EPISODIC AND PROCEDURAL MEMORY CONSOLIDATION DURING SLEEP: CAN MEMORY IMPAIRMENT DURING PREGNANCY BE ATTRIBUTED TO SLEEP DISTURBANCE?

Submitted by Danielle L. Wilson
BSc (Psychology/Psychophysiology), BA (Hons)

A thesis submitted in total fulfilment
of the requirements of the degree of
Master of Science

School of Psychological Science
Faculty of Science, Technology and Engineering

La Trobe University
Bundoora, Victoria, 3086
Australia

May 2011

TABLE OF CONTENTS

LIST OF TABLES

Chapter 2

Chapter 3

Chapter 4

Chapter 5

LIST OF FIGURES

Chapter 2

Chapter 3

Chapter 4

Chapter 5

LIST OF ABBREVIATIONS

AHI/hr	Apnoea/Hypopnoea Index (per hour)
BMI	Body mass index
DASS21	Depression Anxiety Stress Scale – Short Version
EEG	Electroencephalography
EMG	Electromyogram
EOG	Electrooculogram
MAP Index	Multivariate Apnea Risk Index
NREM	Non rapid eye movement
ODI	Oxygen desaturation index (per hour)
OSA	Obstructive sleep apnoea
PLMS	Periodic limb movements of sleep
PSG	Polysomnography
RAVLT	Rey Auditory-Verbal Learning Test
REM	Rapid eye movement
RLS	Restless legs syndrome
SDB	Sleep-disordered breathing
SWS	Slow wave sleep
T1	First trimester of pregnancy
T3	Third trimester of pregnancy
TOMM	Test of Memory Malingering
TOVA	Test of Variables of Attention
TCT	Total cycle time
TST	Total sleep time
UARS	Upper airway resistance syndrome
WASI	Wechsler Abbreviated Scale of Intelligence
WASO	Wake after sleep onset
WMS-III	Wechsler Memory Scale – Third Edition

PUBLICATIONS AND PRESENTATIONS ARISING FROM THIS THESIS

Journal publications
(Published, submitted, and in-preparation)

Wilson, D. L., Barnes, M., Ellett, L., Permezel, M., Jackson, M., & Crowe, S. F. (2011). Decreased sleep efficiency, increased wake after sleep onset and increased cortical arousals in late pregnancy. *Australian and New Zealand Journal of Obstetrics and Gynaecology, 51*, 38-46. DOI: 10.1111/j.1479-828X.2010.01252.x

Wilson, D. L., Barnes, M., Ellett, L., Permezel, M., Jackson, M., & Crowe, S. F. Compromised verbal episodic memory with intact visual and procedural memory during pregnancy. *Journal of Clinical and Experimental Neuropsychology.* First published online 14 March 2011. DOI: 10.1080/13803395.2010.550604

Wilson, D. L., Barnes, M., Ellett, L., Permezel, M., Jackson, M., & Crowe, S. F. Sleep-disordered breathing and periodic limb movements during sleep in normal pregnancy. Manuscript in preparation to be submitted for publication to *Journal of Sleep Research*.

Wilson, D. L., Barnes, M., Ellett, L., Permezel, M., Jackson, M., & Crowe, S. F. Reduced verbal memory retention is unrelated to sleep disturbances during pregnancy. Manuscript submitted for publication to *Australian Psychologist* in April 2011.

Published abstracts

Wilson, D., Crowe, S., Jackson, M., Pierce, R., & Barnes, M. (2009). Sleep and memory deficits during pregnancy: Are they related? *Sleep and Biological Rhythms, 7*(Supp. 1), A27.

Wilson, D., Ellett, L., Barnes, M., Crowe, S., & Permezel, M. (2009). Does pregnancy affect memory and attention? A cross-sectional study. *Australian and New Zealand Journal of Obstetrics and Gynaecology, 49*(5), 574.

Wilson, D., Ellett, L., Crowe, S., Jackson, M., & Barnes, M. (2008). Sleep-disordered breathing in healthy pregnancy: Prevalence and prediction. *Sleep and Biological Rhythms, 6*(Supp. 1), A39-A40.

Presentations at scientific meetings

Australasian Sleep Association Annual Scientific Meeting, Melbourne, Australia, 8-10 October 2009. Oral presentation –
Wilson, D., Crowe, S., Jackson, M., Pierce, R., & Barnes M. Sleep and memory deficits during pregnancy: Are they related?

Australasian Sleep Association Annual Scientific Meeting, Adelaide, Australia, 2-4 October 2008. Poster with oral presentation –
Wilson, D., Ellett, L., Crowe, S., Jackson, M., & Barnes, M. Sleep architecture and sleep-disordered breathing in healthy pregnancy. Awarded 3rd prize for poster presentations.

FORMAT OF THE THESIS

This thesis is submitted in the alternative format approved by La Trobe University (see Appendix A), where it is permissible for candidates to submit a thesis in the form of a series of articles along a central theme that may or may not be already published.

This thesis is presented as a series of six chapters. Chapter 1 is a comprehensive literature review that acts as the introduction in this thesis. Chapters 2, 3, 4, and 5 each correspond to a manuscript that has now been published in, submitted to, or are to be submitted to a peer-review journal for publication. Chapter 6 follows on from the series of four articles as a general discussion that summarises and integrates the main points raised in each study. Preceding each empirical chapter is a short preface that outlines the rationale for each study and draws a logical link between studies in the series. The thesis does not contain a general methods section, however the methods used in each study are detailed within each empirical chapter.

The format and style of Chapters 2, 3, 4, and 5 follow the specific requirements set out by the particular journal to which it was or will be submitted. The only exception to this is that, for the sake of readability, tables and figures are presented in the body of the manuscript rather than at the end. Appendices that were not required in the manuscripts for publication have now been referred to in the text and appended at the end of the thesis. The introduction and general discussion follow the format required by La Trobe University School of Psychological Science, the format of the American Psychological Association.

ABSTRACT

The primary aim of this study was to establish whether memory impairments in pregnancy could be attributed to sleep disturbance, while controlling for confounding variables including attention, mood, hormone level and nocturnal oxygen saturation. Twenty-seven women in the third trimester of pregnancy, 21 women in the first trimester of pregnancy and 24 nonpregnant controls were administered a series of verbal and visual episodic memory tasks and two procedural memory tasks, and underwent an overnight sleep study. Firstly, the results indicated that compared to controls, both pregnant groups had reduced scores on immediate and delayed verbal episodic memory tasks, but were unimpaired on visual and procedural memory tasks. Similarly, both pregnant groups had reduced overnight retention rates on the verbal episodic memory tasks when compared to the control group. Reduced verbal memory retention during pregnancy was not related to measures of attention, mood, progesterone level or nocturnal oxygen saturation. Sleep during pregnancy was characterised by decreased sleep efficiency with increased awakenings and cortical arousals, less time in REM sleep, and less deep sleep in favour of more light, non-restorative sleep. Sleep-related conditions such as snoring and leg movements were also more common in the third-trimester pregnant women. Contrary to prevailing theories regarding memory consolidation during sleep, reduced episodic memory retention during pregnancy was not related to any measure of sleep. This study highlights several issues of pregnancy. Although memory difficulties were minor, the perception of memory problems may have implications for everyday tasks of living for pregnant women. Health professionals should understand the characteristics of sleep during pregnancy, in order to recognise when referral to a sleep specialist may be required. However, the question of why memory difficulties exist during pregnancy remains unanswered, and there remains plenty of scope for further research in this area.

STATEMENT OF AUTHORSHIP

"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 submitted 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. Each article presented here focuses on one part of the overall study conducted for the purpose of this thesis, and so authorship for each article is identical. Professor Simon Crowe and Mr. Martin Jackson provided supervision and intellectual input into the published and submitted manuscripts arising from this thesis. Dr. Maree Barnes provided supervision and intellectual input for research procedures carried out at the Austin Hospital. Professor Michael Permezel, as the Head of the Department of Obstetrics and Gynaecology, supported the involvement of the Mercy Hospital for Women in this research, and Dr. Lenore Ellett assisted with recruitment of participants from the Mercy Hospital for Women. Submission to each research ethics committee, data collection, data analysis, and initial manuscript preparation were almost exclusively undertaken by the candidate.

This thesis has not been submitted for the award of any degree or diploma in any other tertiary institution.

All research procedures in this thesis were approved by the Human Ethics Committee of the Faculty of Science, Technology and Engineering, La Trobe University (Project No. 07-16), and the Human Research Ethics Committees at Austin Health (Project No. 02791) and the Mercy Hospital for Women (Project No. R06/57).

This research was funded by La Trobe University and the Austin Health Medical Research Foundation."

Signed …….. Date…….

Danielle L. Wilson

"As a co-author of the published and prepared manuscripts arising from this thesis, I declare that the above Statement of Authorship accurately states the extent and the nature of the candidate's contribution to this thesis and associated publications."

Signed ……. Date…….

Simon F. Crowe

ACKNOWLEDGMENTS

Firstly, I would like to thank my La Trobe University supervisors, Professor Simon Crowe and Mr. Martin Jackson for their support along the course of my postgraduate journey, and especially to Simon for his ongoing encouragement in the pursuit of having my research published. I would also like to thank Dr. Ben Ong for providing statistical guidance.

Secondly, I would like to express my gratitude and give recognition to my supervisor at Austin Health, Dr. Maree Barnes, and all of my colleagues at the Institute for Breathing and Sleep and the Sleep Disorders Unit. Their unwavering support has been a large part of why this thesis is now complete and has led onto bigger and better things for my future.

In order to make this research possible, we received the support of the Mercy Hospital for Women through Professor Michael Permezel, and for that I am very grateful. I also appreciated the efforts given by Dr. Lenore Ellett to recruit the pregnant participants to our study, especially those tricky first trimesters!

Last but of course not least, I would like to thank my family and friends for their ongoing support and understanding throughout my time as a postgraduate student. To my fiancé Phil, thank-you for supporting and encouraging me through the difficult times as I discovered the career path that was right for me.

Chapter 1

Literature Review

Episodic and Procedural Memory Consolidation during Sleep: Can Memory Impairment during Pregnancy be attributed to Sleep Disturbance?

During pregnancy, many physiological changes occur to meet the demands placed on the mother as the foetus grows. As well as the physical changes that occur, many pregnant women report memory impairments and sleep disturbances. Objective measures of memory performance during pregnancy have found an impairment in declarative memory (de Groot, Hornstra, Roozendaal, & Jolles, 2003; Keenan, Yaldoo, Stress, Fuerst, & Ginsburg, 1998; Sharp, Brindle, Brown, & Turner, 1993), and it has been documented that pregnant women have disturbances in sleep, especially in the third trimester (Brunner, et al., 1994; Hertz, et al., 1992). One common theory is that memory consolidation occurs during sleep (Drosopoulos, Wagner, & Born, 2005; McClelland, McNaughton, & O'Reilly, 1995; Plihal & Born, 1997), and thus disruptions of sleep should also disrupt the long-term storage of memories. Therefore, it is of interest to establish whether memory impairments in pregnancy can be at all attributable to sleep disturbance.

Pregnancy and Memory Changes

Major physiological changes occur to a woman when she becomes pregnant. Among the major changes that occur in the maternal system are rising oestrogen and oxytocin levels, an increase in respiratory rate and blood volume, increased requirements for nutrients and vitamins, and the uterus undergoes a tremendous increase in size (Martini, 1998). While all these physiological changes occur, one interesting phenomenon is the abundance of anecdotal reports by pregnant women that they are plagued with cognitive problems, particularly memory problems (Brett & Baxendale, 2001).

Although popular stereotypes exist of pregnant women who lack concentration or are forgetful, there have been few attempts to investigate cognitive changes during this period (Parsons & Redman, 1991). Cognitive changes may be of particular importance because of their potential to reduce the ability of women to problem-solve at a time when

they are faced with considerable life changes and the necessary adaptive responses (Parsons & Redman, 1991). Also, memory loss in pregnant women could adversely affect their compliance with medical instructions; pregnant women are a particular target for health education (Sharp, et al., 1993).

Pregnancy and Self-Reported Memory Problems

To investigate self-reported cognitive change during pregnancy, Parsons and Redman (1991) invited 236 women to complete a questionnaire assessing cognitive changes during pregnancy, within three days of delivery. Between 50-64% of the sample felt that they had experienced decreases in cognitive function during the last three months of pregnancy. A second study looked further into the cognitive changes reported during pregnancy. Of a sample of 50 pregnant women, 82% reported changes in cognition associated with pregnancy, with 68% reporting changes in recall or memory. Most of the affected women noticed that the onset of changes occurred by the second or third month of gestation. None of the women reported long-term memory loss; only short-term memory was affected.

In their study, Sharp et al. (1993) looked at the subjective awareness of memory disturbances in pregnant women. Eighty-one percent of Sharp et al.'s sample of 48 pregnant women rated their memory during the previous two weeks as worse than normal, whereas only 16% of the control group did so. Comments made by pregnant women regarding memory alterations included difficulty in following the course of a conversation, an inability to remember daily tasks, and an inability to remember friends names.

Crawley, Dennison, and Carter (2003) used self-assessment ratings and found that women in the third trimester of pregnancy reported mild impairments in focused and divided attention, and their ability to remember verbal material compared with the nonpregnant women. However, using an open-ended questionnaire Crawley (2002)

found that when specifically asked to rate their memory, most pregnant women reported no change. Also, women would only report a pregnancy-related impairment in memory, concentration and clarity of thought if they were specifically asked to rate their abilities.

Other studies investigating the prevalence of memory problems during pregnancy have found that pregnant women were far more likely to rate their overall memory performance as worse since pregnancy than were a control group relative to a year ago (Casey, Huntsdale, Angus, & Janes, 1999; Janes, Casey, Huntsdale, & Angus, 1999), and that 59% of a group of pregnant women rated their memory during the last two weeks as worse than normal, whereas only 19% of the control group did so (Brindle, Brown, Griffith, & Turner, 1991). Examination of beliefs about pregnancy-related cognitive decline found that both women and men with and without close experience of pregnancy rated pregnant women's cognitive abilities as slightly worse than before pregnancy, suggesting a widespread belief that cognitive abilities decline during pregnancy (Crawley, Grant, & Hinshaw, 2008).

Although a number of studies have suggested that subjective memory complaints are a significant feature of pregnancy for many women, subjective reports may not reliably indicate actual performance, and pregnant women may be more aware of their cognitive slips due to cultural expectations of cognitive decline during pregnancy (Crawley, et al., 2008). Objective techniques have consequently been employed to more thoroughly investigate memory performance during pregnancy.

Pregnancy and Objectively Measured Memory Performance

Few studies have employed standardised neuropsychological tests to quantify memory abilities during pregnancy (Brett & Baxendale, 2001). The term 'memory' refers to a broad and complex range of abilities and has been conceptualised in a number of ways. Objective memory tests are usually designed to test a particular aspect of memory

and may focus on the acquisition, consolidation and retrieval of information within a particular subsystem (Brett & Baxendale, 2001).

Types of memory.

Memory is commonly conceptualised into two distinct systems, namely explicit (declarative) and implicit (non-declarative) memory. Explicit or declarative memory refers to information encoding and retrieval that is carried out explicitly, or consciously by the individual (Peigneux, Laureys, Delbeuck, & Maquet, 2001). On the other hand, implicit memory, or non-declarative memory, can be acquired and re-expressed without awareness that the new information has been encoded or is retrieved, but behavioural performance is affected by the new memory.

Declarative memory can be further divided into episodic and semantic memory. Episodic memory refers to a system that stores events located in time and space, whereas semantic memory encompasses knowledge of the world regardless of the spatio-temporal context of acquisition (Rauchs, et al., 2004). Tulving's (1983) initial conceptualisation of long-term memory proposed that semantic and episodic memory are based on separate memory systems, but the evidence now seems to point to their reflecting the same system operating under different circumstances. Tulving regards the phenomenological experience of a past event as being crucial to labelling a memory as episodic. Semantic memory stores information that may have originated in many separate experiences, which are no longer individually retrievable. Therefore, semantic memory consists of the accumulation of many episodes (Baddeley, 1995).

A common procedure for testing declarative memory performance is to present the participants with the novel testing materials, and then to assess recall of the information. This type of memory assessment is targeting the individual's ability to mentally travel back in time and recall the features of an experience they previously had. This experience of remembering more closely resembles episodic memory retrieval (remembering an

event which happened in the past), rather than semantic memory retrieval (the accumulation of knowledge and facts). Therefore, to correspond with the methodological procedures most commonly used in declarative memory testing, this review will focus on episodic rather than semantic memory.

Two subsystems of non-declarative memory are clinically relevant; procedural memory and priming or perceptual memory. Procedural memory includes motor and cognitive skill learning and perceptual "how to" learning, whereas priming refers to a form of cued recall in which, without the subject's awareness, prior exposure facilitates the response (Lezak, Howieson, & Loring, 2004). Procedural learning is important as the pregnant woman will be required to learn many new skills as she becomes a parent; hence procedural memory will be the other focus of this review.

Episodic memory during pregnancy.

During objective testing, Sharp et al. (1993) asked participants to remember verbal and visual items for recall and recognition. On word list recall, pregnant women were found to be significantly impaired when compared to nonpregnant controls. The deficit was greater when the learning was incidental than when women were asked explicitly to remember the items. It was therefore suggested that perhaps some of the potential memory loss of those in the pregnant group may be overcome by conscious effort. If so, forgetfulness in everyday living may be greater than that found during formal testing (Brindle, et al., 1991).

Keenan et al. (1998) hypothesised that pregnant women would show decreased explicit memory functioning compared with nonpregnant control women. On paragraph recall, there was a significant decline in performance between the second and third trimester of pregnancy for immediate and delayed recall. Also, third-trimester pregnant women showed significantly worse paragraph recall than the control women.

Another study to find significant memory impairment in pregnancy was conducted by Buckwalter et al. (1999). A comprehensive neuropsychological battery was administered to women during their last two months of pregnancy and again within two months of delivery. In terms of memory, pregnant women performed significantly worse on a verbal learning test as measured by the number of items recalled after the fifth trial. Participants also showed a significantly lower learning slope across the five learning trials when pregnant. Buckwalter et al. also compared performance during pregnancy to published normative data. While the pregnant women performed slightly above average on an intelligence test, performance on indices of verbal memory ranged as low as the fifth percentile when compared with women of similar age and education.

De Groot et al. (2003) focused their investigation of cognitive functioning on early pregnancy. Results showed a clear difference between women in early pregnancy and their matched controls on the mean number of words recalled over three trials, delayed recall of the words, and the word fluency test. A later longitudinal study by de Groot, Vuurman, Hornstra, and Jolles (2006) investigated cognitive performance across multiple time points in pregnancy and at comparable times in a non pregnant group. Memory encoding and retrieval, as assessed with a word learning task, were found to be significantly lower in the pregnant group in all trimesters when compared to the control group.

