Efficacy of acceptance and commitment therapy (ACT) in schizophrenia spectrum and other psychotic disorders: Protocol for a systematic review and meta-analysis

Richard Gray, Ph.D[1, 2, 3*] R.Gray@latrobe.edu.au
Stav Amichai Hillel, MBBS[1] S.Hillel@latrobe.edu.au
Amal Al Ghareeb, Ph.D[1] A.ZuhairAlGhareeb@latrobe.edu.au
Ellie Brown, DCounsPsy[4, 5] Ellie.Brown@unimelb.edu.au

1. The School of Nursing and Midwifery, La Trobe University, Melbourne, Australia
2. Department of Rural Health, The University of South Australia, Adelaide, Australia
3. The University of Essex, Colchester, Essex, United Kingdom
4. Phoenix Australia, The University of Melbourne, Melbourne, Australia
5. IMPACT SRC, Deakin University, Geelong, Australia

*Corresponding author

Abstract

Acceptance and commitment therapy (ACT) has been reported to be efficacious in a number of psychiatric disorders. However, it remains uncertain if ACT is effective in treating psychoses. This protocol describes the methodology for a systematic reviews and meta-analysis on the efficacy of ACT in the treatment of schizophrenia spectrum and other psychotic disorders. The review will be guided by the standards set by the Cochrane Collaboration. We will search on CENTRAL, Embase, MEDLINE, and PsychINFO for randomised controlled trials whose arms are ACT and any comparator, as well as ClinicalTrials.gov, ANZCTR, and ISRCTN for unpublished and ongoing trials. Primary outcome will be any standard measure of psychotic pathology. The meta-analysis will summarise short-term and long-term effects, and different control conditions with or without treatment as usual or comparative to other interventions. If heterogeneity is detected (via χ^2, I^2), we will adopt the random effects model for computation.

Keywords

Acceptance and commitment therapy, cognitive behavioural therapy, psychotherapy, psychosis, schizophrenia

1. Background

There is increasing interest in acceptance and commitment therapy (ACT) in the treatment of psychiatric disorders[1]. Philosophically couched in the cognitive behavioural paradigm, ACT is an empirically-based psychotherapy that aims to effect 'psychological flexibility' through mindfulness, acceptance, commitment, and behavior-changing techniques[2-4]. Psychological flexibility is defined as "the ability to change or to persist with functional behavioral classes when doing so serves valued ends"[5] (p. 15). The therapy claims a modest empirical basis and is reported to have been employed successfully in the treatment of affective disorders, eating disorders, and personality disorders[6]. As for disorders on the schizophrenia-psychosis continuum, however, the evidence is seemingly less robust[7].

The psychoses are perhaps the most challenging phenomena with which psychiatry must tackle; not only does prognosis vary widely from complete recovery to disability[8], the best treatments commonly deliver poor outcomes[9]. Economic and social collolaries are observed too: according to the World Health Organization, 23 million people are affected globally[10], costing the US, by one estimate, approximately $62.7 billion in 2002[11]. At least one factor in this large figure is the early onset of the disease interfering with the most productive years of life[9]. The disorders also continue to bear the stigma that typically is associated with mental illnesses[12]. And according to Catts and McGorry[9], it is advances in treatment that is toward stigma amelioration. ACT is a possible new approach in the treatment of schizophrenia spectrum and other psychotic disorders that must be better understood.

2. Rationale

Systematic reviews and meta-analyses have demonstrated the efficacy of ACT, yet there is some controversy concerning the quality of the therapy's evidence base. Atkins et al., for one,

point out the differing results of two meta-analyses on the progress of the evidence[13], and others have commented about the possibility of missing trials[14-17]. This systematic review synthesises randomised controlled trials of ACT in the treatment of schizophrenia spectrum and other psychotic disorders. This will contribute to the therapy's empirical claims; according to Division 12 of the American Psychological Association, the efficacy of ACT in psychosis enjoys modest research support[7]. It will also report on ACT's effectiveness in the schizophrenia-psychosis spectrum. Insofar as we understand, no systematic review and meta-analysis of ACT in the treatment of schizophrenic/psychotic disorders is available. PROSPERO was searched on 21.05.18 and did not identify any reviews in preparation.

