0.286) but not for affectivity/emotionality. For association with problem behaviors, mean effect size r was significant for affectivity/emotionality ($r = 0.61$, $p < .001$, 95% CI = 0.351, 0.879), self-regulation ($r = -0.26$, $p < .001$, 95% CI = −0.379, −0.138) but not for sociability. For association with overall autism severity, mean effect size r was significant for affectivity/emotionality ($r = 0.28$, $p \leq 0.001$, 95% CI = 0.119, 0.434), self-regulation ($r = -0.22$, $p = .03$, 95% CI = −0.416, −0.022) and sociability ($r = -0.30$, $p = .004$, 95% CI = −0.501, −0.098). Finally, for association with social and communication impairments, mean effect size r was significant for self-regulation ($r = -0.15$, $p = .009$, 95% CI = −0.266, −0.037) and sociability ($r = -0.28$, $p = .025$, 95% CI = −0.535, −0.036) but not for affectivity/emotionality. As can be seen from Table 6, with the exception of sociability-IQ, self-regulation-behavioral problems, and self-regulation-social communication impairments associations, all other mean effect were highly heterogeneous.

4. Discussion

In order to better understand sources of variability in core and comorbid symptom presentation and outcomes among individuals with ASD, we advocate the need to step away from models that concentrate purely on describing group differences and move toward adopting individual differences frameworks that seek to *understand* the variability that presents between people. Gaining insights into the sources of noted heterogeneity is crucial in informing the development of adequate support for individuals with ASD and those who care for them.

In the broader literature, temperament has been shown to have both positive and negative developmental influences, from infancy/toddlerhood through early childhood and into the school years and beyond. For this reason, we suggest temperament may provide a helpful framework for understanding individual differences among individuals with ASD.

In this systematic review, we have attempted to integrate findings from existing studies concerning temperament in the context of ASD, toward a better understanding of the role of temperament across a broad set of positive and negative developmental outcomes. Our aim in conducting a systematic review was to provide a snapshot of the current state of the field of research, rather than to statistically address a specific question/hypothesis. Despite a 30-year history, there is still a great deal more to be understood, with many methodological issues to be considered and research gaps to be filled.

4.1. Limitations of extant research

The large majority of studies identified in this review of temperament and ASD (nearly 90%) used questionnaire or interview measures of temperament. As discussed in more detail elsewhere (Shiner et al., 2012; Zentner & Bates, 2008), questionnaire measures of temperament have numerous advantages over observational and experimental measures, such as the ease of use and the ability to sample behaviors over time and across different contexts to generate rich data that lend themselves easily to group comparisons, factor analyses and person-centered statistical approaches (e.g., cluster analysis). However, research in non-ASD populations has clearly demonstrated that parental characteristics such as stress, anxiety, and depression can substantially bias the reporting of child temperament (Forman et al., 2003), which may be particularly important in the context of ASD, due to elevated levels of affective symptoms in parents of children with ASD and subthreshold ASD-like traits (referred to as the Broader Autism Phenotype; Piven et al., 1994). Hence, we cannot rule out the possible amplification of parent-reported differences in the temperament of individuals with and without ASD as a result of informant bias. Another potential consideration related to parental report – especially in the context of high-risk infant sibling designs – is the potential for parents to either exaggerate (i.e., contrasting effect) or under-estimate (i.e., assimilation effect) differences between their own children, by evaluating them relative to one another (Majdandžić, van den Boom, & Heesbeen, 2008).

Although structured and semi-structured observational protocols for assessing temperament do not suffer from such issues, they also have their own limitations such as potential lack of ecological validity, temporal and contextual restrictedness, and influence of "noise" variables (e.g., the child's transient mood or somatic health issues). The optimal way to assess temperament then may be to combine both observational and questionnaire-based measures, and preferably both maternal and paternal reports (Rothbart & Bates, 1998). Yet, only two among the 64 studies included in this review has adopted this latter method (i.e., Macari et al., 2018; Ratekin, 1993).

Furthermore, the issue of measurement confounding in temperament research is well established in this field (Lemery, Essex, & Smider, 2002; Sanson, Prior, & Kyrios, 1990). Nevertheless, only one study among those reviewed here in the context of ASD (i.e., that of Adamek et al., 2011) addressed potential item overlap between measures of temperament and other constructs of interest. For example, perceptual

Table 5
Summary of prospective studies of ASD diagnostic outcome.

Study	6 Months	12 Months	18 Months	24 Months	36 months
Bolton et al. (2012)	*ASD vs No ASD:* ≈activity, rhythmicity, approach, adaptability, intensity, mood, persistence, distractibility, and threshold (after gender and full-scale IQ controlled).	NA	NA	*ASD vs No ASD:* <adaptability, persistence, and threshold; ≈activity, rhythmicity, approach, intensity, mood, and distractibility (after gender and full-scale IQ controlled).	NA
Clifford et al. (2013)	(7 mths) *HR vs LR:* <surgency (high intensity pleasure and approach subscales); ≈negative affect and effortful control. *HR-ASD vs LR:* ≈surgency, negative affect and effortful control. *HR-Atypical vs LR:* <approach; ≈surgency, negative affect and effortful control. *HR-TD vs LR:* <surgency (approach subscale); ≈negative affect and effortful control. *HR-ASD vs HR-TD:* >surgency (perceptual sensitivity subscale); ≈negative affect and effortful control. *HR-ASD vs HR-Atypical:* ≈surgency, negative affect and effortful control.	(14 mths) *HR vs LR:* <surgency (approach subscale) and effortful control (cuddliness subscale); ≈negative affect. *HR-ASD vs LR:* <smiling and laughter; <effortful control (cuddliness subscale); ≈surgency and negative affect *HR-Atypical vs LR:* ≈surgency, negative affect, and effortful control. *HR-TD vs LR:* <surgency; ≈negative affect and effortful control. *HR-ASD vs HR-Atypical:* <effortful control (cuddliness subscale); ≈surgency and negative affect. *HR-ASD vs HR-TD:* ≈surgency, negative affect, and effortful control.	NA	*HR vs LR:* <effortful control (cuddliness and inhibitory control subscales); ≈surgency and negative affect. *HR-ASD vs LR:* >negative affect (sadness, shyness, and soothability subscales); <effortful control (low intensity pleasure and cuddliness subscales); ≈surgency. *HR-Atypical vs LR:* ≈surgency, negative affect, and effortful control. *HR-TD vs LR:* ≈surgency, negative affect, and effortful control. *HR-ASD vs HR-Atypical & HR-TD:* ≈surgency, negative affect, and effortful control.	NA
*Del Rosario et al. (2014)	*HR-ASD vs HR-TD* <adaptability and approach; ≈activity, mood, intensity, distractibility, persistence, sensory reactivity, rhythmicity.	*HR-ASD vs HR-TD* <adaptability; ≈activity, approach, mood, intensity, distractibility, persistence, sensory reactivity, rhythmicity.	*HR-ASD vs HR-TD* ≈activity, adaptability approach, mood, intensity, distractibility, persistence, sensory reactivity, rhythmicity.	*HR-ASD vs HR-TD* >adaptability and approach; ≈activity, mood, intensity, distractibility, persistence, sensory reactivity, rhythmicity.	*HR-ASD vs HR-TD* >adaptability and approach; ≈activity, mood, intensity, distractibility, persistence, sensory reactivity, rhythmicity.
Garon et al. (2009)	NA	NA	NA	*HR-ASD vs LR:* <behavioral approach and effortful emotion regulation. *HR-ASD vs HR-No ASD:* <behavioral approach; ≈effortful emotion regulation. *HR-No ASD vs LR:* >behavioral approach; <effortful emotion regulation.	NA
Garon et al. (2016)	NA	*HR vs LR:* <distress to limitations; >fear; ≈smiling and laughter, activity level, soothability, and duration of orienting *HR-ASD vs HR-No ASD:* <positive affect; ≈negative affect.	NA	*HR vs LR:* >anger, sadness, and fear; <inhibitory control, soothability, attention focus, high pleasure, and low pleasure; ≈attention shifting, activity level, and positive anticipation. *HR-ASD vs HR-No ASD:* <effortful control and positive affect; ≈negative affect.	NA
Paterson et al. (2019)	*HR-ASD vs LR & HR-No ASD:* <surgency (smiling and laughter subscale) and regulatory capacity (low intensity pleasure subscale); ≈negative affect.	*HR-ASD vs LR:* <surgency (approach, vocal reactivity, and smiling and laughter subscales) and regulatory capacity; >negative affect (sadness	NA	*HR-ASD vs LR:* <surgency (positive anticipation, sociability) and effortful control; >negative affect (discomfort, frustration, sadness).	NA

(*continued on next page*)

Table 5 (*continued*)

Study	6 Months	12 Months	18 Months	24 Months	36 months
		and falling reactivity subscales). *HR-ASD vs HR-No ASD:* <surgency (approach, vocal reactivity, and smiling and laughter subscales) and regulatory capacity; ≈negative affect.		*HR-ASD vs HR-No ASD:* <surgency (positive anticipation and sociability subscales) and effortful control; ≈negative affect.	
Pijl et al. (2019)	(8 months) *HR-ASD > HR-Atypical > HR-TD > LR:* Negative affect.	(14 months) *LR > HR-TD > HR-Atypical > HR-ASD:* Surgency. *HR-ASD > HR-Atypical > HR-TD > LR:* Negative affect; Effortful control.	NA	*HR-ASD > HR-Atypical > HR-TD > LR:* Negative affect; Effortful control.	NA
Yirmiya et al. (2006)	(4 months) *HR-ASD vs HR-TD:* ≈unpredictable, fussy-difficult, inadaptable, and dull.	(14 months) *HR-ASD vs HR-TD:* ≈unpredictable, fussy-difficult, inadaptable, and dull.	NA	NA	NA
Zwaigenbaum et al. (2005)	*HR-ASD vs HR-No ASD & LR:* <activity level; ≈smiling and laughter, fear, distress to limitations, soothability, and duration of orienting	*HR-ASD vs HR-No ASD & LR:* >distress to limitations and duration of orienting; ≈activity level, smiling and laughter, fear, and soothability.	NA	*HR-ASD vs HR-No ASD & LR:* <attention shifting, inhibitory control, positive anticipation and affective responses.	NA

Note. "<" and ">" are signs used to denote that one group shows either higher or lower level of behaviors/traits/problems in question. ASD = Autism Spectrum Disorder; HR-ASD = high-risk siblings diagnosed with ASD; HR-TD = high-risk siblings with typical development; HR-No ASD = high-risk siblings without ASD (without specification of 'TD' or 'Atypical'); HR-Atypical = high-risk siblings without ASD, but with atypical development; LR = low-risk infants/toddlers/siblings.

Table 6
Meta-analysis of studies exploring the relationship between temperament and other factors.