Recently Henry and Rendell (2007) performed a meta-analysis to assess the impact of pregnancy on memory. Overall, they concluded that although pregnancy does impact negatively on memory performance as indexed by objective behavioural measures, this was only true for measures that placed relatively high demands on effortful processing, measures of free recall and the executive component of working memory. They found that the magnitude of the deficits was small and thus the observed impairment may be regarded as relatively subtle.

In contrast to the aforementioned literature, some studies have produced data in an attempt to dispute the hypothesis that memory impairment exists during pregnancy. Brindle et al. (1991) found that pregnant women were unimpaired compared to controls on tests of recall of household objects and word lists, and on recognition of faces. The authors do admit that it was possible that had other tests been used they might have revealed a deficit in explicit memory, as the difficulty of the recall and recognition tasks used was questionable. For example, some participants performed at ceiling in the recognition task and this may have reduced the sensitivity of the comparison between groups. Sharp et al. (1993) also found that pregnant women were unimpaired on tasks of verbal or picture recognition, but again the authors note that the sensitivity of this test was reduced because performances of some of the women were at ceiling.

A study by McDowall and Moriarty (2000) also failed to find any group differences between pregnant and nonpregnant participants, on both data-driven and conceptually-driven memory tests. Although, a closer examination of the study results revealed that the memory tests involved only cued recall. Thus, the memory tasks provided clues that would have encouraged better performances than free recall alone. Also, the authors admit that the relatively low power of the study, with regard to the detection of between-group differences, suggests that further study is warranted.

Janes et al. (1999) and Casey et al. (1999) found no significant differences between a pregnant and nonpregnant group on an explicit memory test which involved answering twelve questions about a short cartoon. The methodology of these studies is questionable. The cartoon was fifty seconds in length, shown to the participants twice, and the groups answered the twelve questions immediately after the viewing. This test appears to be insensitive for detecting group differences in memory performance, could be subject to interpretation, and was the only test of explicit memory utilised by the

authors. Also, the authors did not provide any descriptive or statistical information concerning the explicit memory test to support their conclusion.

Crawley et al.'s (2003) longitudinal study comparing verbal memory in the second and third trimester of pregnancy to a group of nonpregnant controls also found no significant differences between groups on each testing occasion. Verbal memory in this study was tested using a short passage of text with eight questions about the text asked immediately afterwards. Again this test is likely an insensitive measure and also involves a form of cuing, and considering the small sample size the authors were unlikely to find a pregnancy effect. More recently, Crawley et al. (2008) tested women in the second and third trimester of pregnancy on immediate and delayed story recall, and found no significant differences compared to a control group. The authors concede that the memory task used in this study may not have been optimal, as the women knew they were being tested and could concentrate solely on the single task presented, which is a situation rarely encountered in more cognitively complex, real world situations.

In the largest study to date, Christensen, Leach, and Mackinnon (2010) investigated cognition during pregnancy and specifically measured immediate and delayed episodic memory with a list of 16 nouns. No significant differences were found between pregnant women and nonpregnant women, or compared to the prepregnancy baseline. The main limitation of this longitudinal study was that the interval between prepregnancy baseline and testing during pregnancy was variable between participants (up to 4 years apart), and that women were at various stages of pregnancy at the time of testing.

Procedural memory during pregnancy.

All of the above-mentioned studies focus on explicit types of memory, which depend on conscious recollection of a particular episode or a particular learning event. In contrast, implicit memory does not require conscious recollection of any given prior

learning experience. The most commonly used method of testing implicit memory during pregnancy has been word-stem completion priming. This task involves presenting participants with a list of words, but they are told they need not learn them. Later, participants are asked to complete three-letter word stems with the first word that comes to mind. Normal individuals should complete a higher proportion of the word-stems with words from the previously presented list of words than would be expected by chance.

Compared to nonpregnant controls, Brindle et al. (1991) found that women in their first pregnancy used significantly fewer words from the priming list to complete the word stems, with the deficit most marked in the second trimester. Sharp et al. (1993) also found that pregnant women showed a significant impairment in priming as measured by word-stem completion, and found there was no evidence of priming for the pregnant group as their mean score did not differ significantly from chance. Alternatively, in their study Janes et al. (1999) used a similar word-completion priming task and found no differences between pregnant women and nonpregnant controls.

Of the studies investigating implicit memory during pregnancy, priming has been the focus. There appears to be a gap in the literature involving pregnancy and procedural memory; therefore investigation into this field is warranted.

Overall, the majority of existing research studies appears to support the contention that both subjective and objective memory impairments occur during pregnancy. It is possible that methodological flaws are responsible for the few studies which fail to demonstrate this.

Possible factors influencing memory during pregnancy.

The most commonly assumed explanation for the observed memory impairments in pregnancy has been related to the hormonal changes that take place. The hormones oestradiol, progesterone, testosterone, dehydroepiandrosterone, oxytocins, and cortisol change dramatically during pregnancy (Buckwalter, et al., 1999). It has been suggested

that oestrogen plays a role in verbal memory (Sherwin, 1994). There is some evidence that high doses of oxytocin cause deficits in verbal recall (Ferrier, Kennett, & Devlin, 1980), but this finding has not been consistent (Fehm-Wolfsdorf, Bachholz, Born, Voigt, & Fehm, 1988). For example, no correlation between oxytocin concentration and cognitive function during pregnancy was found by Silber, Almkvist, Larsson and Uvnas-Moberg (1990). Little is known of the actions of progesterone on brain memory structures (Brett & Baxendale, 2001). Buckwalter et al. (1999) looked at hormonal levels during pregnancy, and found that changes in hormone levels showed no pattern of associations with cognitive change. Therefore, if hormonal changes are responsible for the cognitive changes during pregnancy, then the evidence has not yet been found.

If hormonal change is not responsible for the observed memory impairments in pregnancy, it is reasonable to propose that some other pregnancy-related change may negatively impact on memory performance. In addition to memory disturbances, a frequently reported problem during pregnancy is that of disrupted sleep. Anecdotal reports from pregnant women and obstetricians indicate that sleep problems during pregnancy are common (Mindell & Jacobson, 2000), and hence the subject of sleep disturbances during pregnancy warrants further investigation.

Sleep Disturbances during Pregnancy

Many of the physiological changes that occur to a woman when she becomes pregnant could be expected to interfere with normal sleeping patterns. Most obviously, the large abdominal mass and associated discomfort that accompanies pregnancy could lead to difficulty in finding a comfortable sleeping position. More than half of women report suffering from low-back pain during pregnancy (Fast, et al., 1987), and nocturnal foetal movements may be disruptive. Increased frequency of urination occurs during the first 12 weeks and in the last month of pregnancy, and nausea and vomiting are commonly accepted symptoms of normal pregnancy (Chamberlain, 1995). Complaints

such as heartburn, oesophageal reflux, increased appetite and minor digestive upsets are also common during pregnancy (Chamberlain, 1995; Nelson-Piercy, 2002), and may result in further sleep disturbances.

Pregnancy and Self-Reported Sleep Problems

Several studies to date have investigated commonly reported sleep complaints in pregnant women. One of the earliest studies by Schweiger (1972) carried out a subjective survey of sleep with 100 women who were at least 38 weeks pregnant. Sixty-eight respondents reported that their sleep was altered from normal during their pregnancy, with most cases reporting the change had occurred only in the third trimester. Sleep problems during the first trimester were mostly attributed to nausea and vomiting, and during the second trimester a variety of causes including discomfort and foetal movements were reported. The most frequently given reasons for sleep alterations in the third trimester were discomfort, urinary frequency, foetal movement and heartburn.

Hertz et al. (1992) presented a detailed investigation of sleep patterns in 12 women in their third trimester of pregnancy. Several sleep complaints were reported significantly more frequently by the pregnant women as compared to a group of age-matched controls, such as low back pain, nocturnal leg cramps, and morning headaches.

Baratte-Beebe and Lee (1999) used sleep diaries to investigate mid-sleep awakenings at four time points across pregnancy. There was a 1.4 fold increase in the number of awakenings from preconception through the first and second trimesters of pregnancy and a twofold increase in the number of mid-sleep awakenings from baseline to the third trimester. Leading sources of midsleep disturbances were awakening to urinate, foetal movements, and general discomforts from pregnancy such as joint pain and muscle cramping. They also found that external stimuli such as co-sleepers, children and outside noises, and internal and psychological sources such as dreams, nightmares, anxiety and restlessness contributed to the problem of disturbed sleep during pregnancy.

With the use of a questionnaire, Mindell and Jacobson (2000) found that the most commonly reported sleep disturbance during pregnancy was night wakings, with 97.3% of women waking at night by the end of pregnancy. The average number of night wakings and their duration increased significantly throughout pregnancy. By the end of pregnancy, 91.9% of women noted that their sleep was restless, and more than two-thirds noted that sleep problems resulted in significant daytime sleepiness. Compared to the first half of pregnancy, women in the second half of pregnancy reported significantly more problems with insomnia-type complaints, including problems falling asleep and staying asleep. Most of the women in this study attributed their sleep problems to common physical complaints during pregnancy, such as the need to urinate, foetal movements, back pain, leg cramps, and difficulty finding a comfortable position.

Lopes et al. (2004) interviewed 300 pregnant women in an effort to establish the prevalence of sleep disorders in pregnancy. When comparing sleep disorders reported during pregnancy to what would be expected in the general population, it was found that insomnia, sleep-disordered breathing, excessive daytime sleepiness, and night awakenings were reported significantly more often in the pregnant sample.

Although the general consensus of previous self-report research is that sleep disruption is common during pregnancy, questionnaire-based studies can give limited information and can be affected by reporting biases and accuracy of recall. In order to look more objectively at sleep patterns during pregnancy, investigators began using polysomnography (PSG) to get a clearer picture.

Pregnancy and Sleep Measurement with Polysomnography

Sleep is not a unitary process; instead it is comprised of physiologically different stages. Polysomnography (PSG) allows objective measurement of sleep stages using electroencephalography (EEG) together with electromyogram (EMG) and electrooculogram (EOG) so that sleep can be classified into different sleep stages

according to a set of criteria (Rechtschaffen & Kales, 1968). Rapid eye movement (REM) sleep is characterised by the presence of rapid eye movements, and a global abolition of muscle tone. Non-REM (NREM) sleep is divided into several stages, corresponding to increasing sleep depth. Stages 1 and 2 correspond to light sleep, with Stage 2 characterised by K complexes and sleep spindles. Stages 3 and 4 (also known as slow-wave sleep (SWS)) have an increase in slow oscillations as sleep deepens, and muscle tone decreases compared to the lighter sleep stages. Through-out the night, the NREM and REM sleep periods alternate following an ultradian cycle, with SWS invariably preceding REM sleep in healthy individuals (Peigneux, et al., 2001). The need for sleep is universally recognised, however the complexities of the function of sleep are still not fully understood.

To date, objective research on sleep during pregnancy has been limited (K. A. Lee, Zaffke, & McEnany, 2000), especially studies that include complete PSG. Two early polysomnographic investigations into sleep during pregnancy were lead by Karacan (Karacan, et al., 1968; Karacan, Williams, Hursch, McCaulley, & Heine, 1969), with similar findings. Both studies monitored pregnant women for three consecutive nights during the last month of pregnancy, and compared them to age-matched nonpregnant controls. Both studies found that the pregnant women spent more time awake and had more awakenings during the night compared to the controls, and that Stage 4 sleep was suppressed during pregnancy. However, Karacan et al. (1968) found that sleep latency was longer for pregnant women, but REM sleep was comparable across groups, whereas Karacan et al. (1969) found no difference in sleep latency, but found that REM sleep was significantly lower in the pregnant group as compared to the nonpregnant controls.

Hertz et al. (1992) also utilised PSG to objectively measure sleep during pregnancy. Firstly, Hertz et al. found that sleep efficiency, defined as the time spent asleep as a percentage of the time allowed for sleeping, was significantly lowered in

pregnancy as compared to controls. Decreased efficiency of sleep was mostly due to a marked increase in wake after sleep onset in the pregnant group. Sleep fragmentation, as defined by the number of awakenings, was found to be significantly higher in the pregnant group as compared to controls. Other sleep changes in the pregnant group included a significant increase in Stage 1 sleep and a significant decrease in REM sleep as compared to the control group. There was also a slight, but non-significant, decrease noted in SWS. Similarly, Brunner et al.'s (1994) analysis of sleep EEG in nine healthy women during each trimester of pregnancy revealed an increase in waking from trimester two to trimester three, and a reduction of REM sleep from trimester one to two.

Driver and Shapiro (1992) performed PSG on five women across each trimester of pregnancy, and used the first six hours of sleep for statistical analysis. In contrast to other studies, they found no reduction in Stage 4 sleep during pregnancy; with SWS actually increasing in the third trimester compared to the first. No significant differences in REM sleep across trimesters were found, however compared to a group of nonpregnant women REM sleep time was decreased during the last two months of pregnancy. During pregnancy, the time spent awake during the first six hours of sleep was increased, but there were no changes in sleep latency.

Schorr et al. (1998) investigated sleep patterns in pregnancy, by performing overnight PSG studies on four pregnant women, at each trimester of pregnancy. When compared to well-matched controls, Schorr et al. found no significant differences between the groups when comparing sleep latency and REM sleep latency. In the pregnant sample, sleep alterations were evident during SWS. Qualitative analysis of all pregnant participants revealed alpha-wave intrusions into the delta-range EEG recordings, whereas normal SWS was seen in the control participants. Abnormalities in Stages 3 and 4 sleep have been implicated in some sleep disorders responsible for symptoms of excessive tiredness and daytime sleepiness. An alteration in this portion of sleep architecture may

play a prominent role in the frequent complaints of excessive tiredness and sleepiness during pregnancy. Schorr et al. also found that the pregnant women spent significantly less mean proportion of their sleep time in SWS when compared to the controls, this finding was evident during the first and third trimester. No other significant differences were found longitudinally throughout pregnancy.

The most recent study in this field by K. A. Lee, et al. (2000) used portable PSG in the home on 33 women prior to and during pregnancy. Compared to prepregnant sleep characteristics, significant changes in sleep patterns were evident by the first trimester, with a significant increase in total sleep time but less deep sleep and more awakenings during sleep. Sleep efficiency continued to decline throughout pregnancy, and deep sleep was diminished throughout pregnancy compared with baseline. However, there was no significant change in the percentage of total sleep time spent in REM sleep throughout pregnancy.

In summary, previous research has consistently and convincingly demonstrated a reduction in sleep efficiency during pregnancy. However, inconsistencies exist as to whether REM sleep and SWS are affected, and if so in which manner. Furthermore, there have been no additional objective investigations into sleep patterns during pregnancy for the past 10 years.

So far there is compelling evidence to conclude that both memory and sleep are compromised during pregnancy. If both of these phenomena co-exist during pregnancy, a relationship may exist between the two functions. One common belief is that sleep participates in the long-term consolidation of recent memory traces. Hence, a disturbance in sleep should disrupt the memory consolidation process. It is, therefore, possible that sleep disturbances during pregnancy are negatively impacting on the observed memory performances. To determine whether sleep plays a role in memory consolidation, a review of the available literature is necessary.

Mechanisms of Memory

To investigate the basis of memory impairments during pregnancy, it is necessary to examine the processes involved in memory and memory consolidation. Although much research exists on the brain regions involved in episodic memory, much remains unclear. Episodes are highly variable in their information content, and it is believed that the neocortical regions activated at encoding depend on the nature of the experience (Mayes & Roberts, 2001). For example, memory for visual elements of the experience is stored in visual processing areas, memory for linguistic elements are stored in language processing areas, and so on. After encoding, the representations of the memory in multiple neocortical sites must interact with the hippocampal complex, located within the mesial temporal lobe.

In terms of the storage of episodic memories, the most widely believed view is that long-term episodic memories are dependent on new protein synthesis and storage changes at synapses, initially occurring in the medial temporal lobes and hippocampus. The small hippocampal network gradually 'trains' the large cortical network with very slow and incremental changes in synaptic weight (McClelland, et al., 1995). As a result, storage changes gradually occur primarily in the posterior neocortex so that retrieval ceases to depend on the medial temporal lobes. It is proposed that the medial temporal lobes initially store a kind of index, which enables the different neocortical regions that represent the distinct components of a remembered episode to be activated together despite the fact that there are no direct links between them initially (Mayes & Roberts, 2001). Direct links develop slowly through the neocortical plastic process, and at this point, cortical representations no longer benefit from hippocampal reactivations, and thus, no longer depend upon the hippocampal system. In this fashion, the model exhibits gradual consolidation which can be thought of as strengthening the memory. In this way,

memory for the entire experience is stored in a distributed fashion across multiple cortical areas (McClelland, et al., 1995).

In contrast, the brain structures thought to be central to the circuitry involved in implicit memory are the basal ganglia. The basal ganglia receive projections from all regions of the neocortex and send projections via the globus pallidus and ventral thalamus to the premotor cortex. The basal ganglia also receive projections from cells in the substantia nigra. The model for implicit memory has been developed from an extensive series of studies using monkeys and rats. Animals with damage to the basal ganglia circuitry appear to display preserved declarative memory, but impaired learning of motor skills, appropriate responses to cues, and association tasks. Further, patients with damage to the basal ganglia, such as in Huntington's chorea, demonstrate impairments in procedural learning tasks but unimpaired verbal-recognition memory (Kolb & Whishaw, 2007).

Memory Consolidation in Sleep

Mechanisms of Memory Consolidation in Sleep

During sleep, a central mechanism for memory consolidation is thought to be the covert reactivation of neuronal populations used for encoding the respective materials during prior learning (Maquet, 2001; McNaughton, et al., 2003; Stickgold, Hobson, Fosse, & Fosse, 2001). It has been proposed that the reactivation of hippocampal memory representations during sleep drives a transfer of information to neocortical networks in which it becomes consolidated and integrated into long-term representations residing in neocortical networks (Buzsaki, 1996; McClelland, et al., 1995; McNaughton, et al., 2003). As described earlier, during wakefulness new information enters the hippocampal region through the entorhinal cortex, where is it stored temporarily without disturbing previously acquired memories. During NREM and SWS, it is proposed that

the flow of information is reversed and hippocampal efferents to the neocortex become predominant.

Similarly, Buzsaki (1989) puts forth the possibility that sharp wave (SPW) bursts carry vital information and the repeated bursts during sleep serve to consolidate the embedded information and transfer it to neocortical structures. SPW bursts are the most synchronous network pattern in the limbic system, and are predominant during sleep (Buzsaki, Leung, & Vanderwolf, 1983). SWS represents the highest coherent neuronal activity in many forebrain structures. The repeated recurrence of the same neuronal activity should strengthen synaptic weights among the active members of the net; a principle known as long-term potentiation. Therefore, it is not difficult to imagine how coherently discharging neurons, binding together various attributes of objects and events in the brain can modify their synaptic connectivity to form long-term memories of the perceived events.