3. Review question

This review seeks to answer the following question: Is acceptance and commitment therapy effective in the treatment of schizophrenia spectrum and other psychotic disorders? 'Schizophrenia spectrum and other psychotic disorders' herein makes reference to the non-affective type. Following recommendations by Schardt et al.[18], our question can be represented schematically as follows in table 1:

P	Schizophrenia spectrum/psychotic disorders
I	ACT
C	Ø
O	Symptom alleviation
R	Randomised controlled trial

Table 1 Review question compartmentalised according to the PICO(R) mnemonic

4. Methods

A systematic review and meta-analysis of randomised controlled trials of ACT in the treatment of patients diagnosed with any schizophrenia spectrum or other psychotic disorder. The review will follow the Preferred Reporting Items for Systematic Reviews and Meta-Analyses Protocols (PRISMA) guidelines[19]. See https://figshare.com/s/81071311ad1421711320 for PRISMA-Protocol checklist. The *Cochrane Handbook for Systematic Reviews of Interventions*[20] will also inform this review. This review was registered on PROSPERO on 21/05/18 by RG (acknowledgement of receipt: 97200). PROSPERO registration number was not available at the time of publication submission.

5. Data sources

5.1 Databases

The following databases will be searched for eligible studies according to a predetermined search strategy (below): Cochrane Central Register of Controlled Trials (CENTRAL), Education Resources Information Center (ERIC), Excerpta Medica database (Embase) via Ovid, MEDLINE (including Ahead of Print, In-Process & Other Non-Indexed Citations) via Ovid, and PsycINFO via Ovid.

5.2 Clinical trial websites

We will supplement these sources by searching on ClinicalTrials.gov, Australian New Zealand Clinical Trials Registry (ANZCTR), and Current Controlled Trials (ISRCTN) for unpublished and ongoing trials. This is but one attempt to attenuate possible publication bias. We searched *psychosis* and *schizophrenia* for condition, and *acceptance and commitment therapy* and *ACT* for intervention.

6. Eligibility criteria

Studies retrieved from databases and clinical trial websites must exhaust the following eligibility criteria to be included in the systematic review and meta-analysis.

6.1 Types of participants

As study is eligible if its sample:

- is 18+ of any sex;
- has a diagnosis of a schizophrenia spectrum or other psychotic disorder (using any standard diagnostic criteria; e.g.: DSM-V, Feighner criteria[21], ICD-10) at any stage of illness.

As study is ineligible if its sample:

- has a schizophrenia spectrum or other psychotic disorder of the affective type;
- has a developmental impairment, intellectual disability, or organic psychosis;
- a primary drug or alcohol addiction;
- any clinically significant medical diseases.

6.2 Types of studies

As study is eligible if it:

- is a randomised controlled trial whose arms (at least two) are ACT delivered via any medium (e.g. individual, group, telephone, online) and any comparator(s);
- provides sufficient statistics to be included in the meta-analysis;
- is in English;
- is published from 1999 to search date.

1999 is not an arbitrary date. 1999 is the date in which Hayes et al. first described ACT[22].

As study is ineligible if:

- less than half of its sample has a primary diagnosis of a psychotic disorder;

- it reports extensions to previously published trials.

7. Search

The search strategy will include the following keywords (italicised) and subject headings (emboldened) on the databases: *acceptance commitment therapy*, *ACT*, *clinical behaviour analysis*, **Cognitive Therapy**/ *psychosis*, *psychotic disorder*, *schizophrenia*, **Psychotic Disorders**/, **Schizophrenia**/. Following recommendations of Wolters Kluwer Health[23], keywords will include special characters in order to capture any spelling variation. Keywords will be associated with subject headings in a highly-sensitive syntax.