	N studies	Mean ES	se	95% CI	*p*	Q	I^2	*p*
IQ								
Negative Affectivity	7	−0.13	0.085	[−0.299, 0.038]	0.13	19.54	78.73%	0.002
Self-regulation	6	0.17	0.058	[0.057, 0.286]	0.003	11.76	57.85%	0.038
Sociability	5	0.12	0.032	[0.055, 0.180]	<0.001	4.52	0.06%	0.34
Problem behaviors								
Negative Affectivity	5	0.61	0.135	[0.351, 0.879]	< 0.001	23.60	83.47%	<0.001
Self-regulation	4	−0.26	0.061	[−0.379, −0.138]	< 0.001	1.27	0.01%	0.736
Sociability	4	−0.10	0.148	[−0.390, 0.190]	0.499	17.55	80.04%	< 0.001
Overall autism severity								
Negative Affectivity	8	0.28	0.08	[0.119, 0.434]	<0.001	32.03	75.28%	<0.001
Self-regulation	9	−0.22	0.10	[−0.416, −0.022]	0.03	41.08	85.35%	<0.001
Sociability	6	−0.30	0.10	[−0.501, −0.098]	0.004	18.52	80.46%	0.002
Social communication impairments								
Negative Affectivity	4	0.05	0.148	[−0.234, 0.345]	0.707	19.20	82.36%	<0.001
Self-regulation	4	−0.15	0.058	[−0.266, −0.037]	0.009	3.59	0.01%	0.308
Sociability	4	−0.28	0.127	[−0.535, −0.036]	0.025	13.39	76.28%	0.004

Note. IQ = Intelligence Quotient.

sensitivity is a subscale within questionnaires based on the Rothbart's model of temperament, and other questionnaire measures contain a number of items related to the reactivity to sensory input (e.g., within the Distractibility and Threshold of Response scales of the Behavioral Style Questionnaire and Carey Infant Temperament Questionnaire). With atypical reactions to sensory input included in the DSM-5 as core diagnostic criteria for ASD, it is clear that there is a significant room for item measurement overlap. This represents a significant limitation of the existing research. In order to understand the nature of the relationship between constructs, it is essential to ensure that measures provide unique rather than overlapping information, lest the strength of the relationship be artificially inflated. Furthermore, this issue speaks to the broader question about the nature of the relationship between temperament and ASD, to which we will return.

Notwithstanding the challenges introduced via different conceptualizations/models of temperament and different measures employed, existing research on temperament and ASD can also be criticized for remaining largely descriptive in nature. The majority of existing studies have focused on identifying how temperament characteristics differ between individuals with ASD and other populations, where relatively fewer studies have explored the relationship between temperament and either ASD traits or co-morbid symptoms. However, associations here are likely to be complex. Indeed, influential alternative models have been developed to explain the potential role of temperament in development, including through indirect (i.e., moderating and mediating) effects, and interactional and transactional models (Belsky & Pluess, 2009; Rothbart & Bates, 1998). All of these emphasize the need to explore interactions between temperament, other intrinsic child characteristics, aspects of the environment (e.g., characteristics of parents and the family) and the wider socio-cultural context, in order to fully characterize developmental pathways.

There is evidence from a prospective study of infant siblings of children with ASD that the quality of parent-infant interaction – which is influenced by both infant temperament and parent responsiveness – is associated with a later diagnosis of ASD (Wan et al., 2013). While this finding requires replication in independent samples, the possibility that infant temperament may be associated with developmental outcomes – including a developmental trajectory toward later ASD diagnosis – provides a potential opportunity for very early intervention in ASD (Green et al., 2015). Future research will also need to go beyond reporting correlational data and simple group comparisons to instead employ refined statistical techniques, such as structural equation modelling, in order to explore the complex developmental relationships and effects likely at play. A good guide for this approach is in work aiming to identify profiles or clusters of temperamental traits that might predict positive and negative aspects of development (Putnam & Stifter, 2005).

4.2. Current state of the field and future directions

Most existing studies have examined the presence or absence of differences on certain dimensions of temperament among groups of children with and without ASD, and these seem to show that, at a higher-order level, individuals with ASD may be temperamentally different from those without ASD – whether TD individuals or those presenting with other conditions.

Some studies have started to look at the extent to which temperamental variation corresponds to variation in both core symptoms (Bölte et al., 2008; Fenning et al., 2018; Kerekes et al., 2013) and co-morbid features (Adamek et al., 2011; De Pauw et al., 2011; Millea et al., 2013; Schwartz et al., 2009) and other characteristics such as cognitive level (Faja & Dawson, 2015; Kasari & Sigman, 1997) among groups of children with ASD However, findings have been inconsistent. Furthermore, due to methodological limitations and inconsistent and incomplete reporting of the relevant statistics, the number of studies that we were able to include in the meta-analytic investigation was limited. Therefore, significant methodological improvements are needed before studies of this type can begin to provide insights into the extent to which temperament can explain variability in development and learning. In addition, in order to fully understand the potential value of temperament as a predictive variable, longitudinal investigation is required from infancy through the toddlerhood and preschool years.

Some researchers have begun to investigate temperament within prospective longitudinal designs, exploring the potential value of early individual differences as indicators of later diagnostic outcome status, suggesting that temperamental differences may be observed in individuals with ASD from as early as 6-months of age. Longitudinal studies hold the exciting potential to establish the extent to which variability in early temperament might correspond to individual differences characteristics and skills and may inform our understanding of predictors of treatment outcome in ASD. As shown in other neuropsychiatric disorders (Joyce, Mulder, & Cloninger, 1994; Karalunas et al., 2014), this approach might thus be critical for increasing our understanding of the impact of temperament on clinical characteristics and long-term outcomes in ASD. Indeed, two recent studies (Berkovits et al., 2017; Bos et al., 2018) showed that emotion regulation abilities contribute to the development and maintenance of internalizing and externalizing symptoms in children with ASD.

Including existing models linking temperament dimensions with specific brain regions and networks (see Whittle, Allen, Lubman, & Yücel, 2006) within future research could be especially powerful when incorporated into longitudinal designs. A very good illustration of the value of this approach has been offered by Karalunas et al. (2014) who first employed a community detection clustering method, identifying three subgroups of children with ADHD based on their temperament profiles (mild, surgent and irritable subtypes). This group then validated their identified subgroups in terms of their distinctive neurobiological profiles, incorporating cardiac physiological indices and resting-state functional brain connectivity, and predicting clinical outcomes 1 year later. Of note, the identified subtypes were independent of DSM-5 clinical demarcations.

Despite diversity among theories of temperament and a wide variety of nominated traits, as we have shown in the taxonomy proposed in the introduction, there is a good degree of coherence in the way we conceive of this construct and can observe its effects on development. As we have suggested above, *affectivity/emotionality*, *sociability* (including concepts related to activity level), and what can be broadly termed *self-regulation* present as almost universal dimensions among different theories of temperament. These have been shown to be associated with particular brain areas/networks (Whittle et al., 2006) and to have at least some distinct genetic underpinnings (Saudino, 2005). Furthermore, these constructs are largely covered by measures based on the four temperament models proposed by Rothbart (Rothbart & Goldsmith, 1985), Thomas and Chess (1968), Buss and Plomin (1975, 1984), and Cloninger (1986, 1987). They align closely with the domains shown by Karalunas et al. (2014) to be useful in parsing heterogeneity in ADHD, and map well onto the key domains of function identified by the National Institute of Mental Health (NIMH) Research Domain Criteria (RDoC) initiative (Insel et al., 2013; for a discussion, see Chetcuti et al., 2019), which is increasingly being adopted as a framework for describing clinical phenomenology. Hence, we suggest that researchers exploring temperament in ASD should adopt these dimensions in their work to enable generalization of findings across studies and future meta-analysis.

The systematic integration of existing work within a unified higher-order taxonomy has brought to light a rather consistent pattern of relations between temperament and ASD across studies. The evidence indicates that individuals with ASD may be distinguished from other groups by high affectivity/emotionality, low sociability, and low self-regulation. The question of precisely *how* ASD and temperament are related is thus an important question for the field. As mentioned above, there are four explanatory models for the link between temperament and psychopathology: the *predisposition/vulnerability* model, the *continuity/spectrum* model, the *pathoplasty/exacerbation* model, and the *complication/scar* model (see Watson et al., 1994).

Evidence linking early temperament characteristics to the later severity of ASD symptoms (Garon et al., 2016; Macari et al., 2017) suggests that a predisposition/vulnerability model represents a viable explanation for the relation between temperament and ASD. Nevertheless, it is difficult to tease apart competing explanations from behavioral quantifications alone; such that the same temporal relationship may not be apparent when measurement is taken at the level of underlying neurobiology. Indeed, ASD-driven perturbations in brain architecture and functional connectivity appear to unfold before behavioral disorder symptoms (Hazlett et al., 2011; Hazlett et al., 2017; O'Reilly, Lewis, & Elsabbagh, 2017).

4.3. Conclusion

Despite nearly three decades of research, challenges remain for the drawing of strong conclusions on the topic of temperament in individuals with ASD. Nevertheless, work in this area holds promise to further our knowledge of the early developmental pathway/s toward ASD diagnosis, and predictors of outcomes beyond this point. Our review has identified limitations in the existing work on this topic and proposed directions for future research efforts. The unified typology of temperament suggested here has well-theorized relationships to neurobiological systems and holds promise for providing a superior description of heterogeneity in ASD compared to current clinical nosologic criteria.

Dedication

This paper is dedicated to Professor Margot Prior, a pioneer of autism and temperament research and an inspirational mentor who helped and guided many generations of researchers and clinicians. She will be greatly missed, but her spirit, generosity, integrity and ideas will continue to inspire the ones who were fortunate to know her and generations to come.

Declaration of competing interest

The authors declare no conflicts of interest.

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Mirko Uljarević is Australian Research Council Discovery Early Career Researcher Award Senior Research Fellow in in the Faculty of Medicine, Dentistry and Health Sciences, Melbourne University. He has completed PhD in Developmental Psychology at Cardiff University and prior to joining Melbourne University he was a Research Fellow in the Department of Psychiatry and Behavioral Sciences, School of Medicine, Stanford University. His research work has focused on the following research themes: (i) taxonomy and mechanisms underlying restricted and repetitive patterns of behaviors across both typical and atypical development, in particular, Autism Spectrum Disorder (ASD), (ii) understanding of risk and resilience factors underpinning co-occurring mental health problems in individuals with ASD, with particular foci on anxiety, depression, and more recently suicidal ideation; (iii) identifying sources of heterogeneity among individuals with ASD, in particular individual variability in sensory processing and temperament domains of affectivity, self-regulation, and sociability, in order to inform the design of individually tailored intervention programs; and (iv) mental health, well-being, and support for families of children with neurodevelopmental disorders.

Appendix D - Published Manuscript (Chapter 2)

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Editorial Perspective: Furthering research on temperament in autism spectrum disorder

Lacey Chetcuti,[1] Mirko Uljarević,[2] and Kristelle Hudry[1,3]

[1]Olga Tennison Autism Research Centre, School of Psychology and Public Health, La Trobe University, Melbourne, Vic., Australia; [2]Stanford Autism Center, Division of Child and Adolescent Psychiatry, Department of Psychiatry and Behavioral Sciences, School of Medicine, Stanford University, Stanford, CA, USA; [3]Victorian Autism Specific Early Learning and Care Centre, La Trobe University, Melbourne, Vic., Australia

Heterogeneity is a long-recognised feature of autism spectrum disorder (ASD), observed in the presentation and severity of core/associated symptoms as well as trajectories of symptom onset and life span course. Identifying the sources of variation in ASD symptomatology and clinical/life outcomes is critical for the development of more targeted and individually tailored recommendations and interventions that will, in turn, improve life outcomes for individuals with ASD. It is becoming increasingly clear that maintaining the search for disorder-specific sources of heterogeneity may not be an effective means of achieving this goal. Although philosophically different, the framework of developmental psychopathology and National Institute of Mental Health's (NIMH) Research Domain Criteria (RDoC; Insel et al., 2010) initiative both emphasise the need to go beyond current symptom-based categorical demarcations of mental health/illness to explain clinical phenomenology at the fundamental biobehavioural level. We propose that captilising on both traditions holds promise for providing a richer mechanistic understanding of heterogeneity in ASD, and specifically nominate temperament as a relevant construct for future such work.