In humans it is difficult to demonstrate signs of a replay of newly acquired memories during sleep. Therefore, evidence for an off-line reactivation has been provided mainly from studies in rats using hippocampus-dependent spatial tasks. By using single and multiple unit recordings in rats, many researchers have found that hippocampal activity observed during encoding was replayed during subsequent periods of SWS (Kudrimoti, Barnes, & McNaughton, 1999; Pavlides & Winson, 1989; Qin, McNaughton, Skaggs, & Barnes, 1997; Stickgold, et al., 2001; Wilson & McNaughton, 1994). With the use of functional neuroimaging in humans, it has been posited that the deactivation of mesio-temporal areas during SWS compared to wakefulness reflects local slow synchronous oscillations (Maquet, 2000), already observed in the hippocampal formation of rats during SWS and possibly related to offline reactivation of labile memory traces during sleep for consolidation into more permanent knowledge structures in the neocortex (Buzsaki, 1989, 1998; Wilson & McNaughton, 1994).

Another popular theory regarding the assembly of a long-term memory involves the neurotransmitter acetylcholine (Ach), which is involved in the regulation of the NREM/REM sleep cycle (Hobson, Stickgold, & Pace-Schott, 1998), and has received considerable attention in memory research. According to a model of cholinergic memory modulations proposed by Hasselmo and McClelland (1999), Ach inhibits feedback loops within the hippocampus and between the hippocampus and neocortex. Thus, high cholinergic activity during waking allows encoding of new declarative memories, whereas low cholinergic activity during SWS supports the spontaneous replay of newly acquired information in the hippocampus. This replay then leads to the transfer of information from the temporary hippocampal to the permanent neocortical storage and to memory consolidation. In line with this model, Gais and Born (2004b) found that by increasing levels of cholinergic tone during SWS by infusion of the cholinesterase inhibitor physostigmine, the recall of a word list task was significantly impaired.

Although REM sleep is not as frequently related to declarative memory as SWS, there still exists reason to explore its role in episodic memory consolidation. Buzsaki (1998) hypothesised that every new REM sleep episode with a new neocortical (dream) content may alter the functional connectivity of the CA3 circuit of the hippocampus. The newly created synaptic weights after each REM sleep episode, in turn, determine the recruitment order of the discharging neurons in subsequent SPW events associated with the ensuing SWS cycle. Therefore, Buzsaki (1989) hypothesised that the goal of REM sleep is to 'update' connectivity of the CA3 recurrent matrix, which information will be consolidated and transferred back to the neocortex during the following SWS period. From his perspective, both REM and SWS stages are critical for memory formation, representing the 'loading' and 'consolidating' stages of the physiology-based model.

Significantly activated cortical areas in REM sleep include the anterior cingulate cortex, the parietal lobule, the inferior temporal and fusiform gyri and the hippocampal

formation, which all receive an important number of amygdalar projections (Maquet & Phillips, 1999). The strong activation of amygdaloid complexes observed during REM sleep suggests that they modulate the activity of cortical areas during REM sleep and that this amygdalo-cortical interplay reflects the processing of some type of memory trace, mainly emotional or procedural memories (Peigneux, et al., 2001).

The Role of Sleep Stages in Memory Consolidation

The role of sleep stages implicated in memory systems has been interpreted in two different ways. The dual-process hypothesis argues that REM sleep and NREM sleep act differently on memory traces, depending on the memory system they belong to. The most common hypothesis is that SWS facilitates the consolidation of declarative memory, whereas REM sleep facilitates consolidation of non-declarative memory (Plihal & Born, 1997). Alternatively, the double-step process view contends that SWS and REM sleep play complementary roles and have to act serially in order to consolidate the memory trace (Stickgold, Whidbee, Schirmer, Patel, & Hobson, 2000). In other words, each state would subserve a part of a process which requires both to be fully effective (Ficca, Lombardo, Rossi, & Salzarulo, 2000).

The dual-process hypothesis of memory consolidation in sleep has received much support for the specific role of SWS sleep in episodic memory consolidation. One way to investigate the effects of sleep stages on memory processes is by dividing the retention interval into either early night sleep versus late night sleep. In humans, sleep in the early part of the night is dominated by extensive epochs of SWS, whereas periods of sleep later in the night are characterised by high amounts of REM sleep. One of the earliest studies to use this technique was by Yaroush, Sullivan, and Ekstrand (1971), who compared the first and second half of the night of sleep using a verbal paired associates task. Participants who were allowed to sleep during the first half of the night (dominated by Stage 4 sleep) showed superior memory to those who were only allowed sleep in the later,

REM sleep dominant part of the night. A totally sleep deprived group did not perform as well on the memory task as those who received large amounts of Stage 4 sleep.

Fowler, Sullivan, and Ekstrand (1973) compared the first half and second half of the night of sleep as retention intervals for paired associate learning and visual memory for nonsense shapes. They found that memory retention for word pairs was inferior following an interval of relatively high amounts of REM sleep compared to an interval with relatively high amounts of Stage 4 sleep. There was no memory effect of retention interval condition for the nonsense shapes task. Plihal, Pietrowsky, and Born (1999) partly replicated these findings in their study, showing that recall of a paired associate word list was substantially improved following early sleep filled with SWS, in contrast to the marginal and nonsignificant improvements seen following late sleep filled with REM sleep.

By using the same research technique, Drosopoulos et al. (2005) used a word recognition task to demonstrate that explicit recollection was generally enhanced after 3-hour retention intervals of sleep compared to wake intervals of the same duration, and that the enhancing effect of sleep on explicit memory was particularly pronounced after early night retention sleep. Similarly, Plihal and Born (1997, 1999) found that recall for a verbal paired associates task and a mental spatial rotation task was better after sleep than after wakefulness, and that recall was better when the retention interval was filled with SWS (early sleep) rather than with REM (late) sleep.

Barrett and Ekstrand (1972) contend that many sleep studies looking at memory consolidation have confounded the sleep-awake variable with time of day. To control for the influences of circadian and other biological rhythms, Barrett and Ekstrand compared forgetting over intervals of sleep with forgetting over intervals of wakefulness, when the intervals for both conditions occurred at the same time during the day. The sleep interval was further divided into two different conditions, one with high Stage 4 sleep and low

REM sleep, and the other with high REM sleep and low Stage 4 sleep, again run at the same time of day. The results of the study led the researchers to conclude that retention of a paired associate word list over the high REM sleep interval was inferior to retention over the high Stage 4 sleep interval, and that these two effects cannot be explained as artefacts of a circadian rhythm effect on memory.

Alternatively, the dual-process hypothesis that REM sleep facilitates consolidation of non-declarative or implicit memory has also received support. For example, a study by Karni, Tanne, Rubenstein, Askenasy, and Sagi (1994) showed that performance on a basic visual discrimination task (perceptual learning) improved after a normal night of sleep. However, selective disruption of REM sleep resulted in no performance gain during a comparable sleep interval, whereas SWS disruption did not affect improvement. Also, a study examining post-training sleep in humans following memory training demonstrated increases in the number and density of rapid eye movements in REM sleep during the night of sleep following cognitive procedural/implicit task acquisition (C. T. Smith, Nixon, & Nader, 2004).

Fischer, Hallschmid, Elsner, and Born (2002) used a sequential motor task to show that sleep after task practice, independent of whether sleep occurred during daytime or nighttime, enhanced speed of sequence performance and reduced rate of errors compared with corresponding intervals of wakefulness. Correlation coefficients indicated that greater performance gains were noted in participants with high amounts of REM sleep, pointing to a particular relevance of REM sleep in procedural memory formation.

Plihal and Born (1997) and Plihal et al. (1999) assessed the consolidation of mirror-tracing skill (procedural learning) using the partial sleep deprivation paradigm in which the retention interval is either placed in the first or the second half of the night, dominated by SWS and REM sleep respectively. The authors found that mirror-tracing skill improved more after REM sleep than after SWS. Using the same partial sleep

deprivation paradigm, Plihal and Born (1999) found that priming, a form of non-declarative memory, was more effective after a 3-hour period of late retention sleep compared to early retention sleep.

C. Smith (2001) reviewed the relationship between procedural memory and REM sleep, and revealed that 14 out of 16 studies utilising tasks of a procedural nature all reported increases in some component of REM sleep. Some of the studies reported increases in the number of minutes of REM sleep or percentage of REM sleep, while others observed increases in the number of actual REM's and REM densities. Further, studies involving total REM sleep deprivation reported a lack of effect on declarative memory, whereas studies involving procedural memory reported impairment of memory.

The double-step process of memory consolidation in sleep postulates that SWS and REM sleep play complementary roles and have to act serially in order to consolidate the memory trace (Giuditta, et al., 1995; Stickgold, et al., 2000). Using a basic visual discrimination task, Gais, Plihal, Wagner, and Born (2000) were able to show that performance on the task improved significantly after early (SWS rich) sleep, but improvement was even more important after a whole night of sleep, suggesting that both SWS and REM sleep may be necessary for an optimal consolidation process. Using the same visual discrimination task, Stickgold et al. (2000) found that performance improvement correlated with the amount of both SWS in the first quarter of the night, and the amount of REM sleep in the last quarter. A two-step process, modelling throughput as the product of the amount of early SWS and late REM sleep, accounted for 80% of inter-subject variance, suggesting that both SWS and REM are required for consolidation of this task.

Ficca et al. (2000) have shown that recall of pairs of unrelated words is impaired after fragmented sleep leading to a disruption of the sleep cycle, but not if awakenings during the night preserved the sleep cycle. In both conditions, the amount of REM and

NREM sleep was similar. This emphasises the importance of sleep organisation of NREM-REM sleep cycles, rather than a specific stage of sleep. Mazzoni et al. (1999) investigated the importance of sleep structure for sleep-related memory processes by studying recall of words in a sample of 30 elderly people. They found that recall was positively related to the average duration of sleep cycles, and the proportion of total sleep time spent in sleep cycles.

So far, results support either the dual-process or the double-step hypotheses of memory consolidation in sleep. Even so, the relationship between individual sleep stages and memory consolidation is probably not that simple (Gais & Born, 2004a), as demonstrated by some contradictory findings. For example, Empson and Clarke (1970) found that the recall of words, grammatically correct but meaningless sentences, and prose passages was significantly impaired after selective REM sleep deprivation. The recall of short stories was also sensitive to REM sleep deprivation (Tilley & Empson, 1978). A beneficial effect of REM sleep has also been found for the recall of words belonging to different semantic categories (Tilley, 1981), and for the retention of emotional texts (Wagner, Gais, & Born, 2001). In a review of the literature, Rauchs, Desgranges, Foret and Eustache (2005) concluded that while substantial evidence for the role of REM sleep in the consolidation of non-declarative memories exists, some studies concerning perceptual motor learning indicate a relationship to features of NREM sleep. For example, in a finger-tapping task where subjects were required to type a simple numeric sequence on a computer keyboard, subsequent retesting 4-12 hours later the same day showed no significant improvement. In contrast, after a night of sleep a significant 20 percent increase in speed was seen, an increase that correlated with the amount of Stage 2 NREM sleep in the last quarter of the night (Walker, Brakefield, Morgan, Hobson, & Stickgold, 2002).

Objection to the Relationship between Sleep and Memory

Although support has been shown for memory consolidation in sleep, there are a handful of studies disputing this relationship. For example, Chernik (1972) and Castaldo, Krynicki, and Goldstein (1974) found that verbal paired associate learning was unaffected by selective REM sleep deprivation, with Castaldo et al. also observing no changes in any REM or NREM sleep parameter following task acquisition. Also using a verbal paired associate task, Ekstrand, Sullivan, Parker, and West (1971) found that learning was unaffected by deprivation of either Stage 4 sleep or REM sleep following task acquisition. Zimmerman, Stoyva, and Reite (1978) conducted a series of closely related experiments designed to investigate possible REM sleep augmenting effects of spatially rearranged vision. They concluded that there was no consistent effect of distorted daytime vision on the amount or percentage of REM sleep, REM latency, or the number of rapid eye movements during REM sleep periods. Most recently, Genzel, Dresler, Wehrle, Grozinger, and Steiger (2009) tested verbal paired associate learning and sequential finger tapping by depriving participants once each of REM sleep and SWS, and once letting them sleep undisturbed through the night. They found that although REM sleep and SWS awakenings led to a significant reduction of the respective sleep stages, both declarative and procedural memory consolidation measured 60 hours later remained unaffected. However, Genzel et al. did find a positive association between verbal paired associate learning and sleep spindles in the first third of the undisturbed night.

In their reviews, Vertes (2004) and Vertes and Eastman (2000) present several arguments against a role for sleep in memory consolidation. Firstly, Vertes argues that as the mental or cognitive content of sleep is dreams, then the hypothesis that sleep serves a role in memory consolidation would be more appealing if dreams reproduced waking experiences, but they do not. Vertes also argues that the contents of sleep are poorly

remembered, which suggests that structures responsible for encoding and storage of information in waking are suppressed or absent in sleep.

Schwartz (2003) provides a possible explanation for episodic memory consolidation during sleep. During the waking state, information flows to the hippocampus, which links together the various elements of an episodic memory that will be stored in different neocortical areas. During SWS, the memory trace is transferred to the neocortex through neuronal bursts initiated in the hippocampus. In contrast, during REM sleep (when dreaming is most common), the hippocampal outflow to the neocortex is blocked, and information flows mainly in the opposite direction. During REM sleep, the information arriving in the hippocampus, at least for recent memories, probably flows from independent cortical modules. Because of this, there is no reason to expect a report of complete and integrated episodic memories during REM sleep. The results would be different for older, consolidated memories, this is, stored within inter-connected cortical modules. Moreover, recall processes depend on the integrity of the prefrontal cortex, which is deactivated during sleep. Thus, one can assume that episodic elements will be reactivated during sleep in a fragmented fashion, rather than in the form of an integrated life episode.

In regards to animal studies of memory consolidation in sleep, Vertes (2004) proposed that "stress" due to the sleep deprivation method used, rather than sleep loss, largely accounts for the learning impairments in many of these studies. Specifically, it has been argued that impairments with sleep deprivation were not true memory deficits, but merely performance deficits as the animals were unable to perform the required tasks due to the physically debilitating effects of the deprivation. Although human sleep deprivation methods are not as severe as those used with animals, participant stress levels are an important variable in studies of sleep and memory and should be considered.

Vertes (2004) and Vertes and Eastman (2000) also use the case of a patient with lesions in the left prepontine cistern, medial left temporal lobe, and left thalamus (Lavie, Pratt, Scharf, Peled, & Brown, 1984) to provide support for their contention. An examination of the patients' patterns of sleep revealed a virtual absence of REM sleep. Vertes and Eastman claimed that despite this, the man led a normal life. A closer look at Lavie et al.'s (1984) study reveals that no neuropsychological testing whatsoever was performed on the patient to assess his cognitive functioning; the only hint to his functioning was that 'the patient had a relatively normal life' (Lavie et al., 1984, pg. 120).

Another attempt to refute memory consolidation during sleep by Vertes (2004) and Vertes and Eastman (2000) involved research into antidepressant drugs. Virtually all major antidepressant drugs suppress REM sleep, and it is claimed that they have no detrimental effect on cognitive functions. Within their argument, the authors state that the general cognitive status of individuals on one class of anti-depressant drugs has not been systematically examined.

In all, it appears that Vertes (2004) and Vertes and Eastman (2000) have not covered sufficient ground to make their assertion that there is no compelling evidence to support a relationship between sleep and memory consolidation. Many of their supporting studies did not employ systematic methods of investigating cognitive functioning to confirm their standpoint. Most notably, Vertes, and Vertes and Eastman focused their review on REM sleep deprivation to argue their case, and almost neglected to mention SWS. The authors do not make a very persuasive argument against the hypothesis of memory consolidation during sleep.

On the whole, the research detailing the process of memory consolidation during sleep seems very feasible. As discussed previously, difficulties with both memory and sleep are experienced during pregnancy. It is possible that these processes are linked; in that disturbance of sleep during pregnancy is responsible for the memory problems

encountered. These findings logically lead to an investigation of whether this is in fact the case.

Can Memory Impairment during Pregnancy be attributed to Sleep Disturbance?

To date, no studies have investigated whether sleep disturbances during pregnancy are responsible for the observed memory impairments. Janes et al. (1999) observed that pregnant participants reported significantly more sleep disruption (as assessed by one question) and that this was a significant predictor of reported memory change. Keenan et al. (1998) reported that all of the pregnant women in the study noted difficulty with sleep, but there was no significant correlation between sleep loss and paragraph recall. This result is questionable however, as Keenan et al. neglect to mention how they measured difficulty with sleep, and provide no statistical evidence.

Based on the assertion that sleep facilitates memory consolidation, it is proposed that as sleep disturbances are commonly reported and objectively measured in pregnant women, and as pregnant women have been shown to have memory impairments, it is reasonable to investigate whether sleep disruptions contribute to memory impairment in pregnancy.

Possible Confounders

One potential problem with this investigation is that during pregnancy, there are alterations in respiratory function that can lead to alterations in maternal oxygenation during sleep (Connolly, et al., 2001; Izci, et al., 2003; Prodromakis, Trakada, Tsapanos, & Spiropoulos, 2004). The brain receives a significant portion of the cardiac output of oxygen, but it does not store oxygen. Therefore, sustained oxygen deprivation may render cerebral autoregulatory mechanisms ineffectual and the brain may become injured (Caine & Watson, 2000). Even lower levels of oxygen deprivation can be associated with brain damage if the hypoxic episodes continue or frequently recur (Gibson, Pulsinelli,

Blass, & Duffy, 1981). The hippocampus, which is heavily implicated in memory consolidation, is particularly vulnerable to oxygen deprivation (Caine & Watson, 2000).

Prodromakis et al. (2004) and Schorr et al. (1998) found no significant differences in mean and minimal oxygen saturation in pregnancy compared to postpartum and controls. There were also no significant sleep-stage related oxygen saturation differences. Bourne, Ogilvy, Vickers and Williamson (1995) did find that mean overnight oxygen saturation in the pregnant group was significantly lower than that in the nonpregnant group, although the pregnant group still showed oxygen saturation levels ranging from 91%-98%, with a mean of 95.2%. The normal range for oxygen saturation at sea level is approximately 95-99% (Crapo, Jensen, Hegewald, & Tashkin, 1999), therefore the pregnant group should not display any ill effects due to saturation levels. Even so, oxygen saturation will need to be monitored and controlled for when examining memory consolidation in sleep.

Another consideration to be made in regards to the relationship between sleep deprivation and memory consolidation is the role of attention. The clearest effect of sleep loss is sleepiness, and the major outcome of the literature relating sleepiness and behavioural functioning has been response slowing and attentional lapses (Bonnet, 2000). Performance decrements after sleep deprivation include a decrease in the ability of the sleep-deprived person to focus the attention and effort necessary to complete the task successfully (Johnson, 1982; Meddis, 1982). Results from experiments examining the relationship between sleep and mental performance generally show that sleep deprivation is associated with increases in lapses of attention (Banks & Dinges, 2007; Polzella, 1975; Williams & Lubin, 1967). The impairments are thought to reflect the reduced level of alertness produced by sleep deprivation and the increased propensity to take microsleeps (Tilley & Brown, 1992). It is therefore conceivable that any memory deficits found after sleep disruption have been somewhat influenced by attentional failures. The role of

attention needs to be investigated as a confounding variable to see if it mediates the relationship between sleep deprivation and memory impairment.