7.1 Search strategy

The complete search strategy is as follows (keywords are italicised; subject headings are emboldened; Boolean operators are capitalised):

1	*'acceptance commitment therapy'* OR *act* OR *'clinic* behavi?r analy*'*.mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms]
2	*psychos?s* OR *'psychotic disorder*'* OR *schizophrenia*.mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms]
3	exp **Cognitive Therapy**/
4	exp **Psychotic Disorders**/ or exp **Schizophrenia**/
5	1 OR 3

6 2 OR 4

7 5 AND 6

8 limit 7 to randomized controlled trial

Subject heading **Cognitive Therapy**/ is **Acceptance and Commitment Therapy**/ in PsycINFO. ERIC does not allow the use of subject headings. Accordingly, the search strategy for ERIC is:

(*'acceptance commitment therapy'* OR *act* OR *'clinic* behavi?r analy*'*) AND (*psychos?s* OR *'psychotic disorder*'* OR *schizophrenia*)

9. Outcomes

9.1 Primary outcome, timing and effect measures

The review's primary outcome is any standard measure of psychotic pathology that may include, but is not limited to, the Positive and Negative Syndrome Scale (PANSS), The Brief Psychiatric Rating Scale (BPRS), The Psychotic Symptom Rating Scales (PSYRATS). Measurement is from baseline to end of treatment or the nearest available follow-up.

9.2 Secondary outcome, timing and effect measures

The review's secondary outcome is any validated measure of personal recovery such as The Recovery Style Questionnaire or Harms (adverse and serious adverse events). Measurement is from baseline to end of treatment or the nearest available follow-up.

10. Data

10.1 Data retrieval

The data retrieved by the database and clinical trial websites searchers will be uploaded to the referencing manager EndNote (https://endnote.com/). EndNote will remove duplicates from the review's sample. We will make the remaining data publically available on Figrshare (https://figshare.com/), an online repository for academic outputs.

10.2 Data screening

RG and SAH will independently screen titles and abstracts in Covidence (https://www.covidence.org/). Covidence is a screening software tool developed for systematic reviews. Any disagreements will be resolved by AAG/EB. RG and SAH will independently screen full texts. Any disagreements will be resolved by AAG/EB. A flow diagram following the PRISMA statement will document the data management.

10.3 Data extraction

A standardised form will be used to extract data for evidence synthesis. Data will be extracted by RG and SAH. Risk of bias will be determined using the Cochrane (performance, detection, attrition, reporting, other) risk of bias tool. The extracted data will be made publically available on Figshare. The following data items will be extracted:

- study citation
- disorder of interest
- setting
- dose of intervention
- delivery medium of intervention
- primary endpoint
- number of participants allocated to intervention and control groups

- number of analysed participants allocated to intervention and control groups
- calculation of sample size
- pre- and post-intervention/control summary statistics
- intervention and control harm
- quality of blinding
- quality of randomization
- bias
- analysis type
- registration status
- country of origin

11. Synthesis

11.1 Meta-analysis

We will undertake meta-analyses for short-term (outcome measures taken closest to 4 weeks after the intervention) and long-term effects (closest to 12 months after the intervention), and different control conditions with or without treatment as usual or comparative to other interventions. Meta-analysis will be conducted if at least three RCTs for a specific comparison are available.

11.2 Heterogeneity and modeling

Dependent on summary statistic type, Pearson's χ^2 will measure heterogeneity due to chance. A *p*-value (0.0000) less than the significance level (0.05) will motivate a random effects model. Higgins's I^2 will measure heterogeneity due to variance in true effect sizes. Conservatively, less that 25% will motivate a random effects model. Following the *Cochrane Handbook of*

Systematic Reviews of Interventions[20], we will test for funnel plot asymmetry if minimally ten studies are included in the meta-analysis.