Temperament reflects early emerging emotional and behavioural traits that result from interactions among genetic, biological and environmental influences (Shiner et al., 2012). While the structure of temperament remains a topic of continuing debate, we consider temperament to be a composite of three high-order dimensions: (a) *negative emotionality*, the tendency to experience negative emotions, (b) *sociability*, the tendency to actively and surgently engage with others and (c) *self-regulation*, the capacity to regulate cognitions, emotions and action. We illustrate in Table 1 how these high-order dimensions map onto different domains of functioning proposed within the RDoC framework, have distinct neurological substrates, and are encompassed within the dominant theoretical models of temperament (for a review, see Shiner et al., 2012).

These high-order temperament dimensions interact in complex ways to affect positive and negative developmental outcomes, such as academic achievement and social-emotional competence (Shiner &

Unified high-order framework of temperament traits

	Negative emotionality	Sociability	Self-regulation
RDoC domain/s of function	Negative valence systems	Positive valence systems Social processes	Cognitive systems (cognitive control construct)
Neural substrates	Bed nucleus of the stria terminalis Basolateral and central amygdala Dorsomedial prefrontal cortex	Midbrain ventral tegmental area Ventral striatum (nucleus accumbens) Orbitofrontal cortex	Caudate Anterior cingulate cortex Dorsolateral prefrontal cortex
Conceptual model			
Alexander Thomas and Stella Chess	Mood Adaptability	Activity Intensity Approach/withdrawal	Attention span/persistence Threshold Distractibility Rhythmicity
Arnold H. Buss and Robert Plomin	Emotionality	Sociability Activity	-
Mary K. Rothbart	Negative affectivity	Surgency	Effortful control Orienting/regulation
H. Hill Goldsmith and Joseph Campos	Anger proneness	Social fearfulness Pleasure Activity level	Interest/persistence
C. Robert Cloninger	Harm avoidance	Reward dependence	Persistence Novelty seeking

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Caspi, 2003). Extensive literature also suggests that temperamental variation may be associated with differences in susceptibility and resilience towards psychopathological outcomes. For instance, in two-independent samples of children and adolescents, Hankin et al. (2017) found that high negative emotionality and low self-regulation conferred broad-based, transdiagnostic risk towards general psychopathology (i.e. *p* factor). Moreover, low self-regulation was uniquely related to externalising liability while high negative emotionality and low sociability were linked more specifically to internalising liability. Considerably less is known, however, about how temperament relates to the variance of core and associated ASD features.

We have recently reviewed 40 studies on temperament in the context of ASD and found that much existing research has been descriptive in nature – comparing the temperamental attributes of ASD-diagnosed individuals to those with normative development and/or other clinical/developmental conditions (Uljarević et al., 2018). This conventional strategy of between-group comparison is predicated on the assumption that all individuals with ASD diagnoses share the same temperamental attributes. However, such a possibility seems highly unlikely given that the aetiology and consequent phenotypic expression of ASD symptoms is highly heterogeneous. We therefore argue that there is a need to reorient research efforts towards exploring temperament as a predictor of individual differences *within* the ASD-diagnosed population. As an illustration, we identified a small number of studies reporting concurrent associations between temperament and the severity of core and noncore/associated ASD features (Uljarević et al., 2018) – that is, an emerging evidence base broadly supporting our position that temperament constitutes a *transdiagnostic* factor contributing to heterogeneity in outcomes for individuals with and without ASD alike. Nevertheless, this line of research remains in its infancy. Here, we highlight how the RDoC approach may further our understanding of temperament in ASD. We begin by identifying key conceptual and methodological avenues for improvement and conclude by raising some unanswered questions for the field.

There is a need to acknowledge and address confounding in the conceptualisation and measurement of temperament and core/associated ASD symptoms. For example, most measures of temperament and internalising psychopathology tap behaviours related to social withdrawal and inhibition, which form part of the ASD diagnostic criteria. A failure to address such overlap might artificially inflate the strength of associations. While one straightforward solution is to eliminate overlapping items from temperament and outcome measures, we propose that estimates of item similarity should be empirically derived (e.g. through joint confirmatory factor analyses) rather than based solely on researcher judgment.

Next, it is crucial to select temperament measures that tap the biologically based, high-order traits of negative emotionality, sociability and self-regulation. Parent-report questionnaires represent a long-standing measurement tradition, and those based on Mary K. Rothbart's conceptualisation are one appropriate option. While this set of measures includes slightly different fine-grained subscales for specific temperament traits, there is convergence around three overarching dimensions – surgency, negative affectivity and effortful control (referred to as orienting/regulation in infancy) – that are grounded in biology and align closely with our proposed three-factor taxonomy (Table 1). Nevertheless, we advocate the need to supplement questionnaire information with other, more objective data.

In the context of ASD research, most studies of temperament have relied soley on the parent-report of temperament, offering numerous practical advantages over observational/laboratory-based indices, and drawing on parents' extensive knowledge of their children to provide a rich picture of behaviour across contexts. However, parental response biases may well be at play. For instance, parent ratings on temperament scales may be influenced by dispositional characteristics, transient mood state, mental health and perceptions of the parent–child relationship. Research comprising multiplex ASD families – including studies of high-risk infant siblings – should also consider the potential of parents to either inflate (i.e. assimilation effect) or underestimate (i.e. contrasting effect) the degree of temperamental similarity between siblings by evaluating them relative to one another. While this bias likely operates across all parent-rated temperament measures, questionnaires that call for global judgements (e.g. 'child cries easily') may be more susceptible than those seeking reports on behaviour within specified contexts (e.g. 'child cries before going to sleep'; Saudino, Wertz, Gagne, & Chawla, 2004).

The principal alternative approach is direct observation of child behaviour in the home or during laboratory-based assessments. While this method may afford greater objectivity than parent-report questionnaires, this nevertheless carries limitations in terms of test–retest reliability and ecological validity. Hence, we advocate a multimethod/multi-informant approach to measuring temperament in the context of ASD diagnosis, combining self/other reports and behavioural observations. We also encourage the continuing development of ecologically valid indices tapping these traits. For example, experience-sampling methods could provide a way of measuring temperament on multiple occasions while 'in-the-moment', circumventing retrospective recall biases and behavioural artefacts created by the laboratory environment.

Moreover, it will be important to incorporate temperament measures across different units of analysis – from observable behaviour to underlying neurobiological systems (i.e. genes, cells, molecules and circuits; Insel et al., 2010) – to gain a more *mechanistic* understanding of individual differences in ASD-diagnosed samples. Different neuroimaging modalities capture different structural and functional properties of the brain, and multimodal neuroimaging indices are necessary to achieve a comprehensive understanding of how individual differences in temperament domains map onto variation in the structural and functional integrity of the specific features and circuits. More specifically, while structural magnetic resonance imaging (MRI) and diffusion tensor imaging (DTI) capture structural properties of brain features and connectivity, task-evoked and resting-state functional MRI capture different aspects of functional dynamics and integrity of particular circuits. Hence, utilising these methods in isolation to explore, for example, the neurobiological underpinnings of cognitive control will not provide comprehensive mapping across the unit of analysis.

Going beyond measurement-related issues, the question of precisely *how* temperament and ASD are associated is an important one for the field. Several theoretical models seem plausible: that temperament (a) represents a predisposition towards the development of ASD (i.e. vulnerability association), (b) alters the manifestation of ASD symptoms *after* their onset (i.e. pathoplastic association) or even (c) exists on the same continuum as ASD, such that ASD is an extreme variant of continuously distributed temperament traits (i.e. spectrum association). Shiner and Caspi (2003) provide a detailed review of these competing accounts. Characterising the nature of the temperament-psychopathology relationship can only be addressed through prospective longitudinal research design. For instance, empirical evidence providing support for the possibility of a spectrum – rather than vulnerability or pathoplastic – association would come from evidence of corresponding longitudinal changes in temperament and ASD features.

We also emphasise that research seeking to understand associations between temperament and features of ASD need not be restricted to the examination of diagnosed individuals who have 'clinical' levels of ASD symptoms. There is growing recognition that the ASD phenotype has a spectrum of expression in the neurotypical population and across samples of people with many different neurodevelopmental/psychiatric disorders. That is, the diagnostic features of ASD are themselves *transdiagnostic*. Hence, research on the temperament-ASD relation is well-suited to an RDoC-informed design, involving the recruitment of study participants spanning multiple disorder categories. Even while maintaining a core objective of understanding heterogeneity in the context of ASD *diagnosis*, researchers need *not* recruit solely on the basis of DSM-defined diagnostic categories. Rather, recruiting transdiagnostically, the ASD diagnostic label would effectively be invisible, allowing the examination of how neural circuits and systems (e.g. temperament) contribute to *individual differences* in social-communicative skills and/or restricted/repetitive behavioural features. While this research design deviates from the between-group comparison approach familiar to researchers with an interest in ASD, it holds the exciting potential to achieve true mechanistic understanding of development that cuts across diagnostic boundaries.

Future research should also employ person-centred statistical techniques to identify 'natural' subgroups of individuals who share similar temperamental attributes, rather than maintaining the traditional focus on variable-centred analyses. Person-centred methods – such as cluster and profile analysis – are well-suited to the study of temperament because, unlike variable-centred regression analysis, they take into account the nonorthogonal nature of temperament traits which may be critical in seeking to draw conclusions about predictive associations with other factors within a given sample. The value of this approach has recently been exemplified by Karalunas et al. (2014), who used a community detection clustering technique and identified three temperament subtypes among children with ADHD diagnoses. *Mild*, *Surgent* and *Irritable* subtypes were distinguished by unique patterns of cardiac physiological response and resting-state functional brain connectivity, stable over time and predictive of clinical outcomes 1 year later. Notably, these subtypes were also independent of clinical demarcations of ADHD symptom severity and presentation.

Finally, it will be important to consider the role of the environment on associations among temperament and core/associated features of ASD. In the broader literature, child temperament and parenting behaviours have been shown to shape one another over time and to interact in predicting child outcomes. While the association between temperament and parenting has received little empirical attention in the context of ASD, emerging evidence suggests that dyadic parent-child interaction may be less synchronous when children with ASD have higher negative emotionality and lower self-regulation (e.g. Hirschler-Guttenberg, Golan, Ostfeld-Etzion, & Feldman, 2015). Further longitudinal research is needed to clarify how the interplay of child temperament and the parenting environment contributes to heterogeneity in ASD; specifically, whether parenting practices may attenuate or intensify the effects of child temperament on outcomes, and/or whether the effects of parenting may vary as a function of child temperament.

In conclusion, it is our view that research in the context of ASD lags well behind that being conducted in other clinical fields in maintaining an almost exclusive focus on describing group-level differences in temperament across samples of participants with/without a diagnosis. We call into question the utility of this conventional approach and recommend that future research efforts be directed towards more comprehensive exploration of temperament as a predictor of individual differences. This will necessitate a shift towards a multimethod/multi-informant measurement approach, informed selection of instruments, more person-centred statistical methods, and the application of more rigorous research designs informed by the transdiagnostic RDoC framework.