Depressive symptomatology in the prenatal period is a significant problem with reported prevalence rates between 14% and 37% (Andersson, et al., 2003; A. M. Lee, et al., 2007; Priest, Austin, Barnett, & Buist, 2008), and has the potential to impact on both sleep patterns and memory performance. Individuals with depressive mood disorders have been shown to exhibit significant impairments in explicit memory function (Bearden, et al., 2006), particularly episodic memory (Sweeney, Kmiec, & Kupfer, 2000). Pregnant women identified as being depressed report poorer sleep quality than their nondepressed counterparts (Field, et al., 2007; Jomeen & Martin, 2007), and researchers have also begun to assess sleep deprivation as a contributor to both prenatal (Skouteris, Germano, Wertheim, Paxton, & Milgrom, 2008) and postnatal mood changes (Wilkie & Shapiro, 1992; Wolfson, Crowley, Anwer, & Bassett, 2003). Therefore, the mood state of the pregnant women also needs to be taken into account.

Rationale of the Study

The purpose of this research is to examine the relationship between sleep and memory during pregnancy. It is widely known that pregnant women report memory problems during pregnancy (Casey, et al., 1999; Parsons & Redman, 1991; Sharp, et al., 1993), and these difficulties have been confirmed with objective measures (Buckwalter, et al., 1999; Keenan, et al., 1998; Sharp, et al., 1993). It has also been documented that pregnant women have disturbances in sleep, especially during the third trimester (Brunner, et al., 1994; Hertz, et al., 1992). Memory impairment has consistently been linked to measures of sleep deprivation (Drosopoulos, et al., 2005; Plihal & Born, 1997; Yaroush, et al., 1971). In summary, the aim of this research study is to establish whether memory impairments in pregnancy can be attributed to sleep disturbances, while

controlling for variables such as attention, mood, hormone level and nocturnal oxygen saturation levels.

References

Andersson, L., Sundström-Poromaa, I., Bixo, M., Wulff, M., Bondestam, K., & åström, M. (2003). Point prevalence of psychiatric disorders during the second trimester of pregnancy: a population-based study. *American Journal of Obstetrics and Gynecology, 189*(1), 148-154.

Baddeley, A. D. (1995). The psychology of memory. In A. D. Baddely, B. A. Wilson & F. N. Watts (Eds.), *Handbook of memory disorders* (pp. 3-26). West Sussex: John Wiley & Sons Ltd.

Banks, S., & Dinges, D. F. (2007). Behavioral and physiological consequences of sleep restriction. *Journal of Clinical Sleep Medicine, 3*(5), 519-528.

Baratte-Beebe, K., & Lee, K. A. (1999). Sources of midsleep awakenings in childbearing women. *Clinical Nursing Research, 8*(4), 386-397.

Barrett, T. R., & Ekstrand, B. R. (1972). Effect of sleep on memory: III. Controlling for time-of-day effects. *Journal of Experimental Psychology, 96*(2), 321-327.

Bearden, C. E., Glahn, D. C., Monkul, E. S., Barrett, J., Najt, P., Villarreal, V., et al. (2006). Patterns of memory impairment in bipolar disorder and unipolar major depression. *Psychiatry Research, 142*((2-3)), 139-150.

Bonnet, M. H. (2000). Sleep deprivation. In M. Kryger, T. Roth & W. C. Dement (Eds.), *Principles and practice of sleep medicine 3rd edition*. Philadelphia, Pennsylvania: W. B. Saunders Company.

Bourne, T., Ogilvy, A. J., Vickers, R., & Williamson, K. (1995). Nocturnal hypoxaemia in late pregnancy. *British Journal of Anaesthesia, 75*, 678-682.

Brett, M., & Baxendale, S. (2001). Motherhood and memory: A review. *Psychoneuroendocrinology, 26*, 339-362.

Brindle, P. M., Brown, M. W., Brown, J., Griffith, H. B., & Turner, G. M. (1991). Objective and subjective memory impairment in pregnancy. *Psychological Medicine, 21*, 647-653.

Brunner, D. P., Münch, M., Biedermann, K., Huch, R., Huch, A., & Borbély, A. A. (1994). Changes in sleep and sleep electroencephalogram during pregnancy. *Sleep, 17*(7), 576-582.

Buckwalter, J. G., Stanczyk, F. Z., McCleary, C. A., Bluestein, B. W., Buckwalter, D. K., Rankin, K. P., et al. (1999). Pregnancy, the postpartum, and steroid hormones: effects on cognition and mood. *Psychoneuroendocrinology, 24*, 69-84.

Buzsaki, G. (1989). Two-stage model of memory trace formation: A role for "noisy" brain states. *Neuroscience, 31*(3), 551-570.

Buzsaki, G. (1996). The hippocampo-neocortical dialogue. *Cerebral Cortex, 6*, 81-92.

Buzsaki, G. (1998). Memory consolidation during sleep: a neurophysiological perspective. *Journal of Sleep Research, 7*(Suppl. 1), 17-23.

Buzsaki, G., Leung, L. S., & Vanderwolf, C. H. (1983). Cellular bases of hippocampal EEG in the behaving rat. *Brain Research Reviews, 6*, 139-171.

Cahill, L., Babinsky, R., Markowitsch, H. J., & McGaugh, J. L. (1995). The amygdala and emotional memory. *Nature, 377*(6547), 295-296.

Cahill, L., Haier, R. J., Fallon, J., Alkire, M. T., Tang, C., Keator, D., et al. (1996). Amygdala activity at encoding correlated with long-term, free recall of emotional information. *Proceedings of the National Academy of Science USA, 93*(15), 8016-8021.

Caine, D., & Watson, J. D. (2000). Neuropsychological and neuropathological sequelae of cerebral anoxia: A critical review. *Journal of the International Neuropsychological Society, 6*, 86-99.

Casey, P., Huntsdale, C., Angus, G., & Janes, C. (1999). Memory in pregnancy. II: Implicit, incidental, explicit, semantic, short-term, working and prospective memory in primigravid, multigravida and postpartum women. *Journal of Psychosomatic Obstetrics and Gynaecology, 20*, 158-164.

Castaldo, V., Krynicki, V., & Goldstein, J. (1974). Sleep stages and verbal memory. *Perceptual and Motor Skills, 39*, 1023-1030.

Chamberlain, G. V. P. (Ed.). (1995). *Obstetrics by Ten Teachers* (16th ed.). London: Edward Arnold.

Chernik, D. A. (1972). Effect of REM sleep deprivation on learning and recall by humans. *Perceptual and Motor Skills, 34*, 283-294.

Christensen, H., Leach, L. S., & Mackinnon, A. (2010). Cognition in pregnancy and motherhood: Prospective cohort study. *The British Journal of Psychiatry, 196*, 126-132.

Connolly, G., Razak, A. R. A., Hayanga, A., Russell, A., McKenna, P., & McNicholas, W. T. (2001). Inspiratory flow limitation during sleep in pre-eclampsia: Comparison with normal pregnant and nonpregnant women. *The European Respiratory Journal, 18*, 672-676.

Crapo, R. O., Jensen, R. L., Hegewald, M., & Tashkin, D. P. (1999). Arterial blood gas references values for sea level and an altitude of 1,400 meters. *American Journal of Respiratory and Critical Care Medicine, 160*(5), 1525-1531.

Crawley, R. A. (2002). Self-perception of cognitive changes during pregnancy and the early postpartum: Salience and attentional effects. *Applied Cognitive Psychology, 16*, 617-633.

Crawley, R. A., Dennison, K., & Carter, C. (2003). Cognition in pregnancy and the first year post-partum. *Psychology and Psychotherapy, 76*, 69-84.

Crawley, R. A., Grant, S., & Hinshaw, K. (2008). Cognitive changes in pregnancy: Mild decline or societal stereotype? *Applied Cognitive Psychology, 22*, 1142-1162.

de Groot, R. H. M., Hornstra, G., Roozendaal, N., & Jolles, J. (2003). Memory performance, but not information processing speed, may be reduced during early pregnancy. *Journal of Clinical and Experimental Neuropsychology, 25*(4), 482-488.

de Groot, R. H. M., Vuurman, E. F. P. M., Hornstra, G., & Jolles, J. (2006). Differences in cognitive performance during pregnancy and early motherhood. *Psychological Medicine, 36*, 1023-1032.

Driver, H. S., & Shapiro, C. M. (1992). A longitudinal study of sleep stages in young women during pregnancy and postpartum. *Sleep, 15*(5), 449-453.

Drosopoulos, S., Wagner, U., & Born, J. (2005). Sleep enhances explicit recollection in recognition memory. *Learning & Memory, 12*, 44-51.

Ekstrand, B. R., Sullivan, M. J., Parker, D. F., & West, J. N. (1971). Spontaneous recovery and sleep. *Journal of Experimental Psychology, 88*(1), 142-144.

Empson, J. A. C., & Clarke, P. R. F. (1970). Rapid eye movement and remembering. *Nature, 227*, 287-288.

Fast, A., Shapiro, D., Ducommun, E. J., Friedmann, L. W., Bouklas, T., & Floman, Y. (1987). Low-back pain in pregnancy. *Spine, 12*(4), 368-371.

Fehm-Wolfsdorf, G., Bachholz, G., Born, J., Voigt, K., & Fehm, H. L. (1988). Vasopressin but not oxytocin enhances cortical arousal: An integrative hypothesis on behavioral effects of neurohypophyseal hormones. *Psychopharmacology, 94*, 496-500.

Ferrier, B. M., Kennett, D. J., & Devlin, M. C. (1980). Influence of oxytocin on human memory processes. *Life Sciences, 27*, 2311-2317.

Ficca, G., Lombardo, P., Rossi, L., & Salzarulo, P. (2000). Morning recall of verbal material depends on prior sleep organization. *Behavioural Brain Research, 112*, 159-163.

Field, T., Diego, M., Hernandez-Reif, M., Figueiredo, B., Schanberg, S., & Kuhn, C. (2007). Sleep disturbances in depressed pregnant women and their newborns. *Infant Behavior and Development, 30*(127-133).

Fischer, S., Hallschmid, M., Elsner, A. L., & Born, J. (2002). Sleep forms memory for finger skills. *Proceedings of the National Academy of Sciences of the United States of America, 99*(18), 11987-11991.

Fowler, M. J., Sullivan, M. J., & Ekstrand, B. R. (1973). Sleep and Memory. *Science, 179*, 302-304.

Gais, S., & Born, J. (2004a). Declarative memory consolidaton: Mechanisms acting during human sleep. *Learning & Memory, 11*, 679-685.

Gais, S., & Born, J. (2004b). Low acetylcholine during slow-wave sleep is critical for declarative memory consolidation. *Proceedings of the National Academy of Sciences of the United States of America, 101*(7), 2140-2144.

Gais, S., Plihal, W., Wagner, U., & Born, J. (2000). Early sleep triggers memory for early visual discrimination skills. *Nature Neuroscience, 3*(12), 1335-1339.

Genzel, L., Dresler, M., Wehrle, R., Grözinger, M., & Steiger, A. (2009). Slow wave sleep and REM sleep awakenings do not affect sleep dependent memory consolidation. *Sleep, 32*(3), 302-310.

Gibson, G. E., Pulsinelli, W., Blass, J. P., & Duffy, T. E. (1981). Brain dysfunction in mild to moderate hypoxia. *American Journal of Medicine, 70*, 1247-1254.

Giuditta, A., Ambrosini, M. V., Montagnese, P., Mandile, P., Cotugno, M., Grassi Zucconi, G., et al. (1995). The sequential hypothesis of the function of sleep. *Behavioral Brain Research, 69*(1-2), 157-166.

Hasselmo, M. E., & McClelland, J. L. (1999). Neural models of memory. *Current Opinion in Neurobiology, 9*, 184-188.

Henry, J. D., & Rendell, P. G. (2007). A review of the impact of pregnancy on memory function. *Journal of Clinical and Experimental Neuropsychology, 29*(8), 793-803.

Hertz, G., Fast, A., Feinsilver, S. H., Albertario, C. L., Schulman, H., & Fein, A. M. (1992). Sleep in normal late pregnancy. *Sleep, 15*(3), 246-251.

Hobson, J. A., Stickgold, R., & Pace-Schott, E. F. (1998). The neuropsychology of REM sleep dreaming. *Neuroreport, 9*(3), R1-R14.

Izci, B., Riha, R. L., Martin, S. E., Vennelle, M., Liston, W. A., Dundas, K. C., et al. (2003). The upper airway in pregnancy and pre-eclampsia. *American Journal of Respiratory and Critical Care Medicine, 167*, 137-140.

Janes, C., Casey, P., Huntsdale, C., & Angus, G. (1999). Memory in pregnancy. I: Subjective experiences and objective assessment of implicit, explicit and working memory in primigravid and primiparous women. *Journal of Psychosomatic Obstetrics and Gynaecology, 20*, 80-87.

Johnson, L. C. (1982). Sleep deprivation and performance. In W. B. Webb (Ed.), *Biological rhythms, sleep and performance*. New York: John Wiley & Sons Ltd.

Jomeen, J., & Martin, C. R. (2007). Assessment and relationship of sleep quality to depression in early pregnancy. *Journal of Reproductive and Infant Psychology, 25*(1), 87-89.

Karacan, I., Heine, W., Agnew, H. W., Williams, R. L., Webb, W. B., & Ross, J. J. (1968). Characteristics of sleep patterns during late pregnancy and the postpartum periods. *American Journal of Obstetrics and Gynecology, 101*(5), 579-586.

Karacan, I., Williams, R. L., Hursch, C. J., McCaulley, M., & Heine, M. W. (1969). Some implications of the sleep patterns of pregnancy for postpartum emotional disturbance. *The British Journal of Psychiatry, 115*, 929-935.

Karni, A., Tanne, D., Rubenstein, B. S., Askenasy, J. J. M., & Sagi, D. (1994). Dependence on REM sleep of overnight improvement of a perceptual skill. *Science, 265*, 679-682.

Keenan, P. A., Yaldoo, D. T., Stress, M. E., Fuerst, D. R., & Ginsburg, K. A. (1998). Explicit memory in pregnant women. *American Journal of Obstetrics and Gynecology, 179*, 731-737.

Kolb, B., & Whishaw, I. Q. (2007). *Fundamentals of human neuropsychology*. New York, NY: Worth Publishers.

Kudrimoti, H. S., Barnes, C. A., & McNaughton, B. L. (1999). Reactivation of hippocampal cell assemblies: Effects of behavioral state, experience, and EEG dynamics. *The Journal of Neuroscience, 19*(10), 4090-4101.

Lavie, P., Pratt, H., Scharf, B., Peled, R., & Brown, J. (1984). Localized pontine lesion: Nearly total absenceof REM sleep. *Neurology, 34*, 118-120.

Lee, A. M., Lam, S. K., Sze Mun Lau, S. M., Chong, C. S., Chui, H. W., & Fong, D. Y. (2007). Prevalence, course and risk factors for antenatal anxiety and depression. *Obstetrics and Gynecology, 110*(5), 1102-1112.

Lee, K. A., Zaffke, M. E., & McEnany, G. (2000). Parity and sleep patterns during and after pregnancy. *Obstetrics and Gynecology, 95*(1), 14-18.

Lezak, M. D., Howieson, D. B., & Loring, D. W. (2004). *Neuropsychological Assessment* (4th ed.). New York: Oxford University Press, Inc.

Lopes, E. A., Carvalho, L. B., Seguro, P. B., Mattar, R., Silva, A. B., Prado, L. B., et al. (2004). Sleep disorders in pregnancy. *Arquivos de Neuro-psiquiatria, 62*(2-A), 217-221.

Maquet, P. (2000). Functional neuroimaging of normal human sleep by positron emission tomography. *Journal of Sleep Research, 9*, 207-231.

Maquet, P. (2001). The role of sleep in learning and memory. *Science, 294*, 1048-1052.

Maquet, P., & Phillips, C. (1999). Rapid eye movement sleep: From cerebral metabolism to functional brain mapping. In B. N. Mallick & S. Inoue (Eds.), *Rapid eye movement sleep* (pp. 276-285). New York: Marcel Dekker, Inc.

Martini, F. H. (1998). *Fundamentals of anatomy and physiology* (4th ed.). New Jersey: Prentice Hall Inc.

Mayes, A. R., & Roberts, N. (2001). Theories of episodic memory. In A. Baddeley, M. Conway & J. Aggleton (Eds.), *Episodic memory: New directions in research* (pp. 86-109). New York: Oxford University Press Inc.

Mazzoni, G., Gori, S., Formicola, G., Gneri, C., Massetani, R., Murri, L., et al. (1999). Word recall correlates with sleep cycles in elderly subjects. *Journal of Sleep Research, 8*(3), 185-188.

McClelland, J. L., McNaughton, B. L., & O'Reilly, R. C. (1995). Why there are complementary learning systems in the hippocampus and neocortex: Insights from the successes and failures of connectionist models of learning and memory. *Psychological Review, 102*(3), 419-457.

McDowall, J., & Moriarty, R. (2000). Implicit and explicit memory in pregnant women: An analysis of data-driven and conceptually driven processes. *The Quarterly Journal of Experimental Psychology, 53A*(3), 729-740.

McNaughton, B. L., Barnes, C. A., Battaglia, F. P., Bower, M. R., Cowen, S. L., Ekstrom, A. D., et al. (2003). Off-line reprocessing of recent memory and its role in memory consolidation: A progress report. In P. Maquet (Ed.), *Sleep and brain plasticity* (pp. 225-246). New York: Oxford University Press.

Meddis, R. (1982). Cognitive dysfunction following loss of sleep. In A. Burton (Ed.), *The pathology and psychology of cognition* (pp. 225-252). London: Methuen.

Mindell, J. A., & Jacobson, B. J. (2000). Sleep disturbances during pregnancy. *Journal of Obstetric, Gynecologic, and Neonatal Nursing, 29*(6), 590-597.

Nelson-Piercy, C. (2002). *Handbook of Obstetric Medicine* (2nd ed.). London: Martin Dunitz Ltd.

Parsons, C., & Redman, S. (1991). Self-reported cognitive change during pregnancy. *The Australian Journal of Advanced Nursing, 9*(1), 20-29.

Pavlides, C., & Winson, J. (1989). Influences of hippocampal place cell firing in the awake state on the activity of these cells during subsequent sleep episodes. *The Journal of Neuroscience, 9*(8), 2907-2918.

Peigneux, P., Laureys, S., Delbeuck, X., & Maquet, P. (2001). Sleeping brain, learning brain. The role of sleep for memory systems. *Neuroreport, 12*(18), A111-A124.

Plihal, W., & Born, J. (1997). Effects of early and late nocturnal sleep on declarative and procedural memory. *Journal of Cognitive Neuroscience, 9*(4), 534-547.

Plihal, W., & Born, J. (1999). Effects of early and late nocturnal sleep on priming and spatial memory. *Psychophysiology, 36*, 571-582.