11.3 Summary statistic and weights

The weighted average of the most common summary statistic across the eligible studies will be reported. Whilst methods obtain that allow differing summary statistics to be pooled together [24-26], it is unclear how to establish the contextual environments that would facilitate re-expression. Any uncommon summary statistic, then, will receive its own forest plot (provided at least three values are available) or be ignored by the meta-analysis. In order to account for heterogeneity (determined by χ^2 and I^2), we will assign the following weight to each study: $w_i^* = \frac{1}{v_i + v^*}$ (where v_i is within-study variance and v^* between study variance); alternatively, $w_i = \frac{1}{v_i}$.

12. Conclusion

ACT is employed in the treatment of a number of psychiatric disorders. Whilst treatment outcomes for affective, eating, and personality disorders are said to be positive, there is more uncertainty of its efficacy in treating schizophrenia spectrum and other psychotic disorders. This systematic review aims to measure the efficaciousness of ACT in psychoses and add to the therapy's evidence base.

Author contributions

RG, SAH, AAG, and EG equally conceived and designed the study. RG wrote the initial draft of this paper. SAH, AAG, and EG edited and revised the paper.

Approval

All authors approve of the submitted version of the manuscript.

Conflicts of Interest

Prof Richard Gray is on the editorial board of Journal of Psychiatric and Mental Health Nursing since 2014. SAH and EG declare no conflicts of interest.

References

1. Webster, M. Introduction to acceptance and commitment therapy. *Adv Psychiatr Treat* **2018**, *17*, 309-316.
2. Hayes, S.C.; Strosahl, K.; Wilson, K. G. *Acceptance and commitment therapy: An experiential approach to behavior change*. 2003, The Guilford Press: New York, United States of America, 2003; ISBN 9781572309555.
3. Hayes, S.C. Acceptance and commitment therapy, relational frame theory, and the third wave of behavioral and cognitive therapies. *Behavior Therapy* **2004**, *35*, 639-665.
4. Hayes, S.C.; Luoma, J.B.; Bond, F.W; Masuda, A.; Lillis, J. Acceptance and commitment therapy: Model, processes and outcomes. *Behav Res Ther* **2006**, *44*, 1-25.
5. Hayes, S. C. Acceptance and commitment therapy and the new behavior therapies: Mindfulness, acceptance, and relationship. In *Mindfulness and acceptance. Expanding the cognitive-behavioral tradition*. Hayes, S. C., Follette, V. M., Linehan, M. M., Eds.; The Guilford Press: New York, United States of America, 2004, pp. 1-29; ISBN 9781609189891.
6. Twohig, M.P. Acceptance and commitment therapy: Introduction. *Cogn Behav Pract* **2012**, *19*, 499-507.

7. Acceptance and commitment therapy for psychosis. Available online: https://www.div12.org/treatment/acceptance-and-commitment-therapy-for-psychosis/ (accessed on 31 May 2018).

8. Stroup, T.S.; Lawrence, R.E.; Abbas, A.I.; Miller, B.R.; Perkins, D.O.; Lieberman, J.A. Schizophrenia spectrum and other psychotic disorders. In *The American psychiatric publishing textbook of psychiatry*, 6th ed.; Hales, R.E., Yudofsky, S.C., Weiss Roberts, L., Eds.; American Psychiatric Publishing: Washington, DC, 2014, pp. 273-310; ISBN 9781585624447.

9. Charlson, F.J.; Ferrari, A.J.; Santomauro, D.F.; Diminic, S.; Stockings, E.; Scott, J.G.; McGrath, J.J.; Whiteford, H. A. Global epidemiology and burden of schizophrenia: Findings from the global burden of disease study 2016. *Schizophrenia Bulletin*, **2018**, *sby058*, https://doi.org/10.1093/schbul/sby058. Available online: https://academic.oup.com/schizophreniabulletin/advance-article/doi/10.1093/schbul/sby058/4995547 (accessed 31 May 2018).

10. Schizophrenia. Available online: http://www.who.int/news-room/fact-sheets/detail/schizophrenia (accessed on 31 May 2018).