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Correspondence

Kristelle Hudry, Olga Tennison Autism Research Centre, School of Psychology and Public Health, La Trobe University, Kingsbury Drive, Bundoora, Vic. 3086, Australia; Email: k.hudry@latrobe.edu.au

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SHORT REPORT

Subgroups of Temperament Associated with Social–Emotional Difficulties in Infants with Early Signs of Autism

Lacey Chetcuti, Mirko Uljarević, Kandice J. Varcin, Maryam Boutrus, Ming Wai Wan, Jonathan Green, Teresa Iacono, Cheryl Dissanayake, Andrew J. O. Whitehouse, Kristelle Hudry, and the AICES Team†

Links between temperament and social–emotional difficulties are well-established in normative child development but remain poorly characterized in autism. We sought to characterize distinct temperament subgroups and their associations with concurrent internalizing and externalizing symptoms in a sample of 103 infants (M_{age} = 12.39 months, SD = 1.97; 68% male) showing early signs of autism. Latent profile analysis was used to identify subgroups of infants with distinct temperament trait configurations on the Infant Behavior Questionnaire-Revised. Derived subgroups were then compared in terms of internalizing and externalizing symptoms on the Infant–Toddler Social and Emotional Assessment. Three distinct temperament subgroups were identified: (a) *inhibited/low positive* (*n* = 22), characterized by low Smiling and Laughter, low High-Intensity Pleasure, low Vocal Reactivity, and low Approach; (b) *active/negative reactive* (*n* = 23), characterized by high Activity Level, high Distress to Limitations, high Sadness, high Fear, and low Falling Reactivity; and (c) *well-regulated* (*n* = 51), characterized by high Cuddliness, high Soothability, and high Low-Intensity Pleasure. There were no differences in infant sex ratio, mean age or developmental/cognitive ability. Inhibited/low-positive infants had significantly more behavioral autism signs than active/negative reactive and well-regulated infants, who did not differ. Inhibited/low-positive and active/negative reactive infants had higher internalizing symptoms, relative to well-regulated infants, and active/negative reactive infants also had higher externalizing symptoms. These findings align closely with those garnered in the context of normative child development, and point to child temperament as a putative target for internalizing and externalizing interventions. ***Autism Res** 2020, 00: 1–8.* © 2020 International Society for Autism Research and Wiley Periodicals LLC

Lay Summary: This study explored whether infants with early signs of autism could be grouped according to temperament characteristics (i.e., emotional, behavioral, and attentional traits). Three subgroups were identified that differed with respect to emotional and behavioral difficulties. Specifically, "inhibited/low-positive" infants had high emotional difficulties, "active/negative reactive" infants had high emotional *and* behavioral difficulties, while "well-regulated" infants had the lowest difficulties.

Keywords: autism spectrum disorder; externalizing; infants; internalizing; temperament

Introduction

Symptoms of autism spectrum disorder (hereafter, autism) co-occur at high rates with internalizing (anxiety and/or depression) and externalizing (inattentive/hyperactive, oppositional, and/or aggressive behavior) symptoms, at both a subclinical level and a clinical level [Joshi et al., 2010; Lundström et al., 2011]. Social–emotional difficulties are heightened among autistic children from very early childhood [Rescorla et al., 2019] and may contribute to functional impairment [Chiang & Gau, 2016], prognosis, and differential treatment response [Vivanti, Prior, Williams, & Dissanayake, 2014]. Therefore, it is critical to identify, early on in life, those children with

From the Department of Psychology and Counselling, School of Psychology and Public Health, La Trobe University, Melbourne, Victoria, Australia (L.C., K.H.); Cooperative Research Centre for Living with Autism (Autism CRC), Brisbane, Queensland, Australia (L.C., M.B., C.D., A.J.O.W.); Melbourne School of Psychological Sciences, The University of Melbourne, Melbourne, Victoria, Australia (M.U.); School of Allied Health Sciences, Griffith University, Gold Coast, Queensland, Australia (K.J.V.); Telethon Kids Institute, Nedlands, Western Australia, Australia (M.B., A.J.O.W.); University of Western Australia, School of Psychological Science, Crawley, Western Australia, Australia (M.B.); Division of Psychology and Mental Health, School of Health Sciences, University of Manchester, Manchester, UK (M.W.W.); Division of Neuroscience and Experimental Psychology, School of Biological Sciences, University of Manchester, Manchester, UK (J.G.); Manchester Academic Health Science Centre, Manchester University NHS Foundation Trust, Greater Manchester Mental Health NHS Trust, Manchester, UK (J.G.); La Trobe Rural Health School, Bendigo, Victoria, Australia (T.I.); Olga Tennison Autism Research Centre, School of Psychology and Public Health, La Trobe University, Melbourne, Victoria, Australia (C.D.)

†The AICES team in alphabetical order: Josephine Barbaro, Stefanie Dimov, Murray Maybery, Michelle Renton, Nancy Sadka, Leonie Segal, Vicky Slonims, Scott Wakeling, and John Wray.

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Address for correspondence and reprints: Lacey Chetcuti, School of Psychology and Public Health, La Trobe University, Melbourne, VIC, Australia. E-mail: lchetcuti@ltu.edu.au

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autism features at greatest risk of internalizing and/or externalizing symptoms so appropriate supports can be allocated.

Existing literature on normative development suggests that individual variation in children's temperament may be associated with social–emotional difficulties; that is, early emerging emotional and behavioral traits in domains of *negative emotionality*, the tendency to experience negative emotions, *sociability*, the tendency to engage actively with others, and *self-regulation*, the capacity to regulate emotions and action [Chetcuti, Uljarević, & Hudry, 2018]. High negative emotionality and low self-regulation confer susceptibility toward both internalizing and externalizing symptoms, whereas low sociability more strongly relates to internalizing symptomatology [De Pauw & Mervielde, 2010; De Pauw, Mervielde, & Leeuwen, 2009]. A similar pattern of relations has been reported among school-aged children and adolescents with autism [Burrows, Usher, Schwartz, Mundy, & Henderson, 2016; De Pauw & Mervielde, 2010; Schwartz et al., 2009]. However, no studies have explored associations between temperament and social–emotional difficulties in infancy, when key differences in temperament associated with autism first become apparent [Clifford et al., 2013].

Furthermore, studies of normative development provide some indication that person-centered statistical methods (cluster/profile analysis) may be a useful alternative means of characterizing relations among temperament and social–emotional difficulties [Chetcuti et al., 2018]. In the seminal work of Thomas, Chess, and Birch [1968], three subgroups were identified by (top-down) qualitative analysis of temperament data collected through clinical observations and interviews with parents of 141 normative infants. Temperamentally *difficult* children were characterized by high and intense negative emotionality and activity, low sociability, and low self-regulation, while *easy* children showed the opposite trait pattern—low negative emotionality, high sociability, and high self-regulation. *Slow-to-warm-up* children showed a qualitatively different trait configuration—high negative emotionality (but of lesser intensity than difficult children), low sociability and activity, and average self-regulation. This typology was subsequently supported through factor analysis [Thomas & Chess, 1977] and replicated using data-driven (bottom-up) statistical techniques [Mcdevitt & Carey, 1978]. Using person-centered statistical methods, recent studies have identified thematically similar temperament subgroups among other normative cohorts [e.g., Robins, John, Caspi, Moffitt, & Stouthamber-Loeber, 1996] that meaningfully map onto internalizing and externalizing outcomes. A slow-to-warm-up disposition appears to confer susceptibility towards internalizing symptoms/disorders, while a difficult temperament is associated with heightened externalizing symptoms/disorders. Temperamentally difficult children also appear more susceptible to both co-occurring internalizing *and* externalizing symptoms, while children with an easy disposition seem least prone toward the development of either [Putnam & Stifter, 2005; Robins et al., 1996; Thomas et al., 1968].

Only a few studies have examined patterns of multiple temperament traits in the context of autism. Kasari and Sigman [1997] found that children with an autism diagnosis scored higher than normative children and children with Down syndrome on a composite score reflecting difficult temperament (a constellation of irregularity, withdrawal from new stimuli, low adaptability, high intensity, and negative mood). Similarly, Chuang, Tseng, Lu, and Shieh [2012] found that a higher percentage of autistic children had a difficult temperament trait constellation (34.3%) than children with normative development (18.2%). To our knowledge, only one study has characterized children into temperament subgroups that were not predefined by existing theory, but rather emerged "bottom-up" from the analyzed data. Garon et al. [2009] used discriminant function analysis to identify temperament trait constellations that prospectively distinguished infants who did and did not go on to receive an autism diagnosis at preschool age. Two temperament functions differentiated children with autism from normative children at 24-months: lower scores were apparent among children with autism for a 'behavioral approach' function reflecting sensitivity to social reward cues, and 'effortful emotion regulation' function reflecting the ability to manage negative emotions and behavior. Garon et al. [2009] also investigated whether temperament function scores differed within their autism-diagnosed sample according to timing of autism diagnosis. A combination of higher autism symptoms, lower IQ, and lower behavioral approach was found to differentiate among children with autism diagnosed earlier versus later in life.

Taken together, evidence from existing studies suggests differences across multiple temperament traits among autistic children compared to non-autistic controls, and according to timing of autism diagnosis. Apart from Garon et al. [2009], there have been no other efforts to characterize temperamentally distinct subgroups of children with autism features or explore the potential relevance of such subgroups for explaining variability in children's social–emotional outcomes. Therefore, among a unique cohort of infants referred with early autism signs we sought to (a) identify temperament subgroups using person-centered methods and (b) explore associations between these and concurrent social–emotional difficulties. We expected heightened internalizing symptoms among infants presenting with low sociability-related temperament traits, and elevated internalizing and externalizing symptoms among those with high negative emotionality and low self-regulation. In contrast, we expected the lowest internalizing and externalizing symptom levels among infants with high temperamental sociability and self-regulation.

Method

Participants were 103 infants aged 9–16 months (M = 12.39, SD = 1.97; 68% male) recruited into a larger study (Whitehouse et al., 2019), for which prospective ethical approval was granted by institutional review boards. Referral to the study was by community healthcare providers, on the basis of infants showing ≥3 (of 5) key autism behaviors on the Social Attention and Communication Surveillance-Revised (SACS-R) tool (i.e., atypical/absent pointing, waving, imitation, eye contact, response to name) [Barbaro & Dissanayake, 2013]. The SACS-R is a revised version of the SACS [Barbaro & Dissanayake, 2010] designed as an autism surveillance tool for implementation by primary health professionals during routine well-child checks. The original SACS tool has excellent estimated sensitivity (84%) and specificity (99%) for detecting autism in childhood (based on a general population prevalence estimate of 1:100) [Barbaro & Dissanayake, 2010]. Similarly, in a more recent study, the SACS-R has shown good positive predictive value (72%) for subsequent autism diagnosis among 12-month olds [Barbaro, Dissanayake, & Sadka, 2018; also see Mozolic-Staunton, Donelly, Yoxall, & Barbaro, 2020]. Each infant was administered the Mullen Scales of Early Learning (MSEL) [Mullen, 1995] to ascertain cognitive/developmental level, and the Autism Observation Scale for Infants (AOSI) [Bryson, Zwaigenbaum, McDermott, Rombough, & Brian, 2008] to quantify early behavioral autism signs.

Caregivers (72% mothers) completed the Infant–Toddler Social and Emotional Assessment (ITSEA) [Carter & Briggs-Gowan, 2006] to ascertain infant symptoms in Internalizing and Externalizing domains, and the Infant Behavior Questionnaire-Revised (IBQ-R) [Gartstein & Rothbart, 2003] to measure fine-grained temperament traits: Activity Level, Smiling and Laughter, High-Intensity Pleasure, Vocal Reactivity, Approach, Perceptual Sensitivity (reflecting aspects of sociability), Distress to Limitations, Fear, Sadness, Falling Reactivity (aspects of negative emotionality), Duration of Orienting, Low-Intensity Pleasure, Cuddliness, and Soothability (aspects of self-regulation).