Plihal, W., Pietrowsky, R., & Born, J. (1999). Dexamethasone blocks sleep induced improvement of declarative memory. *Psychoneuroendocrinology, 24*, 313-331.

Polzella, D. J. (1975). Effects of sleep deprivation on short-term recognition memory. *Journal of Experimental Psychology. Human learning and memory, 104*(2), 194-200.

Priest, S. R., Austin, M. P., Barnett, B. B., & Buist, A. (2008). A psychosocial risk assessment model (PRAM) for use with pregnant and postpartum women in primary care settings. *Archives of Women's Mental Health, 11*(5-6), 307-317.

Prodromakis, E., Trakada, G., Tsapanos, V., & Spiropoulos, K. (2004). Arterial oxygen tension during sleep in the third trimester of pregnancy. *Acta Obstetricia et Gynecologia Scandinavica, 83*, 159-164.

Qin, Y., McNaughton, B. L., Skaggs, W. E., & Barnes, C. A. (1997). Memory reprocessing in corticocortical and hippocampocortical neuronal ensembles. *Philosophical Transactions of the Royal Society of London. Series B, Biological Sciences, 352*, 1525-1533.

Rauchs, G., Bertran, F., Guillery-Girard, B., Desgranges, B., Kerrouche, N., Denise, P., et al. (2004). Consolidation of strictly episodic memories mainly requires rapid eye movement sleep. *Sleep, 27*(3), 395-401.

Rauchs, G., Desgranges, B., Foret, J., & Eustache, F. (2005). The relationships between memory systems and sleep stages. *Journal of Sleep Research, 14*, 123-140.

Rechtschaffen, A., & Kales, A. (1968). *A manual of standardized terminology, techniques, and scoring system for sleep stages of human subjects*. Los Angeles: Brain Information Service.

Schorr, S. J., Chawla, A., Devidas, M., Sullivan, C. A., Naef III, R. W., & Morrison, J. C. (1998). Sleep patterns in pregnancy: A longitudinal study of polysomnography recordings during pregnancy. *Journal of Perinatology, 18*(6), 427-430.

Schwartz, S. (2003). Are life episodes replayed during dreaming? *Trends in Cognitive Sciences, 7*(8), 325-327.

Schweiger, M. S. (1972). Sleep disturbance in pregnancy: A subjective survey. *American Journal of Obstetrics and Gynecology, 114*(7), 879-882.

Sharp, K., Brindle, P. M., Brown, M. W., & Turner, G. M. (1993). Memory loss during pregnancy. *British Journal of Obstetrics and Gynaecology, 100*, 209-215.

Sherwin, B. B. (1994). Estrogenic effects on memory in women. *Annals of the New York Academy of Sciences, 743*, 213-230.

Silber, M., Almkvist, O., Larsson, B., & Uvnas-Moberg, K. (1990). Temporary peripartal impairment in memory and attention and its possible relation to oxytocin concentration. *Life Sciences, 47*, 57-65.

Skouteris, H., Germano, C., Wertheim, E. H., Paxton, S. J., & Milgrom, J. (2008). Sleep quality and depression during pregnancy: a prospective study. *Journal of Sleep Research, 17*, 217-220.

Smith, C. (2001). Sleep states and memory processes in humans: procedural versus declarative memory systems. *Sleep Medicine Reviews, 5*(6), 491-506.

Smith, C. T., Nixon, M. R., & Nader, R. S. (2004). Posttraining increases in REM sleep intensity implicate REM sleep in memory processing and provide a biological marker of learning potential. *Learning & Memory, 11*, 714-719.

Stickgold, R., Hobson, J. A., Fosse, R., & Fosse, M. (2001). Sleep, learning, and dreams: Off-line memory reprocessing. *Science, 294*, 1052-1057.

Stickgold, R., Whidbee, D., Schirmer, B., Patel, V., & Hobson, J. A. (2000). Visual discrimination task improvement: A multi-step process occurring during sleep. *Journal of Cognitive Neuroscience, 12*(2), 246-254.

Sweeney, J. A., Kmiec, J. A., & Kupfer, D. J. (2000). Neuropsychologic impairments in bipolar and unipolar mood disorders on the CANTAB neurocognitive battery. *Biological Psychiatry, 48*, 674-685.

Tilley, A. J. (1981). Retention over a period of REM or non-REM sleep. *British Journal of Psychology, 72*, 241-248.

Tilley, A. J., & Brown, S. (1992). Sleep deprivation. In A. P. Smith & D. M. Jones (Eds.), *Handbook of human performance* (Vol. 3). London: Academic Press.

Tilley, A. J., & Empson, J. A. C. (1978). REM sleep and memory consolidation. *Biological Psychology, 6*, 293-300.

Tulving, E. (1983). *Elements of episodic memory*. New York: Oxford University Press.

Vertes, R. P. (2004). Memory consolidation in sleep: Dream or reality. *Neuron, 44*, 135-148.

Vertes, R. P., & Eastman, K. E. (2000). The case against memory consolidation in REM sleep. *Behavioral and Brain Sciences, 23*(6), 867-876.

Wagner, U., Gais, S., & Born, J. (2001). Emotion memory formation is enhanced across sleep intervals with high amounts of rapid eye movement sleep. *Learning & Memory, 8*, 112-119.

Walker, M. P., Brakefield, T., Morgan, A., Hobson, J. A., & Stickgold, R. (2002). Practice with sleep makes perfect: sleep-dependent motor skill learning. *Neuron, 35*, 205-211.

Wilkie, G., & Shapiro, C. M. (1992). Sleep deprivation and the postnatal blues. *Journal of Psychosomatic Research, 36*(4), 309-316.

Williams, H. L., & Lubin, A. (1967). Speeded attention and sleep loss. *Journal of Experimental Psychology, 73*(2), 313-317.

Wilson, M. A., & McNaughton, B. L. (1994). Reactivation of hippocampal ensemble memories during sleep. *Science, 265*(5172), 676-679.

Wolfson, A. R., Crowley, S. J., Anwer, U., & Bassett, J. L. (2003). Changes in sleep patterns and depressive symptoms in first-time mothers: Last trimester to 1-year postpartum. *Behavioral Sleep Medicine, 1*(1), 54-67.

Yaroush, R., Sullivan, M. J., & Ekstrand, B. R. (1971). Effect of sleep on memory II: Differential effect of the first and second half of the night. *Journal of Experimental Psychology, 88*(3), 361-366.

Zimmerman, J. T., Stoyva, J. M., & Reite, M. L. (1978). Spatially rearranged vision and REM sleep: a lack of effect. *Biological Psychiatry, 13*(3), 301-316.

Chapter 2

Compromised Verbal Episodic Memory with Intact Visual and Procedural Memory during Pregnancy

Manuscript published online in

Journal of Clinical and Experimental Neuropsychology,

March 2011 (see Appendix G).

Preface

Memory problems are reported by pregnant women so frequently that this phenomenon is commonly joked about, and has even been given labels such as "baby brain" or "placenta brain". Ask any new mother and she will likely have an amusing anecdote about a lapse in memory which she attributed to her pregnancy. Studies have consistently found that pregnant women report memory difficulties more frequently than nonpregnant women or when compared to their pre-pregnant state. The research investigating objectively measured memory performance during pregnancy is not as clear cut however, with varying levels of impairment reported on a number of different memory tasks.

The purpose of the first empirical chapter of this thesis is to report the initial findings of an investigation into memory consolidation during sleep in pregnancy. In particular, Chapter 2 aims to investigate episodic and procedural memory performance during the first and third trimesters of pregnancy, whilst accounting for possible confounding factors.

Compromised Verbal Episodic Memory with Intact Visual and Procedural Memory during Pregnancy

Danielle L. Wilson

School of Psychological Science, La Trobe University, Bundoora, Victoria, Australia

Institute for Breathing and Sleep, Austin Health, Heidelberg, Victoria, Australia

Maree Barnes

Institute for Breathing and Sleep, Austin Health, Heidelberg, Victoria, Australia

Lenore Ellett and Michael Permezel

Mercy Hospital for Women, Heidelberg, Victoria, Australia

Martin Jackson and Simon F. Crowe

School of Psychological Science, La Trobe University, Bundoora, Victoria, Australia

Address correspondence to: Simon F. Crowe, School of Psychological Science, La Trobe University, Bundoora, VIC, 3086, Australia. Tel: 613 9479 1380; Fax: 613 9479 1956; E-mail: s.crowe@latrobe.edu.au

Running head – Episodic and Procedural Memory in Pregnancy

Abstract

This study investigated episodic and procedural memory performance in early and late pregnancy. Twenty-six women in the third trimester of pregnancy, 20 women in the first trimester of pregnancy and 24 nonpregnant controls were administered a battery of verbal and visual episodic memory tasks and two procedural memory tasks. Results indicated that compared to controls, both pregnant groups had reduced scores on immediate and delayed verbal episodic memory tasks, but were unimpaired on visual and procedural memory tasks. Verbal memory differences could not be accounted for by mood state or attention; however progesterone level accounted for a small amount of the variation. Although memory differences were minor, the perception of memory problems may have implications for everyday living for pregnant women.

Keywords: Pregnant, Explicit, Implicit, Recall, Recognition, Attention

Anecdotal reports of memory problems during pregnancy are abundant. In particular, pregnant women frequently rate their memory as worse than normal (Crawley, Dennison, & Carter, 2003; McDowall & Moriarty, 2000; Parsons & Redman, 1991) and are more likely than nonpregnant women to have memory complaints (Brindle, Brown, Brown, Griffith, & Turner, 1991; Casey, Huntsdale, Angus, & Janes, 1999; Janes, Casey, Huntsdale, & Angus, 1999; Sharp, Brindle, Brown, & Turner, 1993). However, subjective reports may not reliably indicate actual performance, and pregnant women may be more aware of their cognitive slips due to cultural expectations of cognitive decline during pregnancy (Crawley, Grant, & Hinshaw, 2008). Objective techniques have consequently been employed to investigate memory performance during pregnancy.

Explicit memory refers to the conscious recall or recognition of facts (semantic memory) or events (episodic memory) and is commonly tested in experimental settings. Compared to controls, pregnant women have shown significant deficits on explicit memory tasks such as word-list learning (Buckwalter, et al., 1999; de Groot, Vuurman, Hornstra, & Jolles, 2006; Sharp, et al., 1993), paragraph recall (Keenan, Yaldoo, Stress, Fuerst, & Ginsburg, 1998) and semantic fluency (de Groot, Hornstra, Roozendaal, & Jolles, 2003). Difficulty in discriminating relevant from irrelevant responses led Buckwalter et al. (1999) to conclude that pregnancy is associated with less effective, more haphazard learning styles. A recent meta-analysis indicated that pregnant women are specifically impaired on memory measures that place high demands on executive cognitive control (Henry & Rendell, 2007). In contrast to explicit memory, implicit memory can be acquired and re-expressed without conscious awareness but behavioural performance is affected. Priming has been a focus, with pregnant women using significantly fewer words from a priming list to complete word stems than do controls (Brindle, et al., 1991; Sharp, et al., 1993).

Physiological and psychological factors differ as a function of stage of pregnancy and parity. Some investigators describe memory impairments appearing as early as the first trimester (de Groot, et al., 2003; de Groot, et al., 2006; Sharp, et al., 1993) whereas others describe a maximal decline in memory in the second trimester (Shetty & Pathak, 2002) or the third trimester (Keenan, et al., 1998). Memory performance is often unrelated to prior pregnancy history (Casey, et al., 1999; McDowall & Moriarty, 2000; Parsons, et al., 2004; Sharp, et al., 1993), however Brindle et al. (1991) found that only primigravid women were impaired on implicit memory measures.

Impaired memory function during pregnancy is not always observed (Casey, 2000; Casey, et al., 1999; Christensen, Poyser, Pollitt, & Cubis, 1999). Specifically, pregnant women have been unimpaired on measures of verbal and visual recognition (Sharp, et al., 1993), recall of visually presented objects (Brindle, et al., 1991; Sharp, et al., 1993) word-list recall (Brindle, et al., 1991), story recall (Crawley, et al., 2003; Crawley, et al., 2008) and priming (Casey, et al., 1999; Janes, et al., 1999; McDowall & Moriarty, 2000). Prospective memory, or remembering to remember, is largely unimpaired during pregnancy (Casey, et al., 1999; Crawley, et al., 2008), although Rendell and Henry's (2008) data suggest that prospective memory difficulties may be context dependent. A large experimental study conducted recently concluded that pregnancy and motherhood are not associated with persistent cognitive deterioration (Christensen, Leach, & Mackinnon, 2010).

Pregnancy is associated with dramatic hormonal changes; both oestrogen and progesterone influence brain regions that subserve learning and memory (Dohanich, 2003). Oestrogen administration appears to help enhance verbal memory and capacity for new learning (Kampen & Sherwin, 1994; Sherwin, 1997), however there is little evidence to suggest that very high oestrogen levels like those in pregnancy have a beneficial effect on memory (Brett & Baxendale, 2001). The actions of progesterone on memory

structures has been rarely studied, though progesterone concentrations equivalent to term pregnancy levels in healthy premenopausal women have been associated with decreased verbal memory function (Freeman, Weinstock, Rickels, Sondheimer, & Coutifaris, 1992). Despite this, no consistent associations between hormones and cognition during pregnancy have been found (Buckwalter, et al., 1999; Silber, Almkvist, Larsson, & Uvnas-Moberg, 1990).

Depressive symptomatology in the prenatal period is a significant problem, with reported prevalence rates between 14% and 37% (Andersson, et al., 2003; Lee, et al., 2007; Priest, Austin, Barnett, & Buist, 2008). Individuals with depressive mood disorders have been shown to exhibit significant impairments in explicit memory function (Bearden, et al., 2006), particularly episodic memory (Sweeney, Kmiec, & Kupfer, 2000). Mood symptoms experienced by some women during pregnancy may plausibly impact on memory function. Pregnancy also triggers a major lifestyle adjustment and the mother-to-be is likely to focus on their current state of pregnancy rather than on the world around them (Crawley, 2002). This high degree of introspection may result in attentional fluctuations and make encoding new information and learning new skills more difficult.

The experience of cognitive difficulties can be frustrating and upsetting for an individual. During a time such as pregnancy, women need to learn new information and skills pertaining to the care of their newborn infant and are required to comply with specific medical instructions. Memory problems at such a time would disadvantage the mother-to-be.

A discrepancy currently exists between the consistently reported memory problems during pregnancy and the conflicting findings on objective testing. Only a limited number of studies using well-established neuropsychological techniques exist, but variations in their methodologies and choice of memory tasks may have led to their contradictory conclusions. Furthermore, procedural memory, a type of implicit memory

which includes motor and cognitive skill learning and perceptual "how to" learning (Lezak, Howieson, & Loring, 2004), has not been investigated in pregnancy.

This article aims to report the initial findings from a study looking at the impact of sleep on memory consolidation during pregnancy. Specifically, the purpose of this study is to investigate episodic and procedural memory performance during early and late pregnancy, whilst accounting for possible contributors to memory impairment including attentional deficits, hormonal change and mood disturbance. Based on consistent reports of memory problems during pregnancy and objectively measured memory deficits in much of the literature, it is hypothesised that pregnant women will show impairments on memory tasks in comparison to the nonpregnant controls.

Method

Participants

The Human Research Ethics Committees at Austin Health, Mercy Hospital for Women and La Trobe University approved this study, and informed consent was obtained from all participants (See Appendix B). Four hundred and thirty pregnant women from the Outpatient Obstetrics Clinic at the Mercy Hospital for Women were consecutively approached to participate in the study; of these 56 agreed. Participant declination was mostly due to the requirements of the broader study. After volunteering to participate, 10 pregnant women withdrew prior to data collection due to pregnancy-related complications or inability to attend the testing session. Nonpregnant women were recruited from advertisements in the hospital newsletter and from friends of the pregnant participants. Participants were excluded if they had a multiple pregnancy or pregnancy complicated by hypertension, diabetes or pre-eclampsia, a significant medical, psychological or psychiatric co-morbidity, a history of head injury or memory problems, poor English language skills, or if they were taking anti-depressant medication. In total, 26 women in the third trimester of pregnancy (T3: 30-38 weeks gestation), 20 women in the first

trimester of pregnancy (T1: 9-14 weeks gestation) and 24 nonpregnant women (control group) participated in the study.

Materials

Memory tasks were chosen for their widespread use in standardised neuropsychological testing and the availability of age- and sex-specific norms. As procedural memory has not yet been tested in pregnant women, task selection was based on previous research examining procedural memory consolidation and sleep in nonpregnant samples.

Memory questionnaire. Participants rated their current and general (or when not pregnant) memory quality on a scale of 1 (*extremely poor*) to 10 (*extremely good*), and indicated whether they had noticed changes in memory and in attention and concentration since becoming pregnant (or over the past six months for control participants; See Appendix C). Frequency of memory lapses over the past fortnight was rated on a scale of "always", "often", "rarely", or "never".

Depression Anxiety Stress Scale – Short version (DASS21; Lovibond & Lovibond, 1995). Current state of depression, anxiety and stress was measured using 21 items scored on a 4-point severity/frequency scale to rate the extent to which they have experienced each state over the past week. The score range for each scale is 0-42.

Wechsler Abbreviated Scale of Intelligence (WASI; The Psychological Corporation, 1999). The WASI is a short and reliable measure of intelligence, consisting of four subtests which combine to yield the Full Scale IQ score. The WASI IQ scores are scaled on a metric of a mean of 100 and a standard deviation of 15.

Test of Memory Malingering (TOMM; Tombaugh, 1996). This test assesses effort and feigning of memory complaints in adults. Each of two learning trials contains the same 50 line drawings of common objects shown for three seconds each. Following each trial, recognition is tested with the presentation of 50 paired pictures with one target

item plus a new line-drawn object. Participants in this study were deemed to be giving sufficient effort if they scored at least 45 out of 50 (90%) on the second trial.

Wechsler Memory Scale – Third Edition (WMS-III; Wechsler, 1997). The scaled scores from the four primary subtests of Logical Memory, Faces, Verbal-Paired Associates and Family Pictures were used to assess episodic memory. The Rarely Missed Index for Logical Memory Recognition (Killgore & DellaPietra, 2000) was also calculated as a measure of response validity.

Austin Maze (Milner, 1965; Walsh, 1985). The maze consists of a grid of 10 x 10 buttons that must be pressed in a certain order to get from one corner to the opposite corner. When the participant presses a button that is in the correct order they receive a green light, and when they venture off track the light turns red and they must try another path. Errors per trial are calculated as the number of times the participant presses a button that is not on the correct path. A maximum of 10 trials were allowed to complete two errorless trials; with the total score as the overall number of errors for the 10 trials. Delayed recall was assessed by the number of errors made on one further trial.

Rey Auditory-Verbal Learning Test (RAVLT; Rey, 1964). A list of 15 unrelated nouns is read aloud for five consecutive trials; each trial is then followed by a free-recall test. Only List A was used for this study. After the delay period, the participant is required to recall words without further presentation of the word list. Delayed recognition was tested whereby the participant must identify the 15 words from a list of 50 words read aloud containing all items from List A and 15 words phonemically and/or semantically similar to those in the list. Identified words that were not on List A were scored as "false positive" responses.