11. Wu, E.Q.; Birnbaum, H.G.; Shi, L.; Kessler, R.C.; Moulis, M.; Aggarwal, J. The economic burden of schizophrenia in the United States in 2002. *J Clin Psychiatry*, **2005**, *66*, 1122-9.

12. Catts, S.; Weickert, C. S. Schizophrenia and related psychotic disorders. In *Foundations of Clinical Psychiatry*, 4th ed.. Bloch, S., Green, S.A., Jance, A., Mitchell, P.B., Robertson, M., Eds.; Melbourne University Publishing: Melbourne, Australia, 2017; ISBN 0522870953.

13. Atkins, P.W.B.; Ciarrochi, J.; Gaudiano, B.A.; Bricker, J.B.; Donald, J.; Rovner, G.; Smout, M.; Livheim, F.; Lundgren, T.; Hayes, S.C. Departing from the essential

features of a high quality systematic review of psychotherapy: A response to Öst (2014) and recommendations for improvement. *Behav Res Ther*, **2017**, *97*, 259-272.

14. Editor's Note. *Behav Res Ther*, **2018**, *102*, 67.
15. Öst, L.G. The efficacy of acceptance and commitment therapy: An updated systematic review and meta-analysis. *Behav Res Ther*, **2014**, *61*, 105-21.
16. Öst, L.G., Rebuttal of Atkins et al. (2017) critique of the Öst (2014) meta-analysis of ACT. *Behav Res Ther*, **2017**, *97*, 273-281.
17. Hacker, T.; Stone, P.; MacBeth, A. Acceptance and commitment therapy - Do we know enough? Cumulative and sequential meta-analyses of randomized controlled trials. *J Affect Disord*, **2016**, *190*, 551-565.
18. Schardt, C.; Adams, M.B; Owens, T.; Keitz, S.; Fontelo, P. Utilization of the PICO framework to improve searching PubMed for clinical questions. *BMC Medical Informa and Decis Mak*, **2007**, *7*, doi:10.1186/1472-6947-7-16. Available online: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC1904193/ (accessed 31 May 2018).
19. Moher, D.; Liberati, A.; Tetzlaff, J.; Altman, D.G. Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. *PLoS Med*, **2009**, doi.org/10.1371/journal.pmed.1000097. Available online: http://journals.plos.org/plosmedicine/article?id=10.1371/journal.pmed.1000097 (accessed 31 May 2018).
20. Higgins J.P.T.; Green, S.; Eds. *Cochrane Handbook for Systematic Reviews of Interventions Version*, 5.1.0 [updated March 2011]. The Cochrane Collaboration, 2011. Available online: http://training.cochrane.org/handbook (accessed 31 May 2018).
21. Feighner, J.P.; Robins, E.; Guze, S.B.; Woodruff, R.A. Jr.; Winokur, G.; Munoz, R. Diagnostic criteria for use in psychiatric research. *Arch Gen Psychiatry*, **1972**, *26*, 57-63.

22. Hayes, S. C.; Strosahl, K. D.; Wilson, K. G., Eds. *Acceptance and commitment therapy: An experiential approach to behavior change*. The Guilford Press: New York, United States of America, 1999; ISBN 978-1572304819

23. MEDLINE ® 2018 Database guide. Available online: http://ospguides.ovid.com/OSPguides/medline.htm#advanced (accessed 31 May 2018).

24. Chinn, S. A simple method for converting an odds ratio to effect size for use in meta-analysis. *Stat Med*, **2000**, *19*, 3127-31.

25. Ofuya, M.; Sauzet, O.; Peacock, J.L. Dichotomisation of a continuous outcome and effect on meta-analyses: illustration of the distributional approach using the outcome birthweight. *Sys Rev*, **2014**, *3*, 63-63.

26. Whitehead, A.; Bailey A.J.; Elbourne, D. Combining summaries of binary outcomes with those of continuous outcomes in a meta-analysis. *J Biopharm Stat*, **1999**, *9*, 1-16.