To address the issue of measurement confounding, ITSEA items that were conceptually and semantically similar to IBQ-R items were removed prior to calculation of ITSEA domain scores (Appendix A). Internal consistency was good for both scales of the IBQ-R (α = 0.65–0.89) and domains of the ITSEA (Externalizing α = 0.82; Internalizing α = 0.62).

Analytic Strategy

Latent profile analysis (LPA) was conducted in M*plus* [Muthén & Muthén, 1998–2017] using the robust maximum likelihood estimator. Model fit concerning temperament subgroups identified from the 14 IBQ-R scales was assessed with the Akaike Information Criterion (AIC), Bayesian Information Criterion (BIC), and Adjusted BIC, where lower values indicate better fit, and statistically significant Lo–Mendell–Rubin test (LMRT) and Bootstrapped Likelihood Ratio test (BLRT) indicate fit improvement with an additional subgroup (k vs. $k - 1$). Subgroup classification quality was assessed with the entropy statistic, with a value closer to 1 indicating less uncertainty. Model selection was also guided by parsimony and interpretability [Bauer & Curran, 2003]. Once extracted, subgroup-level differences in mean IBQ-R scale scores were determined via bootstrapped (2000 resamples) one-way analysis of variance (ANOVA) with a Bonferroni correction applied for multiple comparisons (i.e., alpha-level of 0.05/14 = 0.0036) and post hoc tests. Pearson's chi-square tests and one-way ANOVAs were then performed to explore differences in infant clinical characteristics and ITSEA domain scores as a function of temperament subgroup. Eta squared (η^2) was the effect size measure computed for each ANOVA, with 0.01 interpreted as small, 0.06 medium, and 0.14 large.

Results

Table 1 summarizes model fit indices. The three-subgroup model was selected as the best fitting solution, with lowest-value BIC and statistically significant BLRT. Although the four- and five-subgroup solutions also had statistically significant BLRT and lower AIC and Adjusted BIC values, Nylund, Asparouhov, and Muthén [2007] advocate better performance of the BIC in smaller samples. Furthermore, the three-subgroup solution was most parsimonious, with accurate subgroup classification (i.e., entropy >0.80; mean posterior membership probabilities >0.70 [Profile 1 = 0.97, 2 = 0.92, 3 = 0.98]) [Clark, 2010; Nagin, 2005].

Infants were assigned to temperament subgroups based on maximum probability of membership. Figure 1 shows IBQ-R scale mean scores for infants in the three identified temperament subgroups with ANOVA results in Table 2. The first subgroup (n = 22) was characterized by low Smiling and Laughter, low High-Intensity Pleasure, low Vocal Reactivity and low Approach; hereafter, labeled *inhibited/low positive*. The second (n = 23) was labeled *active/negative reactive*, given high Activity Level, high Distress to

Table 1. Comparison of Five LPA Models for Infant Temperament

# of subgroups	n for each subgroup	AIC	BIC	Adjusted BIC	LMRT P value	BLRT P value	Entropy
1	$n_1 = 96$	3775.87	3847.67	3759.26	–	–	–
2	$n_1 = 20$ $n_2 = 76$	3603.34	3713.61	3577.84	<0.001	<0.001	0.95
3	$n_1 = 22$ $n_2 = 23$ $n_3 = 51$	3506.26	3654.99	3471.86	0.056	<0.001	0.92
4	$n_1 = 15$ $n_2 = 23$ $n_3 = 20$ $n_4 = 38$	3474.53	3661.72	3431.23	0.471	<0.001	0.90
5	$n_1 = 19$ $n_2 = 10$ $n_3 = 15$ $n_4 = 42$ $n_5 = 10$	3454.23	3679.88	3402.03	0.293	<0.001	0.93

Abbreviations: AIC, Akaike Information Criterion; BIC, Bayesian Information Criterion; BLRT, Bootstrapped Likelihood Ratio test; LMRT = Lo–Mendell–Rubin test; LPA, latent profile analysis.

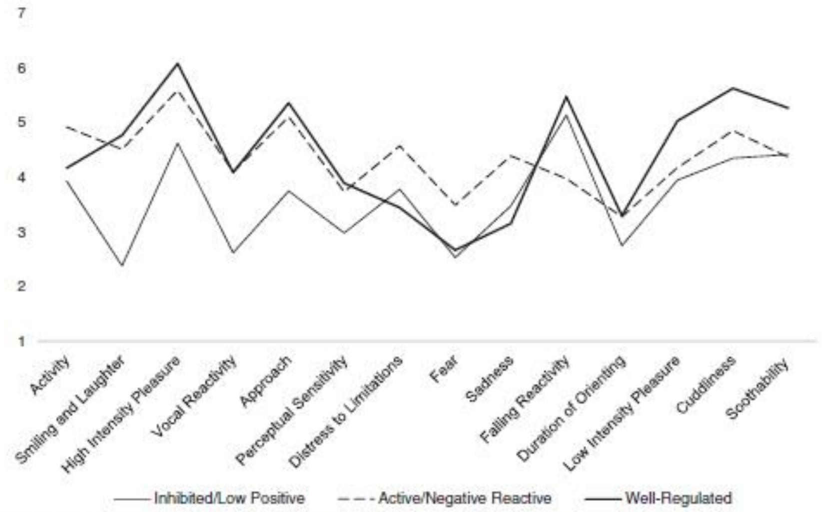

Figure 1. Infant Behavior Questionnaire-Revised (IBQ-R) scale mean scores for each temperament subgroup.

Limitations, high Sadness, and high Fear, and low Falling Reactivity. The third ($n = 51$), with high Cuddliness, high Soothability, and high Low-Intensity Pleasure, was labeled *well-regulated*.

Between-subgroup differences are presented in Table 3. There were no differences in infant sex ratio, mean age,[1] or developmental/cognitive ability (MSEL). *Inhibited/lowpositive* infants had significantly more behavioral autism signs (AOSI) than *active/negative reactive* and *well-regulated* infants, who did not differ. Infants classified as either *inhibited/low positive* or *active/negative reactive* had significantly higher internalizing symptoms than *well-regulated* infants. *Active/negative reactive* infants had higher externalizing symptoms than *well-regulated* infants. Those classified as *inhibited/low positive* had intermediate externalizing symptoms but did not differ from the other two subgroups.

[1]Nonsignificant correlation coefficients were obtained between infant age and each of the 14 IBQ-R subscale continuous scores ($r = 0.000$ [cuddliness] to 0.175 [vocal reactivity]).

Table 2. ANOVA Results Showing Mean IBQ-R Scale Scores for Infants in Each Temperament Subgroup

IBQ-R Scale	Inhibited/ low positive *M* (SD)	Active/negative reactive *M* (SD)	Well-regulated *M* (SD)	*F*	*P*	η^2	BCa 95% CI Contrast *a*	Contrast *b*	Contrast *c*
Activity	3.93 (0.70)	4.92 (0.65)	4.17 (0.61)	15.23	<0.001	0.25	**−1.38, −0.58**	**0.43, 1.04**	−0.1, 0.59
Smiling and Laughter	2.38 (0.66)	4.51 (0.71)	4.77 (0.80)	87.34	<0.001	0.66	**−2.52, −1.74**	−0.66, 0.04	**2.07, 2.79**
High-Intensity Pleasure	4.62 (0.70)	5.59 (0.68)	6.08 (0.55)	41.92	<0.001	0.48	**−1.38, −0.56**	**−0.81, −0.17**	**1.13, 1.78**
Vocal Reactivity	2.63 (0.72)	4.1 (0.96)	4.09 (0.95)	22.09	<0.001	0.32	**−1.98, −0.97**	−0.47, 0.46	**1.05, 1.87**
Approach	3.75 (1.04)	5.11 (0.74)	5.36 (0.86)	25.95	<0.001	0.36	**−1.89, −0.82**	−0.63, 0.14	**1.11, 2.11**
Perceptual Sensitivity	2.98 (1.35)	3.74 (1.10)	3.89 (1.28)	3.88	0.024	0.08	-	-	-
Distress to Limitations	3.78 (1.01)	4.57 (0.75)	3.45 (0.92)	11.86	<0.001	0.20	**−1.35, −0.28**	**0.69, 1.52**	−0.82, 0.21
Fear	2.54 (0.87)	3.49 (0.93)	2.67 (0.86)	8.40	<0.001	0.15	**−1.43, −0.46**	**0.34, 1.23**	−0.29, 0.61
Sadness	3.48 (0.78)	4.39 (0.79)	3.15 (0.97)	14.82	<0.001	0.24	**−1.37, −0.46**	**0.81, 1.64**	−0.75, 0.14
Falling Reactivity	5.14 (0.96)	3.98 (0.8)	5.47 (0.55)	33.20	<0.001	0.42	**0.63, 1.69**	**−1.83, −1.14**	−0.07, 0.74
Duration of Orienting	2.75 (0.76)	3.28 (0.87)	3.3 (1.18)	2.27	0.109	0.05	-	-	-
Low-Intensity Pleasure	3.95 (0.85)	4.18 (0.72)	5.03 (0.81)	18.46	<0.001	0.29	−0.69, 0.25	**−1.24, −0.50**	**0.70, 1.49**
Cuddliness	4.35 (0.79)	4.85 (0.73)	5.63 (0.71)	27.25	<0.001	0.37	**−0.99, −0.01**	**−1.13, −0.45**	**0.91, 1.70**
Soothability	4.42 (0.77)	4.37 (0.48)	5.26 (0.5)	27.60	<0.001	0.38	−0.34, 0.42	**−1.14, −0.65**	**0.5, 1.20**

Note. Contrast *a* = inhibited/low positive versus active/negative reactive. Contrast *b* = active/negative reactive versus well regulated. Contrast *c* = well regulated versus inhibited/low positive. Bolded BCa 95% CIs do not span zero, signifying statistical significance.

Abbreviations: ANOVA, analysis of variance; BCa, bias-corrected and accelerated; CI, confidence interval; IBQ-R, Infant Behavior Questionnaire-Revised; ITSEA, Infant–Toddler Social and Emotional Assessment.

Discussion

The aim of this study was to characterize associations between temperament and concurrent internalizing/externalizing symptoms among a community-referred cohort of infants presenting with early autism symptoms. Three temperament subgroups were identified using a person-centered approach—*inhibited/low positive*, *active/negative reactive*, and *well-regulated*—that aligned closely with those observed in normative samples [e.g., Robins et al., 1996; Thomas et al., 1968; Thomas & Chess, 1977].

The *active/negative reactive* subgroup showed close alignment with Thomas et al.'s [1968] difficult subgroup, sharing a tendency toward temperamental negative affect and self-regulation difficulties. Indeed, such a profile has been consistently replicated [e.g., Beekman et al., 2015; Prokasky et al., 2017]. Similarly, the *well-regulated* subgroup was characterized by effective self-regulation; an attribute shared by Thomas et al.'s easy subgroup and similar other subgroups identified in the literature [Gartstein et al., 2017; Robins et al., 1996]. The *inhibited/low-positive* subgroup shared the low sociability characteristics of Thomas et al.'s slow-to-warm-up subgroup. However, previously identified low-sociability subgroups have also encompassed high trait self-regulation, which was not the case here. Rather, traits related to self-regulation—Low-Intensity Pleasure, Cuddliness, and Soothability—were found to be comparable or even lower among *inhibited/low-positive* infants relative to the remainder of the cohort. Alternatively, high self-regulation may not emerge among *inhibited/low-positive* infants until later childhood, when attention comes under greater effortful control [Posner & Rothbart, 2006].