Motor Sequence Learning. This procedural memory task is the same as the finger-tapping task used by Walker, Brakefield, Morgan, Hobson, and Stickgold (2002), but for the purpose of this study is termed Motor Sequence Learning so as not to confuse

with the Finger Tapping Test (Reitan, 1979) used in neuropsychological test batteries. Motor Sequence Learning requires participants to press four numeric keys on a standard computer keyboard with the fingers of their left (nondominant) hand, repeating the five-element sequence 4-1-3-2-4 as quickly and as accurately as possible for a period of 30 seconds. The numeric sequence was displayed at the top of the screen at all times to exclude any working memory component to the task. Training consisted of ten 30-second trials with 30-second rest periods between trials. The scores (number of sequences and number of errors) from the first trial of training were taken as the "baseline" measure, and the averaged scores from the final two trials were taken as the "posttraining" performance. The averaged scores of two further 30-second trials assessed delayed performance.

Mirror-Tracing Task (Model 31010; Lafayette Instrument Co., Lafayette, Indiana). For this procedural memory task, participants were instructed to trace a flat, six-pointed star with a pencil while only a mirror-inverted image of the star was visible. Participants were instructed to be as quick and accurate as possible. Performance on each of 10 trials was assessed by the number of errors (drawing outside the edges of the star) and the time taken to trace the star. The scores from the first trial were taken as the "baseline" measure, and the averaged scores from the final two trials were taken as the "posttraining" performance. The averaged scores of two further trials assessed delayed performance.

Test of Variables of Attention (TOVA; The TOVA Company, Los Alamitos, California). The TOVA is a computerised attention task that measures responses to visual stimuli for 21.6 minutes. The TOVA contains two test conditions: target infrequent and target frequent. In the first half of the test (target infrequent), the target:nontarget ratio is 1:3.5; a target is presented (randomly) only once every 3.5 nontarget presentations. In the second half of the test (target frequent), the target:nontarget ratio is

reversed (3.5:1). Variables measured include response time, variability of response time (consistency), errors of commission (impulsivity), and errors of omission (inattention).

Procedure

As the current study reports on part of a broader study investigating the impact of sleep on memory consolidation, immediate memory was tested in the evening prior to sleep and delayed memory was tested the following morning.

Participants arrived at the research laboratory in the evening, having refrained from alcohol and caffeine from midday. The demographic questionnaire (see Appendix D), memory questionnaire and the DASS21 were completed before the neuropsychological tests were administered as ordered in Table 1. All participants were tested at the same time of day by the same investigator, who was trained in neuropsychological test administration. The testing session took approximately two hours and participants were given rest breaks as requested. The following morning (approximately nine hours later), the delayed component of the memory tests were administered, and blood samples were taken for serum progesterone levels.

Table 1

Schedule of Neuropsychological Testing and Estimated Administration Time

Order of Testing	Administration Time (mins)
Demographics and DASS21	5
WASI	30
TOMM	10
Motor Sequence Learning	10
Mirror-Tracing Task	10
Austin Maze	10
WMS-III	20
RAVLT	5
TOVA	20

Note. DASS21 = Depression Anxiety Stress Scale 21, WASI = Wechsler Abbreviated Scale of Intelligence, TOMM = Test of Memory Malingering, WMS-III = Wechsler Memory Scale – Third Edition, RAVLT = Rey Auditory Verbal Learning Test, TOVA = Test of Variables of Attention.

Statistical Analysis

All statistical analyses were performed with the Statistical Package for Social Sciences 15.0 (SPSS Inc., Chicago, Illinois). Data were checked for linearity and normality and non-normally distributed variables were transformed as appropriate. The few extreme univariate outliers found (z score > 3.29) were assigned a raw score one unit larger or smaller than the next most extreme score in the distribution, as recommended by Tabachnick and Fidell (2007). There were no extreme outliers on any of the WMS-III or RAVLT variables. A total of four third-trimester women, one first-trimester woman and one control woman were unable to complete the Mirror-Tracing Task due to its difficulty. TOVA data for one first-trimester woman were invalid due to an unanticipated disruption

during the fourth quarter of the test. Up until this point performance was within normal limits and therefore this participant was included in all other analyses. Chi-square tests were used to compare the pregnancy groups on demographic variables and subjective memory ability. One-way between-groups analysis of variance (ANOVA) was used to compare groups on the WMS-III subtests and the DASS21. One-way between-groups multivariate analysis of variance was used to compare groups on overall RAVLT and Austin Maze performance, with between-subjects effects indicating on which task elements the groups differed. Procedural memory was analysed with one-way analysis of covariance in order to control for existing differences in performance across the groups. A mixed 3 (group) x 4 (quarter) analysis of variance was used to analyse TOVA response time and response time variability. As progesterone is strongly linked to pregnancy status it could not be a covariate for ANOVA; therefore the effect of progesterone on memory was investigated using multiple regression. Effect sizes were calculated using eta-squared and partial eta-squared with 95% confidence intervals according to Smithson's (2003) method. Effect sizes of .01, .06 and .14 are considered small, medium, and large in magnitude. In order to determine which groups differed on ANOVAs, post hoc Newman-Keuls tests were set at a significance level of $p < .05$. All values are given in mean ± standard deviation or median and interquartile range (IQR) for non-normally distributed variables.

Results

Participants

The average age in years of the third-trimester ($M = 32.2$, $SD = 3.6$), first-trimester ($M = 29.4$, $SD = 3.3$) and control groups ($M = 29.3$, $SD = 5.9$) did not differ ($p = .09$). Further demographic details for each of the groups are presented in Table 2. The three groups did not differ in terms of handedness, education level, employment status or

whether they already had children. However, significantly more pregnant women were in a stable relationship as compared to the control group.

Table 2

Percentage of Participants in Each Demographic Category

	Control	T1	T3	χ^2	*p*
Right handed	87.5	95.0	96.2	1.60	.45
Relationship status				25.61**	<.001
Married/De facto	37.5	85	92.3		
In a Relationship	25	15	7.7		
Single	37.5	0	0		
Has children	25	55	46.2	4.43	.11
Tertiary educated	87.5	100	76.9	5.38	.07
Employment				8.20	.09
Full time	50	45	38.5		
Part time	50	50	38.5		
Unemployed	0	5	23		

Note. T1 = first trimester of pregnancy. T3 = third trimester of pregnancy.

** $p < .01$

Intellectual Functioning

The third-trimester, first-trimester and control groups were equivalent in terms of Verbal and Performance IQ, and subsequently Full Scale IQ did not differ across the groups (control: $M = 114.8$, $SD = 8.2$; T1: $M = 111.1$, $SD = 8.6$; T3: $M = 114.1$, $SD = 10.7$), $F(2,67) = 0.96$, $p = .39$).

Measures of Effort

All participants scored 45 or greater on the second trial of the TOMM, indicating that no participant was feigning memory difficulties.

Two control participants scored under the cut off of 136 on the Rarely Missed Index for Logical Memory Recognition. However, both of these participants scored above average on overall General Memory on the WMS-III and were deemed to be giving sufficient effort during testing. Several aspects of the RAVLT performance were analysed for signs of malingering or reduced effort. All participants recognised at least 11 words on the recognition component of the task (Berry & Schipper, 2008) and performed better on recognition than they had in the first trial (Greiffenstein, Baker, & Gola, 1996) and delayed recall (Bernard, Houston, & Natoli, 1993; Flowers, Sheridan, & Shadbolt, 1996) further indicating that sufficient effort was given towards testing. Also, no participant demonstrated "exceedingly poor learning" or "lack of primacy effect" as defined by Barrash, Suhr, and Manzel (2004) as part of their Exaggeration Index for auditory-verbal learning tests.

Episodic Memory

The means, standard deviations, significance levels and effect sizes with 95% confidence intervals for each between-group comparison on the WMS-III subtests are presented in Table 3. In terms of immediate memory, both the third- and first-trimester pregnant groups performed significantly worse on the Logical Memory task than did the control group; the effect size for this difference was large. Although the difference in scores across groups on the Verbal Paired Associates task was nearing significance, simple contrast tests showed that the third-trimester pregnant group scored significantly worse than the control group ($p = .018$). The groups did not differ on the Faces or Family Pictures subtests.

Table 3

Mean (± SD) of Immediate and Delayed Recall on the WMS-III Subtests for Each Group and Level of Significance and Effect Sizes for Between-Group Comparisons

Subtest	Control	T1	T3	F^a	*p*	partial $n^{2\,b}$
			Immediate Recall			
LM	$13.4 \pm 2.6_a$	$11.6 \pm 2.0_b$	$11.4 \pm 2.0_b$	5.95**	.004	.15 (.02, .27)
VPA	13.1 ± 1.9	12.4 ± 2.3	11.4 ± 3.0	2.94	.06	.08 (.00, .21)
Faces	11.0 ± 2.7	10.4 ± 1.6	11.7 ± 3.0	1.39	.26	.04 (.00, .14)
Fam Pic	11.3 ± 2.2	10.7 ± 2.8	9.9 ± 3.1	1.57	.22	.05 (.00, .15)
			Delayed Recall			
LM	$12.6 \pm 2.7_a$	$9.8 \pm 2.7_b$	$11.0 \pm 2.6_b$	6.44**	.003	.16 (.02, .30)
VPA[c]	13	13	13	1.93	.15	.05 (.00, .17)
	(12.3-13)	(10-13)	(10.8-13)			
Faces	12.4 ± 2.9	11.3 ± 2.7	12.6 ± 2.1	1.69	.19	.05 (.00, .16)
Fam Pic	11.3 ± 2.3	10.7 ± 3.2	9.8 ± 3.1	1.49	.23	.04 (.00, .15)
Aud Rec	$12.2 \pm 2.7_a$	$10.6 \pm 2.5_b$	$10.4 \pm 2.2_b$	3.71*	.03	.10 (.00, .23)

Note. WMS-III = Wechsler Memory Scale – Third Edition; T1 = first trimester of pregnancy; T3 = third trimester of pregnancy. Means in the same row that do not share subscripts differ at $p < .05$ in the Newman-Keuls significant difference comparison. LM = Logical Memory; VPA = Verbal Paired Associates; Fam Pic = Family Pictures; Aud Rec = Auditory Recognition.

[a] *df* = 2,67. [b] 95% Confidence intervals given in parentheses (upper, lower). [c] values given as *Mdn* (*IQR)* as variable was transformed, where *Mdn* = median, IQR = interquartile range.

* $p < .05$

** $p < .01$

On delay, the third- and first-trimester pregnant groups performed significantly worse on the Logical Memory task but not on the Verbal Paired Associates task, as compared to controls. Again, the effect size for the difference on Logical Memory was large. There was a ceiling effect on the Verbal Paired Associates task, with 92% of controls, 55% of first-trimester women and 62% of third-trimester women recalling all word pairs on delay (See Table 3). The third- and first-trimester pregnant groups also performed significantly worse on the recognition components of the auditory subtests than did the controls; the effect size for this difference was moderate to large. Again, the groups did not differ on the Faces or Family Pictures subtests.

The average number of words recalled on each trial of the RAVLT by each group is shown in Table 4. Measures of immediate memory on the RAVLT (Trial 1, Trial 5, total) differed significantly across the groups, *Wilks* = .82, $F(6,130) = 2.32$, $p = .04$, $n^2 = .10$, with confidence intervals from .00 to .16. Specifically, the control group recalled significantly more words on each trial and in total for the five trials compared to both pregnant groups (apart from Trial 3 on which the controls recalled significantly more words than the third-trimester group only). Measures of delayed memory on the RAVLT also differed significantly across groups, *Wilks*= .77, $F(6,130) = 2.96$, $p = .01$, $n^2 = .12$, with confidence intervals from .01 to .19. On delay, the control group recalled significantly more words, recognised significantly more words, and made fewer false-positives responses on recognition than did both pregnant groups.

Table 4

Mean (± SD) for RAVLT Recall and Recognition for Each Group and Level of Significance and Effect Sizes for Between-Group Comparisons

Subtest	Control	T1	T3	F^a	*p*	partial $n^{2\,b}$
Trial 1	$8.3 \pm 2.1_a$	$7.1 \pm 1.6_b$	$7.0 \pm 2.0_b$	3.28*	.04	.09 (.00, .22)
Trial 2	$13.0 \pm 1.6_a$	$11.0 \pm 2.2_b$	$11.3 \pm 2.1_b$	6.90**	.002	.17 (.03, .31)
Trial 3	$14.2 \pm 1.3_a$	$13.3 \pm 1.7_{ab}$	$13.0 \pm 2.0_b$	3.61*	.03	.10 (.00, .23)
Trial 4	$14.7 \pm 0.6_a$	$14.0 \pm 1.0_b$	$13.8 \pm 1.5_b$	4.53*	.01	.12 (.00, .26)
Trial 5	$15.0 \pm 0.2_a$	$14.2 \pm 1.1_b$	$13.9 \pm 1.7_b$	5.01**	.009	.13 (.01, .27)
Total	$65.1 \pm 4.3_a$	$59.5 \pm 6.0_b$	$58.9 \pm 7.8_b$	6.80**	.002	.17 (.03, .31)
Delay	$13.1 \pm 2.0_a$	$11.3 \pm 3.1_b$	$10.4 \pm 2.7_b$	7.18**	.002	.18 (.03, .32)
Recognition	$15\ (15\text{-}15)_a$	$15\ (14\text{-}15)_b$	$15\ (14\text{-}15)_b$	3.68*	.03	.10 (.00, .23)
Recog FP	$0\ (0\text{-}0.8)_a$	$1\ (0\text{-}3.5)_b$	$2\ (0\text{-}3)_b$	6.19**	.003	.16 (.02, .30)

Note. RAVLT = Rey Auditory Verbal Learning Test; Recog FP = recognition false-positive responses; T1 = first trimester of pregnancy; T3 = third trimester of pregnancy. Means in the same row that do not share subscripts differ at $p < .05$ in the Newman-Keuls significant difference comparison.

[a] $df = 2,67$. [b] 95% Confidence intervals given in parentheses (upper, lower).

* $p < .05$

** $p < .01$

The average number of errors made on each trial of the Austin Maze by each group is shown in Figure 1. Measures of spatial episodic memory on the Austin Maze task (Trial 10 errors, learning over trials, total errors) did not differ across the groups, *Wilks*= .95, $F(6,130) = 0.59$, $p = .74$, $n^2 = .03$, with confidence intervals from .00 to .05, and there was no difference in the number of errors made on delay, $F(2,67) = 1.34$, $p = .27$, $n^2 = .04$, with confidence intervals from .00 to .14.

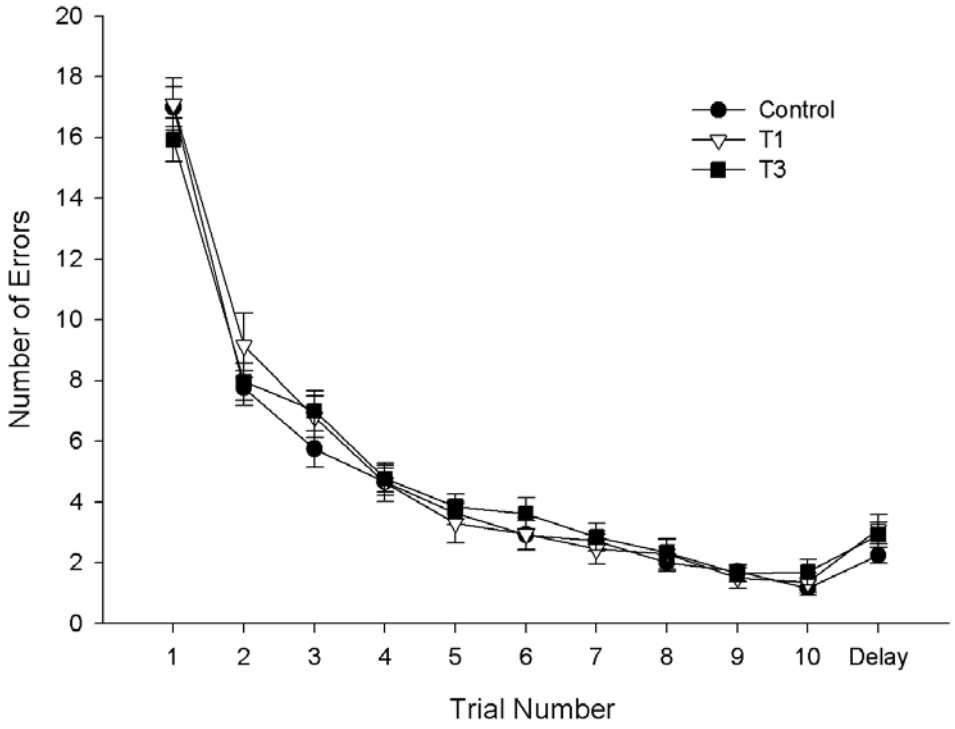

Figure 1. Mean number of errors (± *SE*) for the control (*n* = 24), T1 (*n* = 20), and T3 (*n* = 26) groups for each trial of the Austin Maze. There were no significant differences between groups on any trial of the task. T1 = first trimester of pregnancy. T3 = third trimester of pregnancy.

Procedural Memory

Motor Sequence Learning performance for each group is shown in Figure 2. There were no differences across groups on the posttraining number of sequences, $F(2,65) = 2.29$, $p = .11$, partial $n^2 = .07$, with confidence intervals from .00 to .19, or posttraining number of errors, $F(2,65) = 2.00$, $p = .14$, partial $n^2 = .06$, with confidence intervals from .00 to .18, after controlling for baseline scores. The difference in number of sequences on delay after controlling for posttraining scores was nearing significance, $F(2,65) = 2.95$, $p = .06$, partial $n^2 = .08$, with confidence intervals from .00 to .21, with simple contrast tests revealing the control group performed significantly better than the third-trimester group ($p = .02$). There were no differences across the groups on errors

made on delay after controlling for posttraining scores, $F(2,65) = 2.37$, $p = .10$, partial $n^2 = .07$, with confidence intervals from .00 to .19.

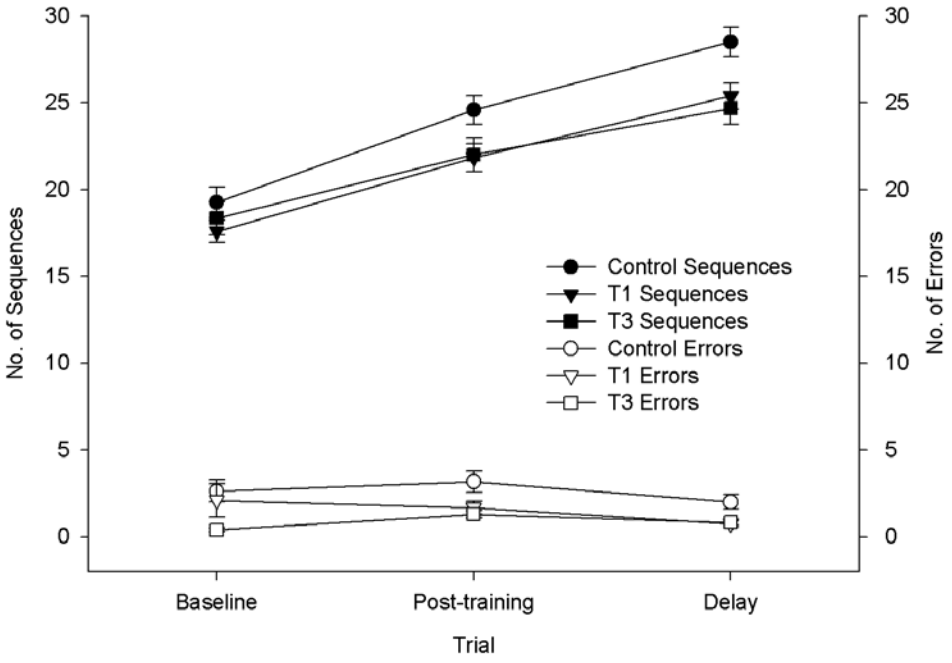

Figure 2. Mean number of sequences (± *SE*) and mean number of errors (± *SE*) for the control ($n = 24$), T1 ($n = 20$), and T3 ($n = 26$) groups for baseline, for posttraining and on delay for the Motor Sequence Learning task. After controlling for posttraining performance, the control group completed significantly more sequences than the T3 group on delay ($p = .02$). T1 = first trimester of pregnancy. T3 = third trimester of pregnancy.

Mirror-Tracing Task performance for each group is shown in Figure 3. No differences across groups were found on time taken to trace the star at posttraining, after controlling for baseline time, $F(2,60) = 1.16$, $p = .32$, partial $n^2 = .04$, with confidence intervals from .00 to .14, or on delay after controlling for posttraining time, $F(2,60) = 1.54$, $p = .22$, partial $n^2 = .05$, with confidence intervals from .00 to .17. There were no differences across groups on posttraining number of errors after controlling for baseline errors, $F(2,60) = .80$, $p = .45$, partial $n^2 = .03$, with confidence intervals from .00 to .12, or

on delay after controlling for posttraining errors, $F(2,60) = 1.46$, $p = .24$, partial $n^2 = .05$, with confidence intervals from .00 to .16.

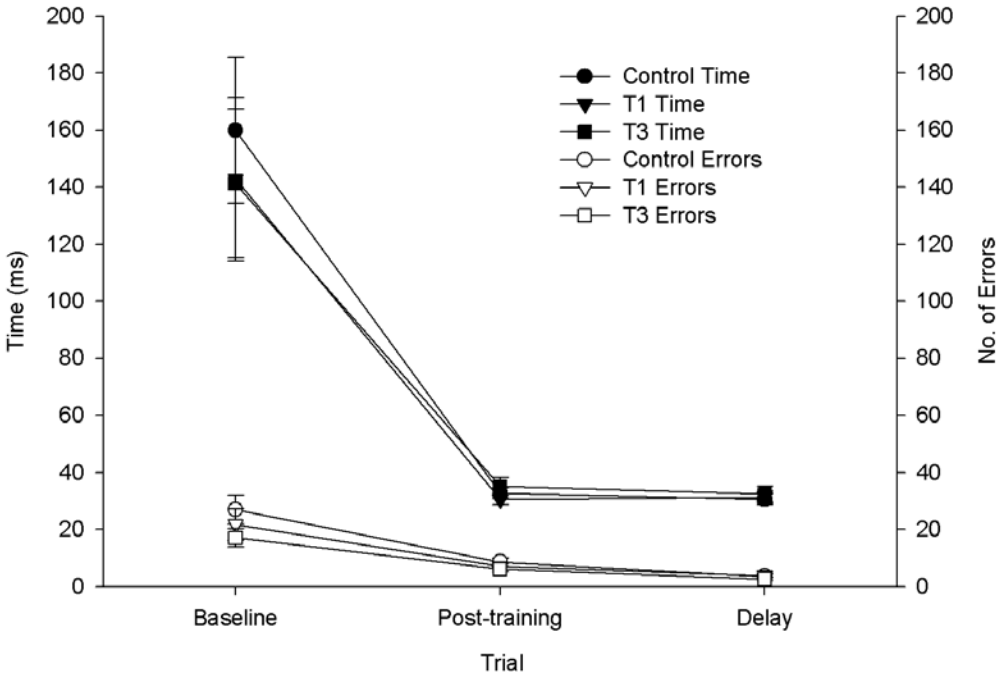

Figure 3. Mean tracing time (± *SE*) and mean number of errors (± *SE*) for the control (*n* = 24), T1 (*n* = 20), and T3 (*n* = 26) groups for baseline, for posttraining and on delay for the Mirror-Tracing Task. The groups did not differ on any trial of the task. T1 = first trimester of pregnancy. T3 = third trimester of pregnancy.

Attention

The average number of omission and commission errors made by each group did not differ on any quarter of the test, and subsequently the total omission errors (control: $M = 0.8$, $SD = 2.5$; T1: $M = 0.4$, $SD = 0.8$; T3: $M = 0.5$, $SD = 0.7$) and commission errors (control: $M = 8.5$, $SD = 6.2$; T1: $M = 9.9$, $SD = 8.0$; T3: $M = 11.7$, $SD = 8.7$) did not differ, *Wilks*= .93, $F(4,130) = 1.15$, $p = .34$.

As shown in Figure 4, there was no interaction effect between the three groups and test quarter on the T.O.V.A. for response time, *Wilks*= .98, $F(6,128) = 0.21$, $p = .97$,

and response time variability, *Wilks*= .93, $F(6,128) = 0.80$, $p = .57$, indicating that the pattern of performance over time was similar across groups. A nonsignificant between-subjects effect indicated that the groups did not differ overall on response time, $F(2,66)= 0.98$, $p = .31$, or response time variability, $F(2,66)= 1.36$, $p = .26$.

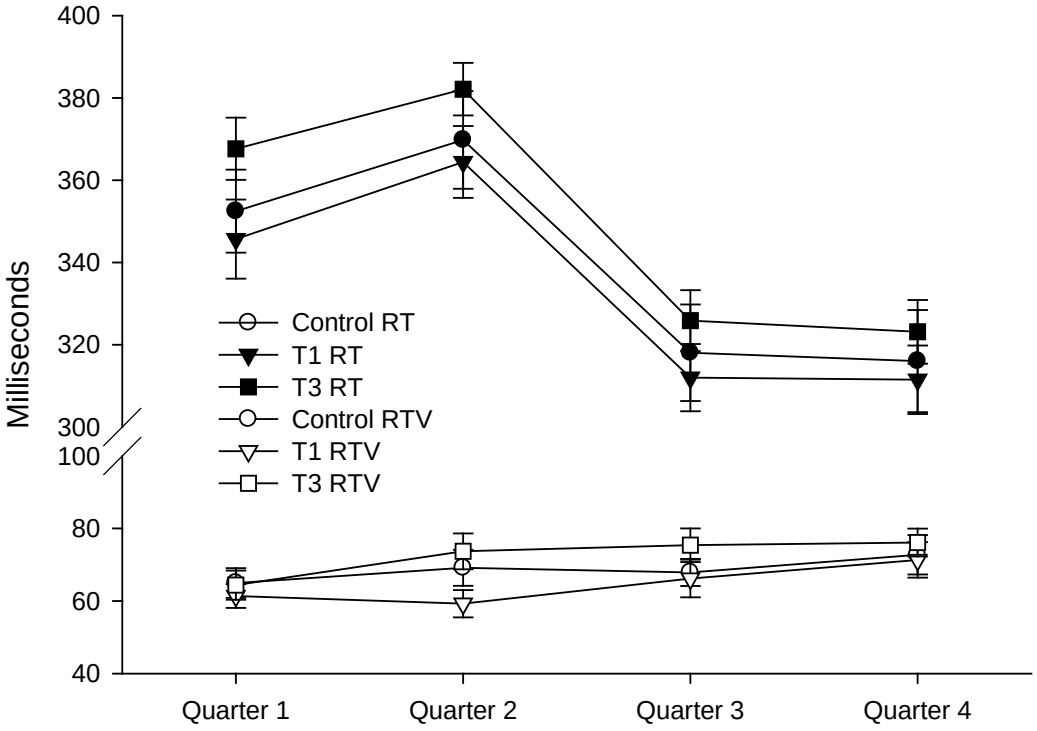

Figure 4. Mean response time (RT) and mean response time variability (RTV) for the control ($n = 24$), T1 ($n = 19$), and T3 ($n = 26$) groups for each quarter of the Test of Variables of Attention (TOVA). The groups performed equivalently on each quarter of the test. Vertical lines depict standard errors of the mean. T1 = first trimester of pregnancy. T3 = third trimester of pregnancy.

Progesterone

Progesterone level was significantly higher in the third-trimester pregnant group (*Mdn* = 413nmol/L, *IQR* = 311.5-509.3) than in the first-trimester pregnant group (68.5, 58.6-82.3), which was significantly higher than that in the control group (4.2, 2.6-7.9);

$F(2,65) = 392.38$, $p < .001$, $n^2 = 0.92$. Within the control group, progesterone level was not associated with verbal, visual or procedural memory. After combining the third- and first-trimester pregnant groups, progesterone significantly explains an additional 19.5% of the variance in Logical Memory immediate recall, $F(1,42) = 10.26$, $p = .003$, and 13% in the Trial 1 score on the RAVLT, $F(1,42) = 6.26$, $p = .016$, over and above that explained by number of weeks gestation. In both instances, increased progesterone level was related to decreased memory performance ($pr = -.44$ and $-.36$ respectively).

Mood State

The average DASS21 scores for each group are shown in Table 5. Mood did not differ across the groups, *Wilks* = .88, $F(6,128) = 1.46$, $p = .20$, $n^2 = .06$., and depression, anxiety and stress did not show any significant associations with memory variables.

Primiparous versus Multiparous

Within the pregnant sample, there were 23 primiparous women (T3: $n = 14$; T1: $n = 9$) and 23 multiparous women (T3: $n = 12$; T1: $n = 11$). Comparison of the primiparous and multiparous participants on measures of IQ, episodic memory and procedural memory revealed no significant differences.

Table 5

Median Scores on the DASS21 for Each Group and Level of Significance and Effect Sizes for Between-Group Comparisons

	Control	T1	T3	F^a	p	n^2
Depression	2 (0-4)	2 (2-5.5)	2 (0-4)	.43	.65	.01
Anxiety	1 (0-4)	2 (0-4)	4 (0-6)	1.72	.19	.05
Stress [b]	9.6 ± 5.9	8.4 ± 7.9	8.3 ± 6.3	.26	.77	.01

Note. Interquartile range (IQR) in parentheses. DASS21 = Depression Anxiety Stress Scale – short version; T1 = first trimester of pregnancy; T3 = third trimester of pregnancy. Normal range: Depression = 0-9, Anxiety = 0-7, Stress = 0-14.

[a] $df = 2,67$. [b] Values given as mean ± standard deviation.

Subjective Memory Abilities

Both pregnant groups reported a significantly greater fall in memory quality on average than did the control group. However, as shown in Table 6, this was because the third-trimester group rated their general memory as significantly better than controls, but their current memory as equivalent.

A total of 60% of women in the first trimester and 80.8% of women in the third trimester of pregnancy reported a change in their ability to recall or remember things since becoming pregnant, as compared to only 25% of controls ($\chi^2 = 15.94$, $p < .001$). A total of 75% of women in the first trimester of pregnancy reported a change in attention and concentration, which was significantly more than the third-trimester group (61.5%) and controls (33.3%; $\chi^2 = 8.25$, $p = .02$). Memory lapses were reported by 65% of the first-trimester group, significantly more than the third-trimester (46.2%) and control groups (25%; $\chi^2 = 7.13$, $p = .03$).

Table 6

Mean (± SD) for Reported Memory Quality for Each Group and Level of Significance and Effect Sizes for Between-Group Comparisons

	Control	T1	T3	F^a	p	n^2
Past 2 weeks	6.6 ± 1.2	6.0 ± 1.6	6.5 ± 2.0	.96	.39	.03
Generally	$7.1 \pm 1.1_a$	$7.5 \pm 1.6_{ab}$	$8.3 \pm 1.2_b$	5.19**	.008	.13
Difference	$0.4 \pm 0.8_a$	$1.5 \pm 1.2_b$	$1.7 \pm 1.5_b$	7.70**	.001	.19

Note. Memory quality was rated on a scale of 1 (*extremely poor*) to 10 (*extremely good*). Means in the same row that do not share subscripts differ at $p < .05$ in the Newman-Keuls significant difference comparison. T1 = first trimester of pregnancy; T3 = third trimester of pregnancy.

[a] $df = 2,67$.

** $p < .01$

Discussion

The results of the current study indicate that women in the first and third trimester of pregnancy demonstrate reduced performance on episodic memory tasks compared to the control group. In particular, pregnant women performed significantly worse on verbal memory tasks comprising of paragraph recall, word-list recall and verbal recognition than did nonpregnant women, supporting previous work (de Groot, et al., 2006; Keenan, et al., 1998; Sharp, et al., 1993). In addition, these group differences persisted after a long delay of time. The magnitudes of the effect sizes of these differences were all moderate to large, indicating that the relationship between pregnancy and reduced verbal memory performance is fairly strong. Apart from the word-pairs task (on which only third-trimester women had difficulty), the first- and third-trimester pregnant women performed similarly on verbal memory tasks, supporting earlier studies showing consistent performance spanning across pregnancy trimesters (de Groot, et al., 2003; de Groot, et al., 2006; Sharp, et al., 1993). Primiparous and multiparous women did not perform

differently on any memory task, supporting the contention that memory performance is unrelated to prior pregnancy history (Casey, et al., 1999; McDowall & Moriarty, 2000; Parsons, et al., 2004; Sharp, et al., 1993).

Our findings contrast those that found no differences on verbal memory tasks between pregnant women and controls (Brindle, et al., 1991; Casey, et al., 1999; Crawley, et al., 2003; Janes, et al., 1999). However, closer inspection of these methodologies revealed that most measured only recognition memory, whilst another used word lists comprising semantic categories presented in both verbal and visual modalities. These cued memory tasks are less difficult than free recall and may explain why no differences in performance between pregnant women and controls could be found.

Pregnant women did not show deficits on any of the visual memory tasks, performing similarly to the nonpregnant women. This study is the first to investigate procedural memory performance during pregnancy. Overall, both pregnant groups were unimpaired on measures of procedural memory, apart from a slightly slower performance by the third-trimester pregnant group on the delayed component of Motor Sequence Learning.

Pregnant women were more likely than controls to notice a recent change in their memory quality. However, as found by Christensen et al. (1999), this difference in the women's ratings appear due to pregnant women over-rating their memory level before pregnancy rather than to underrating their current memory.

Successful completion of memory tasks involves effective encoding, storage and retrieval of information. Reduced immediate recall on all verbal memory tasks by the pregnant groups relative to the controls suggests deficiencies in the encoding process, resulting in a relatively decreased immediate memory span. Despite a reduced immediate memory span, pregnant women displayed normal rates of learning over trials. Comparing the delayed scores to the immediate scores, the first-trimester group showed a higher

degree of forgetting on the paragraph recall task, whereas the third-trimester group had a higher degree of forgetting on the word-list task than did the nonpregnant women. Reduced recognition memory on story recall further implicates encoding problems, but satisfactory recognition memory on the word list suggests that retrieval problems may also contribute to memory difficulties. A high number of false positive responses on recognition suggests a disorganised encoding style, making retrieval less reliable.

The potential cause of memory-related difficulties during pregnancy is up for debate. The possibility that pregnant women are more susceptible to attentional fluctuations was not supported by our findings. First, pregnant women did not show deficits in sustained attention on testing, and verbal recall differences persisted despite this. However, it is acknowledged that testing in the laboratory setting differs from the real world in which pregnant women may be more introspective and readily distractible. Mood state was also unrelated to memory performance, with relatively substandard verbal recall in the absence of mood disturbance demonstrating that even pregnant women with sound mental health may experience memory-related difficulties. In regard to the potential influence of hormonal change, higher progesterone levels were weakly to moderately related to poorer performance on immediate paragraph and word-list recall. However, progesterone level explained less than 20% of the variance in these tasks, implying that several other factors are involved.

There is also the discordant finding that only verbal episodic memory was affected within the pregnant groups, and not visual episodic or procedural memory. Although our study design does not allow for attribution of causality to this discrepancy, we could speculate that as different kinds of memory are thought to have different functional and neuroanatomical systems (Smith, 2001), some neurotransmitter or hormone is acting differently on those areas involved in verbal memory (such as the left hippocampus and nearby cortical areas), as compared to the brain regions thought to be involved in visual

and procedural memory (such as the right hippocampus and temporal lobe, and the neostriatum; Knowlton, Mangels, & Squire, 1996). Conversely, the differences between verbal and visual memory performance may be the result of differences in task difficulty, in that pregnant women may only be underperforming on tasks perceived as more challenging and overwhelming. As mentioned, this study represents the initial findings of an investigation into the impact of sleep on memory consolidation, and it is possible that sleep difficulties during pregnancy explain group differences on delayed memory performance. This hypothesis is currently under investigation by the authors.

It has been argued that women may subconsciously perform more poorly due to cultural expectations of cognitive decline during pregnancy (Crawley, et al., 2008). Incorporating well-validated tests of malingering into our methodology revealed that all pregnant participants in this study were giving sufficient conscious effort towards testing. Unfortunately, sensitivity issues with symptom validity tests such as the TOMM have been raised (Greve, Ord, Curtis, Bianchini, & Brennan, 2008), although the TOMM has been shown to have similar predictive rates to those of other tests of malingering (Greiffenstein, Greve, Bianchini, & Baker, 2008). Furthermore, a slightly diminished performance resulting from negative cognitive expectations may go undetected by symptom validity testing, and therefore this cannot be ruled out as a contributing factor.

The results from the current study should be interpreted with caution. The participant groups in this study averaged a Full Scale IQ within the above-average range and were well educated. While above-average intellectual functioning generally translated to above-average verbal memory scores for the control group, observed weaknesses on verbal recall and recognition in the pregnant groups generally reduced their performances to within the average range. Although these group differences are statistically significant, the question is whether they are clinically important. Despite the long test battery administered, the pregnant women in this study were still able to perform

within normal limits. However, 72% of the pregnant women reported a change in their ability to recall or remember things since becoming pregnant. It is possible that even these small differences may be noticeable, with the pregnant woman finding that her abilities are not up to their usual standard.

Although minor, the observed shortfalls on verbal episodic memory tests and even the perception of memory difficulties may have implications for tasks of everyday living for pregnant women. Pregnant women may lack confidence in their memory abilities and benefit from the use of compensatory techniques such as making lists and using pictorial aids. Differences in verbal memory between the pregnant and nonpregnant women were mostly due to a reduced immediate memory span, so those who feel their memory is below par may want to avoid overwhelming themselves with too much information at one time. Given the inconsistencies in current literature, women should be reassured that significant memory loss is not a proven "side effect" of pregnancy, and they should generally be able to function as per usual. On this note, visual memory, repetitive learning and procedural memory remain unaffected. Approaching motherhood, the pregnant woman has much to learn and many new skills to master, so her ability to improve learning with repetition and to master "how to" tasks without difficulty is important.