A further aim was to investigate whether temperament subgroup membership predicted variability in social–emotional difficulties in our cohort of infants showing early autism symptoms. Infants classified as *inhibited/low positive* and *active/negative reactive* had more co-occurring internalizing symptoms compared to *well-regulated* infants. Externalizing symptoms were similarly elevated in the *active/negative reactive* subgroup, relative to *well-regulated* infants, while *inhibited/low-positive* infants had intermediate externalizing symptom levels which were not significantly different to the two other subgroups. These results are consistent with literature on normative development, suggesting that slow-to-warm-up children are prone towards internalizing symptoms while difficult children are prone toward both internalizing and externalizing symptoms. Moreover, the finding of fewer co-occurring internalizing/externalizing symptoms among well-regulated infants is consistent with findings pertaining to an easy temperament in normative development [Robins et al., 1996; Thomas et al., 1968].

Infants classified as *inhibited/low-positive* presented with more behavioral signs of autism compared to *active/negative reactive* or *well-regulated* infants. This is consistent with evidence that autism severity is negatively

Table 3. Sample and Temperament Subgroup Characteristics and Between-Subgroup Comparisons

	Full sample (N = 103) M (SD)	Inhibited/low positive (n = 22) M (SD)	Active/negative reactive (n = 23) M (SD)	Well-regulated (n = 51) M (SD)	Between-subgroup comparisons			BCa 95% CI		
					χ^2/F	P	φ/η^2	Contrast a	Contrast b	Contrast c
Male (%)	70 (68)	17 (77.27)	17 (77.27)	31 (60.78)	2.44	0.295	0.16	–	–	–
Age	12.39 (1.97)	12.13 (2.18)	12.61 (2.16)	12.39 (1.76)	0.34	0.713	0.01	–	–	–
MSEL ELC	86.02 (16.76)	82.95 (20.44)	84.13 (12.66)	88.18 (13.73)	0.88	0.418	0.02	–	–	–
AOSI Total[a]	8.90 (4.31)	10.91 (4.63)	7.30 (3.56)	7.45 (3.61)	7.73	0.001	0.14	**1.38, 5.97**	−1.96, 1.63	**−5.93, −1.24**
ITSEA Internalizing	0.38 (0.23)	0.45 (0.25)	0.50 (0.23)	0.28 (0.17)	7.04	0.002	0.17	−0.22, 0.12	**0.09, 0.34**	**−0.30, −0.02**
ITSEA Externalizing	0.32 (0.25)	0.33 (0.24)	0.42 (0.27)	0.27 (0.23)	7.16	0.002	0.18	−0.27, 0.01	**0.09, 0.34**	−0.18, 0.02

Note. Contrast a = Inhibited/low positive versus active/negative reactive. Contrast b = active/negative reactive versus well regulated. Contrast c = well regulated versus inhibited/low positive. Bolded BCa 95% CIs do not span zero, signifying statistical significance.

Abbreviations: AOSI, Autism Observation Schedule for Infants; BCa, bias-corrected and accelerated. CI, confidence interval; ELC, Early Learning Composite; EXT, Externalizing; INT, Internalizing; ITSEA, Infant–Toddler Social and Emotional Assessment; MSEL, Mullen Scales of Early Learning.

[a]AOSI temperament items (reactivity and transitions) were removed from the computation of total scores counts prior to ANOVA.

associated with temperamental sociability [Kamio, Takei, Stickley, Saito, & Nakagawa, 2018] and scores on the behavioral approach discriminant function identified by Garon et al. [2009]. The precise nature of associations between temperament and autism features has yet to be elucidated. It may be that low sociability-related temperament traits (characteristic of the *inhibited/lowpositive* subgroup) increase vulnerability toward emergent autism symptoms (i.e., vulnerability association) or, alternatively, exist on the same continuum as autism such that autism represents an extreme variant of low temperamental sociability (i.e., spectrum association) [see Chetcuti et al., 2018]. Another possible explanation is that similarities in the behavioral expression and measurement of social interest/motivation deficits and temperament-related social reticence created a biased inflation of autism symptom ratings among *inhibited/lowpositive* infants. The presence of co-occurring social–emotional difficulties might also contribute to differences in autism severity, such that the heightened internalizing symptoms experienced by *inhibited/lowpositive* infants might exacerbate their autism-related difficulties [Duvekot, van der Ende, Verhulst, & Greaves-Lord, 2018]. Conversely, autism-related difficulties might contribute to the development of internalizing symptoms over time [Pickard, Rijsdijk, Happé, & Mandy, 2017].

This study has several limitations. First, given the relatively modest sample size, replication across larger and phenotypically diverse samples is needed in order to evaluate the robustness of the three-subgroup solution. Second, temperament and social–emotional difficulties were both measured via parent-report; thus, the observed associations may be inflated through common-method variance. A related issue concerns conceptual overlap between temperament and internalizing/externalizing symptoms. Although the sample size precluded formal statistical testing of item content, ITSEA items that were conceptually and semantically similar to IBQ-R items were removed to minimize measurement confounding. Moreover, previous studies have yielded significant associations after conceptual overlap was empirically determined through factor analysis [Lemery, Essex, & Smider, 2002]. Next, it is not possible to draw causal conclusions from the current cross-sectional results. While we conclude that temperament characteristics confer risk towards later social–emotional difficulties through evidence of concurrent associations, it is equally possible that social–emotional difficulties influence the expression of child temperament [see Shiner & Caspi, 2003]. Finally, it remains unknown what proportion or which infants in our sample will go on to receive an autism diagnosis and/or other clinical diagnoses; nonetheless, comparison of AOSI characterization data obtained here (see Table 3) and in familial 'at-risk' infants who went on to autism diagnostic outcome [Gammer et al., 2015] gives us encouragement that infants at elevated likelihood of autism diagnosis were successfully recruited. Future work should explore potential predictive relations between temperament patterns in infancy and clinical outcomes in childhood among large, well-characterized, general-population samples.

The clinical implication of these findings is that inhibited/*lowpositive* and *active/negative reactive* infants with autism features might benefit most from interventions addressing social–emotional difficulties that target *specific* patterns of maladaptive temperamental responding. For example, INSIGHTS into Children's Temperament is a temperament-tailored intervention designed to equip caregivers with child management techniques that "fit" a child's temperament type [McClowry, 2003], and more successfully reduces externalizing symptoms in children with normative development than a comparison program [McClowry, Snow, & Tamis-LeMonda, 2005]. No such temperament-based interventions have been developed or trialed in the context of autism. Nonetheless, the apparent convergence of findings here with studies of normative development suggests a similar treatment approach might also be useful among children with autism features.

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Supporting Information

Additional supporting information may be found online in the Supporting Information section at the end of the article.

Appendix A: Overlapping IBQ-R and ITSEA Items.

Appendix F - Published Manuscript (Chapter 7)

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SHORT REPORT

The Role of Negative Affectivity in Concurrent Relations Between Caregiver Psychological Distress and Social-Emotional Difficulties in Infants With Early Signs of Autism

Lacey Chetcuti, Mirko Uljarević, Kandice J. Varcin, Maryam Boutrus, Ming Wai Wan, Vicky Slonims, Jonathan Green, Leonie Segal, Teresa Iacono, Cheryl Dissanayake, Andrew J.O. Whitehouse, Kristelle Hudry, and the AICES Team

Recent evidence suggests the link between caregiver psychological distress and offspring social-emotional difficulties may be accounted for by offspring temperament characteristics. However, existing studies have only focused on neurotypical children; thus, the current study sought to provide an initial examination of this process among children with varying levels of early autism features. Participants included 103 infants aged 9–16 months (M = 12.39, SD = 1.97; 68% male) and their primary caregiver (96% mothers) referred to a larger study by community healthcare professionals. We utilized caregiver-reported measures of psychological distress (Depression Anxiety Stress Scales), infant temperament (Infant Behavior Questionnaire-Revised) and internalizing and externalizing symptoms (Infant-Toddler Social and Emotional Assessment) and administered the Autism Observation Schedule for Infants (AOSI) at an assessment visit to quantify autism features. Infant negative affectivity was found to mediate positive concurrent relations between caregiver psychological distress and infant internalizing and externalizing symptoms, irrespective of the infants' AOSI score. While preliminary and cross-sectional, these results replicate and extend previous findings suggesting that the pathway from caregiver psychological distress to negative affectivity to social-emotional difficulties might also be apparent among infants with varying levels of autism features. More rigorous tests of causal effects await future longitudinal investigation. ***Autism Res** 2020, 00: 1–9.* © 2020 International Society for Autism Research, Wiley Periodicals, Inc.

Lay Summary: Offspring of caregivers experiencing psychological distress (i.e., symptoms of depression, anxiety, and/or stress) may themselves be at increased risk of poor mental health outcomes. Several previous studies conducted with neurotypical children suggest that this link from caregiver-to-child may be facilitated by children's temperament qualities. This study was a preliminary cross-sectional exploration of these relationships in infants with features of autism. We found that infants' elevated negative emotions were involved in the relation between caregiver heightened psychological distress and children's mental health difficulties, consistent with neurotypical development.

Keywords: autism spectrum disorder; infant; caregivers; temperament; social-emotional difficulties

Introduction

There is a well-established link between caregiver psychological distress and heightened risk toward internalizing (anxiety and/or depression) and externalizing (inattention/hyperactivity, oppositional, and/or aggressive behavior) symptoms among offspring [for meta-analyses, see Goodman et al., 2011; Lawrence, Murayama, & Creswell, 2018]. However, the nature of these associations is currently unclear. One potential mechanism that may account for the relation between caregiver psychological distress and child social-emotional difficulties is children's individual temperament

From the School of Psychology and Public Health, La Trobe University, Melbourne, Victoria, Australia (L.C., K.H.); Cooperative Research Centre for Living with Autism (Autism CRC), Brisbane, Queensland, Australia (L.C., M.B., C.D., A.J.W.); Stanford Autism Center, Department of Psychiatry and Behavioral Sciences, Child and Adolescent Psychiatry, School of Medicine, Stanford University, Stanford, California (M.U.); Melbourne School of Psychological Sciences, Faculty of Medicine, Dentistry and Health Sciences, The University of Melbourne, Melbourne, Victoria, Australia (M.U.); Telethon Kids Institute, University of Western Australia, Subiaco, Western Australia, Australia (K.J.V., M.B., A.J.W.); School of Psychological Science, University of Western Australia, Perth, Western Australia, Australia (M.B.); Division of Psychology and Mental Health, School of Health Sciences, University of Manchester, Manchester, UK (M.W.W.); Children's Neurosciences, Evelina London Children's Hospital, Institute of Psychiatry, Psychology & Neuroscience, Kings College London, London, UK (V.S.); Division of Neuroscience & Experimental Psychology, School of Biological Sciences, University of Manchester, Manchester, UK (J.G.); Manchester Academic Health Science Centre, Manchester University NHS Foundation Trust, Greater Manchester Mental Health NHS Trust, Manchester, UK (J.G.); Australian Centre for Precision Health, School of Health Sciences, University of South Australia, Adelaide, South Australia, Australia (L.S.); La Trobe Rural Health School, Bendigo, Victoria, Australia (T.I.); Olga Tennison Autism Research Centre, School of Psychology and Public Health, La Trobe University, Melbourne, Victoria, Australia (C.D.); The AICES Team in Alphabetical Order: Josephine Barbaro, Stefanie Dimov, Murray Maybery, Michelle Renton, Nancy Sadka, Scott Wakeling, and John Wray

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Address for correspondence and reprints: Lacey Chetcuti, School of Psychology and Public Health, La Trobe University, Melbourne, VIC, Australia. E-mail: l.chetcuti@ltu.edu.au

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characteristics, defined as biologically based differences in reactivity and self-regulation [Rothbart & Derryberry, 1981]. While early theories of temperament emphasized the genetic etiology and stability of traits across developmental periods [Goldsmith et al., 1987], there is growing recognition that temperament is malleable to environmental experience. Indeed, research has shown that caregiver psychological distress symptoms are associated with children's temperamental difficulties [Hanington, Ramchandani, & Stein, 2010], which in turn may confer risk toward child social-emotional difficulties [Hankin et al., 2017]. Nevertheless, few existing studies have specifically tested this pathway.

Among 97 mother–child dyads, Suveg, Shaffer, Morelen, and Thomassin [2011] found that the links between maternal psychological distress and children's internalizing and externalizing symptoms were mediated by child self-regulation (i.e., the capacity to suppress or modulate emotions and behavior). Similar results were garnered by Choe, Shaw, Brennan, Dishion, and Wilson [2014] in a large sample of 677 toddlers and their mothers. Specifically, low levels of self-regulation at age 3 years was found to mediate the association between maternal depression at Age 2 and toddler oppositionality at Age 4. Nevertheless, Choe et al. did not explore the relevance of this pathway to children's internalizing symptoms. Allen, Oshri, Rogosch, Toth, and Cicchetti [2018] found that low child self-regulation mediated the link between maternal depression and child social-emotional difficulties. High levels of child negative affect also acted as a mediator of this association, although there was no effect of offspring positive affect/sociability. Nevertheless, the composite measure of both internalizing *and* externalizing utilized by Allen et al. may have obscured the presence of specific internalizing versus externalizing pathways. Indeed, emerging evidence suggests that low positive affect/sociability may confer internalizing-specific risk [Hankin et al., 2017].

The current study is an initial attempt to extend empirical work on this topic to the context of autism. Our primary objective was to examine whether variation in child temperament is relevant to the links between contemporaneously measured caregiver psychological distress and child social-emotional difficulties in a sample of young infants with features of autism. Examining the relevance of this pathway to autism is important given there is a higher prevalence of internalizing and externalizing symptoms/disorders among autistic individuals than in the general population. Indeed, it is estimated that over 90% of individuals with autism meet DSM criteria for a co-occurring psychiatric disorder [Joshi et al., 2010; Salazar et al., 2015], and although these are not typically diagnosed in children under the age of 2, associated social-emotional difficulties can be identified at a very young age [Briggs-Gowan, Carter, Bosson-Heenan, Guyer, & Horwitz, 2006] suggesting potential for pre-emptive intervention.

While yet to be empirically tested, several lines of evidence suggest that the aforementioned pathway identified in neurotypical children—from caregiver psychological distress to child social-emotional difficulties through child temperament—might extend to young infants with features of autism. Symptoms of psychological distress are higher among caregivers of autistic children than comparison samples [Hayes & Watson, 2013; Yirmiya & Shaked, 2005], and positively associated with children's internalizing and externalizing symptomatology [Carter, Martinez-Pedraza Fde, & Gray, 2009; Herring et al., 2006]. Moreover, autistic children demonstrate higher negative affect, lower positive affect/sociability, and lower self-regulation than nonautistic comparison groups [Chetcuti et al., 2019]—a temperament pattern associated with heightened levels of both caregiver psychological distress [Britton, 2011; Olino et al., 2011] and child social-emotional difficulties [Eisenberg et al., 2001, 2009]. Prospective studies of infants at higher familial likelihood of developing autism (by virtue of having an older autistic sibling) indicate that a temperament profile consisting of higher negative affect, lower positive affect/sociability, and lower self-regulation might predict subsequent autism diagnosis in toddlerhood [Clifford et al., 2013; Garon et al., 2015; Del Rosario, Gillespie-Lynch, Johnson, Sigman, & Hutman, 2014; Paterson et al., 2019; for a review, see Chetcuti et al., 2019]. These findings suggest that there may be an early emerging profile of temperamental susceptibility toward caregiver psychological distress and social-emotional difficulties in autism. However, the relation of temperament characteristics to social-emotional difficulties or caregiver psychological distress has yet to be explored early on in development, among infants with early autism signs.

The establishment of temporal or causal processes is beyond the scope of cross-sectional research. Nevertheless, caregiver-to-child effects were hypothesized and modeled, as studies with longitudinal measures more consistently found an effect of early caregiver attributes on subsequent child temperament than the reverse, when cross-sectional associations and stability of constructs were controlled for [Hanington et al., 2010; Pesonen et al., 2008], particularly in early life [Eisenberg et al., 2010]. In light of evidence suggesting temperament traits function similarly across clinical and nonclinical groups [Burrows, Usher, Schwartz, Mundy, & Henderson, 2016; Schwartz et al., 2009], we expected to replicate the results obtained by Suveg et al. [2011], Choe et al. [2014], and Allen et al. [2018] in a sample of infants with autism features. Specifically, infant negative affectivity and self-regulation were expected to mediate the concurrent relation between caregiver psychological distress and both internalizing and externalizing symptoms, while we anticipated a mediating effect of surgency only for internalizing. A secondary objective was to examine whether results generalize across infants with varying levels of autism features, though we predicted no such effects.

Method

Participants

Participants were 103 infants aged 9–16 months (M = 12.39, SD = 1.97; 68% male) and their primary caregivers recruited into a larger study (Whitehouse et al., 2019). Referral to the study was by community healthcare providers, on the basis of infants showing ≥3 of 5 behavioral markers autism on the Social Attention and Communication Surveillance-Revised (SACS-R) tool (i.e., atypical/absent pointing, waving, imitation, eye contact, response to name; Barbaro & Dissanayake, 2013). The SACS-R is a revised version of the SACS [Barbaro & Dissanayake, 2010] designed as an autism surveillance tool for implementation during routine well-child checks. The SACS-R has an estimated positive predictive value of 72% when used with 12 month olds for subsequent autism diagnosis [Barbaro, Dissanayake, & Sadka, 2018]. Other inclusion criteria were child chronological age between 9- and 14-months 31 days (corrected for prematurity) and caregivers having sufficient English to understand study requirements and participate fully. Exclusion criteria were diagnosed comorbidity known to affect infant neurological and developmental abilities (including gestation < 32 weeks) or family intention to relocate within 2 years of enrolment. Caregivers were on average 34.28 years old (SD = 5.05) and predominantly biological mothers (3% biological fathers, 1% guardians). Most infants (n = 80; 78%) had no family history of autism and, among others, an autism diagnosis was reported for an older sibling/s (n = 20) or cousin (n = 3).

Procedure and measures

This study draws on a subset of the data collected at the baseline assessment for the larger study, for which ethical approval was granted by institutional review boards. Baseline assessments occurred an average of 2.53 weeks (SD = 1.50) after eligibility screening. Caregivers provided informed consent and completed a series of questionnaires.

A short form of the Depression Anxiety Stress Scales [DASS-21; Lovibond & Lovibond, 1995] was used to measure caregiver self-reported psychological distress. DASS-21 items (21) are rated on a 4-point Likert scale, ranging from 0 (*Did not apply to me at all*) to 3 (*Applied to me very much or most of the time*). Responses across three subscales (depression, anxiety, stress) were summed to yield an overall score (range 0–63).

The Infant-Toddler Social and Emotional Assessment [ITSEA; Carter & Briggs-Gowan, 2006] was used to assess infant internalizing and externalizing symptoms. ITSEA items (170) are rated by caregivers on a 3-point Likert scale ranging from 0 (*Not true/rarely*) to 3 (*Very true/often*), and domain subscale mean scores are averaged to form composite internalizing (consisting of depression/withdrawal, general anxiety, separation distress, and inhibition to novelty) and externalizing (consisting of activity/impulsivity, aggression/defiance, peer aggression) scores (range 0–2).

The Infant Behavior Questionnaire-Revised [IBQ-R; Gartstein & Rothbart, 2003] was used to measure child temperament. IBQ-R items (191) are rated by caregivers on a 7-point Likert scale for frequency, ranging from 1 (*Never*) to 7 (*Always*), and fine-grained subscales are averaged to form three higher-order dimension scores: surgency/extraversion (consisting of activity level, smiling and laughter, high intensity pleasure, vocal reactivity, approach, perceptual sensitivity), negative affectivity (consisting of distress to limitations, fear, sadness, falling reactivity), and orienting/regulation (consisting of duration of orienting, low intensity pleasure, cuddliness, and soothability).

Overlapping item content between the ITSEA and IBQ-R was removed to reduce measurement confounding, including the entire inhibition to novelty subscale which measures a temperament-based construct (for more details, see [reference withheld for blinded review]).

Autism features were measured by the Autism Observation Scale for Infants [AOSI; Bryson, Zwaigenbaum, McDermott, Rombough, & Brian, 2008], a direct observational measure that includes a standard set of semi-structured activities. Examiner ratings of (16) target social-communicative, sensory-motor, attentional, and play behaviors, ranging from 0 to 2 or 3, are summed to create a total score (maximum 38). Higher scores on all metrics denoted greater expression of the measured construct(s), including more autism-related behavior.

Results

Descriptive statistics and bivariate correlations are presented in Table 1. Child age and sex were considered as potential covariates but were mostly unrelated to other variables (see Table 1).[1] There were significant intercorrelations among caregiver psychological distress, child social-emotional difficulties (internalizing, externalizing), and negative affectivity in the expected direction. Orienting/regulation and child internalizing and externalizing were negatively correlated, although neither orienting/regulation nor surgency/extraversion were related to parent depression.

Analyses were performed using the PROCESS macro for SPSS [Hayes, 2018]. Internalizing and externalizing symptoms

[1]Child age was significantly correlated with externalizing, r =0.26, P < 0.05. Inclusion of age as a covariate in the mediation model with externalizing as the dependent variable and AOSI Total score as a moderator did not substantively change the results, F (2, 88) = 6.35, R^2 =0.36, P < 0.01. The mediation effect remained significant (B = 0.004, 95% bootstrap CI = 0.001–0.008), and the direct effect of caregiver psychological distress remained nonsignificant (B = 0.005, 95% bootstrap CI = −0.002 to 0.011). Child age had a significant direct effect on child externalizing, B = 0.03, t (85) = 2.54, P < 0.05.

Table 1. Descriptive Statistics and Bivariate Correlations Between Study Variables (N = 103)

	n data	α	n (%) or M (SD)	Range	1	2	3	4	5	6
Child sex (male)	103	-	70 (68%)	-	0.05 [−0.17, 0.26]	0.02 [−0.19, 0.24]	−0.01 [−0.22, 0.20]	−0.03 [−0.24, 0.18]	−0.01 [−0.21, 0.20]	0.02 [−0.19, 0.24]
Child age at baseline (months)	103	-	12.39 (1.97)	9.10–16.30	−0.10 [−0.32, 0.09]	0.06 [−0.15, 0.25]	0.26* [0.08, 0.42]	0.07 [−0.13, 0.27]	0.08 [−0.14, 0.29]	0.04 [−0.18, 0.25]
SACS-R	103			3–5						
3 markers			32 (31%)							
4 markers			34 (33%)							
5 markers		-	37 (36%)							
1. DASS-21 Total	95	0.86	9.41 (7.84)	0–39	-					
2. ITSEA internalizing	91	0.62[a]	0.38 (0.23)	0.00–0.99	0.37** [0.15, 0.56]	-				
3. ITSEA externalizing	88	0.82	0.32 (0.25)	0.00–1.21	0.24* [−0.04, 0.48]	0.23* [0.04, 0.43]	-			
4. IBQ-R surgency/ extraversion	96	0.77	4.40 (0.73)	1.88–5.22	−0.05 [−0.29, 0.16]	−0.11 [−0.33, 0.11]	0.07 [−0.19, 0.31]	-		
5. IBQ-R negative affectivity	96	0.78	3.28 (0.76)	1.88–5.22	0.34** [0.12, 0.53]	0.58** [0.41, 0.72]	0.45** [0.28, 0.60]	0.09 [−0.11, 0.29]	-	
6. IBQ-R orienting/ regulation	96	0.63	4.43 (0.62)	2.95–6.41	−0.11 [−0.30, 0.07]	−0.21* [−0.40, −0.01]	−0.23* [−0.45, 0.01]	0.53** [0.37, 0.67]	−0.34** [−0.51, −0.15]	-
7. AOSI Total	103	0.66	8.90 (4.31)	1–28	0.07 [−0.21, 0.33]	0.29** [0.11, 0.45]	−0.07 [−0.27, 0.13]	−0.36** [−0.54, −0.15]	0.03 [−0.19, 0.22]	−0.05 [−0.24, 0.14]

Note. Correlation coefficients were bootstrapped (5,000 resamples) to account for distributional non-normality.

AOSI, Autism Observation Scale for Infants; DASS-21, Depression Anxiety Stress Scales-21; IBQ-R, Infant Behavior Questionnaire-Revised; ITSEA, Infant-Toddler Social and Emotional Assessment; SACS-R, Social Attention and Communication Surveillance-Revised.

[a]Removal of the item with the lowest corrected item-total correlation increased the value of Cronbach's α from 0.56 to 0.62 for the ITSEA Internalizing domain.

*$P < 0.05$.

**$P < 0.01$.

were examined in separate models as the dependent variable, with caregiver psychological distress as the independent variable and child negative affectivity as the mediator. List-wise deletion of missing values resulted in a sample size of 91 for the internalizing model 88 for the externalizing model. Since significant relations between the proposed mediator(s) and both the dependent and independent variable is a necessary precondition for testing mediation [Hayes, 2018], surgency/extraversion and orienting/regulation were not included in the models.

The full model accounted for a significant proportion of the variance in both infant internalizing symptoms, $F(2, 88) = 25.30$, $R^2 = 0.37$, $P < 0.001$, and externalizing symptoms, $F(2, 85) = 11.11$, $R^2 = 0.21$, $P < 0.001$. There was a significant positive indirect effect ($a \times b$) of caregiver psychological distress on infant internalizing ($B = 0.005$, 95% bootstrap CI = 0.002–0.008) and externalizing ($B = 0.004$, 95% bootstrap CI = 0.001–0.008) through infant negative affectivity. The direct effect (c') of caregiver psychological distress was significant for infant internalizing ($B = 0.005$, 95% bootstrap CI = 0.002–0.011), and nonsignificant for externalizing ($B = 0.003$, 95% bootstrap CI = –0.003 to 0.010).

Next, AOSI Total score was included in the model as a moderator of the association between negative affectivity and social-emotional difficulties (path b) in order to test the equivalence of temperament pathways across the

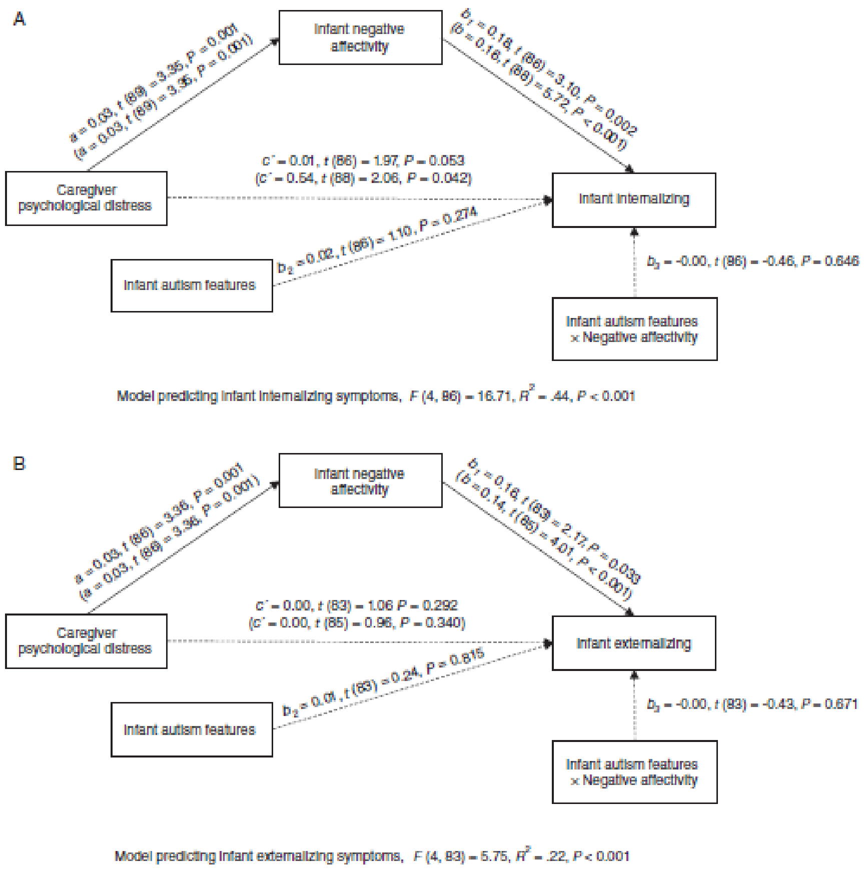

Figure 1. Moderated mediation models investigating infant negative affectivity as a mediator of the relation between caregiver psychological distress and infant internalizing (a; $n = 91$) and externalizing (b; $n = 88$), including infant autism features as a moderator. Results from the initial mediation model (without the moderator) are also presented within brackets. Regression coefficients are unstandardized, and pathways in bold are significant ($P < 0.05$).

spectrum of autism expression (i.e., AOSI Total scores ranging from 1, signifying little-to-no autism features, to ≥9 predictive of clinical diagnosis; Zwaigenbaum et al., 2005). The mediation effect remained statistically significant in both the internalizing (B = 0.01, 95% bootstrap CI = 0.002–0.008) and externalizing models (B = 0.004, 95% bootstrap CI = 0.001–0.009) when AOSI Total score was added as a moderator. However, the direct effect of caregiver psychological distress on infant internalizing was no longer significant. AOSI Total score did not interact with negative affectivity in either model, and there was no direct effect; thus, there was no evidence that the mediating effects of infant negative affectivity—on the relation between caregiver psychological distress and infant social-emotional difficulties—were contingent on infants' autism expression.

Results from these models are depicted in Figure 1.

Discussion

This study explored whether the relation of caregiver psychological distress to child social-emotional difficulties through temperament identified previously among neurotypical children extends to young infants with early signs of autism. Consistent with Allen et al. [2018], infant negative affectivity was found to mediate the positive association between caregiver psychological distress and concurrent infant internalizing and externalizing symptoms. There was no moderating effect of AOSI score on these indirect effects; hence, the pathway from caregiver psychological distress to infant negative affectivity to infant social-emotional difficulties may be shared across young children irrespective of whether they have autism features.

Infant orienting/regulation was negatively correlated with internalizing and externalizing symptoms, though unrelated to caregiver psychological distress. This finding contrasts with prior prospective [Hoffman, Crnic, & Baker, 2006] and mediational analyses [Allen et al., 2018; Choe et al., 2014; Suveg et al., 2011] conducted in later childhood, which have shown that caregiver psychological distress predicts children's subsequent emotional dysregulation and, in turn, social-emotional difficulties. The negative impact of caregiver psychological distress on children's self-regulation might thus be dependent on child developmental stage; such that an effect may be apparent for later-developing top-down (deliberate) aspects of self-regulation (e.g., attention switching) but not early emerging bottom-up (automatic) processes (e.g., attention capture).

Surgency/extraversion was unrelated to caregiver psychological distress and infant social-emotional difficulties in our sample. This is not surprising given previous inconsistencies in the literature linking children's positive affect/sociability to the family environment and developmental outcomes [for reviews, see Putnam, 2012; Davis & Suveg, 2014]. Indeed, Allen et al. [2018] found that positive affect/sociability during childhood did not mediate relations between maternal depression and offspring social-emotional difficulties. Nonetheless, a more nuanced examination of the various facets of positive affect/sociability may help resolve inconsistencies across studies relating these traits to environmental factors and child outcomes.

Level of infant autism features was positively correlated with internalizing symptoms, but unrelated to externalizing symptoms. The latter nonsignificant association might be due to the young age and limited behavioral repertoire of our sample, as a positive correlation between autism and externalizing symptoms been reported among autistic preschoolers [Tureck, Matson, Cervantes, & Turygin, 2015]. Furthermore, level of autism features was negatively correlated with temperamental surgency but unrelated to orienting/regulation and negative affectivity; consequently, the nonsignificant interaction of AOSI Total and negative affectivity in the mediation models was not all that surprising.

The results from this study should be interpreted in light of some methodological limitations. First, the cross-sectional design of this study precludes causal inference. We formulated our hypotheses under the assumption that effects flow from caregiver-to-child, although the reverse might also be true. Indeed, Choe et al. [2014] found that toddlers' oppositionality predicted subsequent difficulties with self-regulation and more depressive symptoms for mothers. Studies that have tested bidirectional relations between child temperament and caregiver psychological distress, however, provide more consistent evidence of caregiver evocative effects than vice versa in early childhood [Hanington et al., 2010; Pesonen et al., 2008]. The presence and magnitude of caregiver-to-child and child-to-caregiver effects should be elucidated in future studies through use of repeated measures multivariate modeling (e.g., structural equation modeling); specifically, evaluating whether initial child temperament and/or caregiver psychological distress predict subsequent levels of the other construct over and above cross-sectional between-construct associations and within-construct stability over time. Controlling for potential shared genetic influences on child temperament and caregiver psychological distress [e.g., through a genetically informed research design such as illustrated by Micalizzi, Wang, & Saudino, 2017] would further the robustness of this approach.

Next, the use of a single informant and method of assessment may have inflated observed relations between measures. It seems unlikely that the current results were solely due to method variance, however, given associations between caregiver and child outcomes have been observed across different methods of assessment [Goodman et al., 2011]. Nonetheless, our results should be interpreted with caution until they are replicated using multiple informants and measurement methods.

Finally, it remains unknown what proportion of infants in our sample will go on to receive an autism diagnosis and/or other clinical diagnoses. The equivalence of the indirect effect of caregiver psychological distress on child social-emotional difficulties (through child temperament) across categorical diagnostic groups should be addressed in future work.

In conclusion, this study is one of few—and, notably, the first in the context of autism—to have explored temperament as a potential mechanism underlying the concurrent relation between caregiver psychological distress and offspring social-emotional difficulties. While preliminary and cross-sectional, these findings suggest the pathway from caregiver psychological distress to child negative affectivity to child internalizing and externalizing identified in neurotypical children might also extend to young infants with early signs of autism. It is hoped that this work will provide impetus for future replications using multiple methods of assessment and longitudinal designs, as the establishment of causal relations would permit clinical translation of these findings. A tentative implication is that child and caregiver affective symptoms should be treated concurrently to promote well-being in the entire family system. Should a caregiver-to-child flow of effects indeed be borne out in longitudinal analyses, the provision of mental health support to caregivers of children with autism symptoms could reduce strain on the caregiver-child relationship and improve children's affective tolerance to, in turn, promote positive social-emotional functioning.

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