A limitation of the current study is its cross-sectional rather than longitudinal design, mostly as a consequence of the broader study that involves overnight sleep studies. Longitudinal memory research is also difficult due to a paucity of rigorous memory tests with multiple equivalent forms (Lezak, et al., 2004). In this study, the delay period for memory testing was approximately nine hours compared to 30 minutes for standardised testing. Our results therefore may be difficult to compare to previous and future research in this area. However, even with a lengthy delay period, performances were generally within the normal ranges, and it could be argued that a longer delay period

is more realistic to real-world demands than the standard 30 minutes. Recruitment difficulties due to the broader study requirements resulted in a reduced sample size. The sample size in this study had less than a 50% chance of finding a medium effect of .06 at a significance level of .05. There is potential that small differences in visual memory may have been undetected due to insufficient power. Measures of procedural memory can be criticised because although they mimic true procedural memory, they may tap into other learning and memory processes and may include components of executive functioning. Tasks such as those used in this study may also be limited by their generalisability to real-world procedural memory tasks, such as riding a bike or driving a car.

Future research is needed to disentangle the discrepant findings on research into memory during pregnancy. If pregnancy can be associated with a particular pattern of memory dysfunction, then ways to overcome their impact on everyday functioning can be developed. The cause of memory differences during pregnancy such as those found in this study still remains to be discovered.

The current study has demonstrated that early and late pregnancy is associated with reduced verbal memory performance compared to nonpregnant women, mostly as a consequence of a reduced immediate span. On the other hand, visual and procedural memory remains intact. Attention difficulties and mood disturbance were ruled out as possible contributors to these findings, but progesterone was found to play a small role. The implications of this research are important for prenatal health and education, in that pregnant women can be reassured that any memory difficulties experienced should be minor, and that those with actual or even perceived memory problems can be taught compensatory techniques to improve confidence in their abilities.

Acknowledgments

The authors would like to thank the staff at the Austin Health Sleep Laboratory for their support of this project and we appreciate the valuable contribution made by each of the research participants.

This research was funded by La Trobe University and the Austin Health Medical Research Foundation. The authors have indicated no financial conflicts of interest.

References

Andersson, L., Sundström-Poromaa, I., Bixo, M., Wulff, M., Bondestam, K., & åström, M. (2003). Point prevalence of psychiatric disorders during the second trimester of pregnancy: a population-based study. *American Journal of Obstetrics and Gynecology, 189(1)*, 148-154.

Barrash, J., Suhr, J., & Manzel, K. (2004). Detecting poor effort and malingering with an expanded version of the Auditory Verbal Learning Text (AVLTX): Validation with clinical samples. *Journal of Clinical and Experimental Neuropsychology, 26*, 125-140.

Bearden, C. E., Glahn, D. C., Monkul, E. S., Barrett, J., Najt, P., Villarreal, V., et al. (2006). Patterns of memory impairment in bipolar disorder and unipolar major depression. *Psychiatry Research, 142(2-3)*, 139-150.

Bernard, L. C., Houston, W., & Natoli, L. (1993). Malingering on neuropsychological memory tests: potential objective indicators. *Journal of Clinical Psychology, 49*, 45-53.

Berry, D. T. R., & Schipper, L. J. (2008). Assessment of feigned cognitive impairment using standard neuropsychological tests. In R. Rogers (Ed.), *Clinical assessment of malingering and deception* (3rd ed.). New York: The Guilford Press.

Brett, M., & Baxendale, S. (2001). Motherhood and memory: A review. *Psychoneuroendocrinology, 26*, 339-362.

Brindle, P. M., Brown, M. W., Brown, J., Griffith, H. B., & Turner, G. M. (1991). Objective and subjective memory impairment in pregnancy. *Psychological Medicine, 21*, 647-653.

Buckwalter, J. G., Stanczyk, F. Z., McCleary, C. A., Bluestein, B. W., Buckwalter, D. K., Rankin, K. P., et al. (1999). Pregnancy, the postpartum, and steroid hormones: effects on cognition and mood. *Psychoneuroendocrinology, 24*, 69-84.

Casey, P. (2000). A longitudinal study of cognitive performance during pregnancy and new motherhood. *Archives of Women's Mental Health, 3*, 65-76.

Casey, P., Huntsdale, C., Angus, G., & Janes, C. (1999). Memory in pregnancy. II: Implicit, incidental, explicit, semantic, short-term, working and prospective memory in primigravid, multigravid and postpartum women. *Journal of Psychosomatic Obstetrics and Gynaecology, 20*, 158-164.

Christensen, H., Leach, L. S., & Mackinnon, A. (2010). Cognition in pregnancy and motherhood: Prospective cohort study. *The British Journal of Psychiatry, 196*, 126-132.

Christensen, H., Poyser, C., Pollitt, P., & Cubis, J. (1999). Pregnancy may confer a selective cognitive advantage. *Journal of Reproductive and Infant Psychology, 17(1)*, 7-25.

Crawley, R. A. (2002). Self-perception of cognitive changes during pregnancy and the early postpartum: Salience and attentional effects. *Applied Cognitive Psychology, 16*, 617-633.

Crawley, R. A., Dennison, K., & Carter, C. (2003). Cognition in pregnancy and the first year post-partum. *Psychology and Psychotherapy, 76*, 69-84.

Crawley, R. A., Grant, S., & Hinshaw, K. (2008). Cognitive changes in pregnancy: Mild decline or societal stereotype? *Applied Cognitive Psychology, 22*, 1142-1162.

de Groot, R. H. M., Hornstra, G., Roozendaal, N., & Jolles, J. (2003). Memory performance, but not information processing speed, may be reduced during early pregnancy. *Journal of Clinical and Experimental Neuropsychology, 25(4)*, 482-488.

de Groot, R. H. M., Vuurman, E. F. P. M., Hornstra, G., & Jolles, J. (2006). Differences in cognitive performance during pregnancy and early motherhood. *Psychological Medicine, 36*, 1023-1032.

Dohanich, G. (2003). Ovarian steroids and cognitive function. *Current Directions in Psychological Science, 12(2)*, 57-61.

Flowers, K. A., Sheridan, M. R., & Shadbolt, H. (1996). Simulation of amnesia by normals on the Rey Auditory Verbal Learning Test. *Journal of Neurolinguistics, 9*, 147-156.

Freeman, E. W., Weinstock, L., Rickels, K., Sondheimer, S. J., & Coutifaris, C. (1992). A placebo-controlled study of effects of oral progesterone on performance and mood. *British Journal of Clinical Pharmacology, 33*, 293-298.

Greiffenstein, M. F., Baker, J., & Gola, T. (1996). Comparison of multiple scoring methods for Rey's malingered amnesia measures. *Archives of Clinical Neuropsychology, 11(4)*, 283-293.

Greiffenstein, M. F., Greve, K. W., Bianchini, K. J., & Baker, W. J. (2008). Test of Memory Malingering and Word Memory Test: A new comparison of failure concordance rates. *Archives of Clinical Neuropsychology, 23*, 801-807.

Greve, K. W., Ord, J., Curtis, K. L., Bianchini, K. J., & Brennan, A. (2008). Detecting malingering in traumatic brain injury and chronic pain: a comparison of three forced-choice symptom validity tests. *The Clinical Neuropsychologist, 22(5)*, 896-918.

Henry, J. D., & Rendell, P. G. (2007). A review of the impact of pregnancy on memory function. *Journal of Clinical and Experimental Neuropsychology, 29(8)*, 793-803.

Janes, C., Casey, P., Huntsdale, C., & Angus, G. (1999). Memory in pregnancy. I: Subjective experiences and objective assessment of implicit, explicit and working memory in primigravida and primiparous women. *Journal of Psychosomatic Obstetrics and Gynaecology, 20*, 80-87.

Kampen, D. L., & Sherwin, B. B. (1994). Estrogen use and verbal memory in healthy postmenopausal women. *Obstetrics and Gynecology, 83(6)*, 979-983.

Keenan, P. A., Yaldoo, D. T., Stress, M. E., Fuerst, D. R., & Ginsburg, K. A. (1998). Explicit memory in pregnant women. *American Journal of Obstetrics and Gynecology, 179*, 731-737.

Killgore, W. I. S., & DellaPietra, L. (2000). Using the WMS-III to detect malingering: Empirical validation of the Rarely Missed Index (RMI). *Journal of Clinical and Experimental Neuropsychology, 22(6)*, 761-771.

Knowlton, B. J., Mangels, J. A., & Squire, L. R. (1996). A neostriatal habit learning system in humans. *Science, 273(5280)*, 1399-1402.

Lee, A. M., Lam, S. K., Sze Mun Lau, S. M., Chong, C. S., Chui, H. W., & Fong, D. Y. (2007). Prevalence, course and risk factors for antenatal anxiety and depression. *Obstetrics and Gynecology, 110(5)*, 1102-1112.

Lezak, M. D., Howieson, D. B., & Loring, D. W. (2004). *Neuropsychological Assessment* (4th ed.). New York: Oxford University Press, Inc.

Lovibond, S. H., & Lovibond, P. F. (1995). *Manual for the Depression Anxiety Stress Scales* (2nd ed.). Sydney: Psychology Foundation.

McDowall, J., & Moriarty, R. (2000). Implicit and explicit memory in pregnant women: An analysis of data-driven and conceptually driven processes. *The Quarterly Journal of Experimental Psychology, 53A(3)*, 729-740.

Milner, B. (1965). Visually-guided maze learning in man: Effects of bilateral hippocampal bilateral frontal, and bilateral cerebral lesions. *Neuropsychologia, 3*, 317-338.

Parsons, C., & Redman, S. (1991). Self-reported cognitive change during pregnancy. *The Australian Journal of Advanced Nursing, 9(1)*, 20-29.

Parsons, T. D., Thompson, E., Buckwalter, D. K., Bluestein, B. W., Stanczyk, F. Z., & Buckwalter, J. G. (2004). Pregnancy history and cognition during and after pregnancy. *International Journal of Neuroscience, 114*, 1099-1110.

Priest, S. R., Austin, M. P., Barnett, B. B., & Buist, A. (2008). A psychosocial risk assessment model (PRAM) for use with pregnant and postpartum women in primary care settings. *Archives of Women's Mental Health, 11(5-6)*, 307-317.

Reitan, R. (1979). *Manual for Administration of Neuropsychological Test Batteries for Adults and Children*. Tucson: Reitan Neuropsychological Laboratory.

Rendell, P. G., & Henry, J. D. (2008) Prospective-memory functioning is affected during pregnancy and postpartum. *Journal of Clinical and Experimental Neuropsychology, 30(8)*, 913-919.

Rey, A. (1964). *L'examen clinique on psychologie [Clinical tests in psychology]*. Paris: Presses Universitaires de France.

Sharp, K., Brindle, P. M., Brown, M. W., & Turner, G. M. (1993). Memory loss during pregnancy. *British Journal of Obstetrics and Gynaecology, 100*, 209-215.

Sherwin, B. (1997). Estrogen effects on cognition in menopausal women. *Neurology, 48(Suppl. 7)*, S21-S26.

Shetty, D. N., & Pathak, S. S. (2002). Correlation between plasma neurotransmitters and memory loss in pregnancy. *The Journal of Reproductive Medicine, 47*, 494-496.

Silber, M., Almkvist, O., Larsson, B., & Uvnas-Moberg, K. (1990). Temporary peripartal impairment in memory and attention and its possible relation to oxytocin concentration. *Life Sciences, 47*, 57-65.

Smith, C. (2001). Sleep states and memory processes in humans: procedural versus declarative memory systems. *Sleep Medicine Reviews, 5(6)*, 491-506.

Smithson, M. (2003). *Confidence Intervals*. Belmont, CA: Sage.

Sweeney, J. A., Kmiec, J. A., & Kupfer, D. J. (2000). Neuropsychologic impairments in bipolar and unipolar mood disorders on the CANTAB neurocognitive battery. *Biological Psychiatry, 48*, 674-685.

Tabachnick, B. G., & Fidell, L. S. (2007). *Using multivariate statistics* (5th ed.). Boston: Pearson Education, Inc.

The Psychological Corporation. (1999). *Wechsler Abbreviated Scale of Intelligence (WASI)*. San Antonio, TX: The Psychological Corporation.

Tombaugh, T. N. (1996). *Test of memory malingering (TOMM)*. New York: Multi Health Systems.

Walker, M . P ., B rakefield, T ., M organ, A ., H obson, J . A ., & S tickgold, R . (2002). Practice with sleep makes perfect: sleep-dependent motor skill learning. *Neuron, 35*, 205-211.

Walsh, K . (1985). *Understanding brain damage. A primer of neuropsychological evaluation*. London: Churchill Livingstone.

Wechsler, D. (1997). *Wechsler Memory Scale. Third Edition manual*. San Antonio, TX: The Psychological Corporation.

Chapter 3

Decreased Sleep Efficiency, Increased Wake after Sleep Onset and Increased Cortical Arousals in Late Pregnancy

Manuscript published in the *Australian and New Zealand Journal of Obstetrics and Gynaecology*, 2011, Vol 51, pp 38-46 (see Appendix H).

Preface

The initial findings from Chapter 2 showed reduced verbal episodic memory performance during the first and third trimester of pregnancy, when compared to nonpregnant women. The most commonly assumed explanation for observed memory impairments in pregnancy has been hormonal change; however there is no evidence as yet to support this. In addition to memory complaints, a frequently reported problem during pregnancy is sleep disturbance. One common theory is that memory consolidation occurs during sleep, and thus disruptions of sleep should also disrupt the long-term storage of memories.

In order to see whether sleep disruption during pregnancy is responsible for observed memory impairments, this study first needs to confirm that changes in sleep do occur during pregnancy. The main purpose of Chapter 3 is to investigate both objective and subjective changes in sleep patterns associated with the first and third trimester of pregnancy, when compared to the nonpregnant state.

Decreased Sleep Efficiency, Increased Wake after Sleep Onset and Increased Cortical Arousals in Late Pregnancy

Short title (running head) – Decreased Sleep Efficiency in Late Pregnancy

Ms. Danielle L. WILSON, BA (Hons.)

Master of Science Candidate/Sleep Scientist

School of Psychological Science, La Trobe University, Bundoora, Victoria, Australia.

Institute for Breathing and Sleep, Austin Health, Heidelberg, Victoria, Australia.

Dr. Maree BARNES, MBBS

Sleep Physician and Senior Research Fellow

Institute for Breathing and Sleep, Austin Health, Heidelberg, Victoria, Australia.

Department of Medicine, University of Melbourne, Parkville, Victoria, Australia.

Dr. Lenore ELLETT, MBBS

Obstetrics and Gynaecology Registrar

Department of Obstetrics and Gynaecology, Mercy Hospital for Women, Heidelberg, Victoria, Australia.

Prof. Michael PERMEZEL MD MRCP (UK) FRANZCOG

Professor and Head

Department of Obstetrics and Gynaecology, Mercy Hospital for Women, Heidelberg, Victoria, Australia.

Department of Obstetrics and Gynaecology, University of Melbourne, Parkville, Victoria, Australia.

Mr. Martin JACKSON, MSc

Clinical Neuropsychologist and Lecturer

School of Psychological Science, La Trobe University, Bundoora, Victoria, Australia.

Prof. Simon F. CROWE, PhD

Professor of Neuroscience and Clinical Neuropsychology

School of Psychological Science, La Trobe University, Bundoora, Victoria, Australia.

Address correspondence to: Simon F. Crowe, School of Psychological Science, La Trobe University, Bundoora, VIC, 3086, Australia. Tel: 613 9479 1380; Fax: 613 9479 1956; E-mail: s.crowe@latrobe.edu.au

If corresponding author unavailable, address correspondence to: Danielle Wilson, Ground Floor Bowen Centre, Austin Health, Studley Rd, Heidelberg, VIC, 3084, Australia. Tel: 613 9496 3517; Fax: 613 9496 5124; E-mail: danielle.wilson@austin.org.au

Word count – 4115

Abstract Word Count – 236

Keywords: Pregnancy, polysomnography, sleep efficiency, cortical arousal, awakenings.

Background: Anecdotal reports of sleep disturbance during pregnancy are abundant, however objective measurement of sleep changes has so far produced conflicting results.

Aims: To objectively measure sleep architecture and investigate subjective sleep quality in the first and third trimester of pregnancy, as compared to the nonpregnant state.

Methods: Twenty-seven women in the third trimester of pregnancy, 21 women in the first trimester of pregnancy and 24 nonpregnant control women underwent overnight polysomnography and completed questionnaires regarding sleep quality and mood.

Results: Women in the third trimester of pregnancy had poorer sleep efficiency, more awakenings, less Stage 4 sleep, more Stage 1 sleep and fewer minutes in rapid eye movement (REM) sleep when compared to the control group. Cortical arousals were seen more often during pregnancy, particularly in response to respiratory events and limb movements. Sleep during the first trimester was affected to a lesser extent, with more wake time after sleep onset and less Stage 4 sleep when compared to the controls.

Conclusions: Sleep during pregnancy is compromised by higher amounts of wake and cortical arousals leading to sleep fragmentation, with greater amounts of light sleep and less deep sleep. Mood state did not have an effect on sleep. Given the impact of sleep on well-being, this study increases our understanding of the characteristics of sleep during pregnancy, to help recognise when severe sleep disruption may warrant referral to a specialist for appropriate diagnosis and treatment.

Pregnancy is marked by considerable physiological changes and a multitude of symptoms, many of which are likely to disrupt sleep. Research utilising self-reported questionnaires has demonstrated that sleep complaints are more frequent during pregnancy as compared to the nonpregnant state[1] and that sleep disturbance increases as pregnancy progresses.[2-5] Frequent night awakenings are reported by as many as 90% of women by the end of pregnancy, [3] due to general discomfort and pain, urinary frequency, nausea and vomiting, foetal movements and shortness of breath. [2,3] However, self-report methodologies are limited by their subjective nature and may be prone to bias, as the pregnant women may be more aware of changes in sleeping habits due to cultural expectations of sleep-deprivation during pregnancy. Furthermore, people who believe they have a sleeping problem will tend to overestimate the extent of their sleep disruption. [6,7]

Polysomnography (PSG) has been utilised to objectively measure sleep changes during pregnancy. The use of electroencephalography (EEG) together with the use of electromyogram (EMG) and electrooculogram (EOG) allows sleep to be classified into different stages according to objective criteria.[8] Rapid eye movement (REM) sleep is characterised by cortical activation, the presence of rapid eye movements and a global abolition of muscle tone,[9] and is often associated with dreaming. Non-REM (NREM) sleep is subdivided into four stages; Stages 1 and 2 correspond to light sleep and Stages 3 and 4 are often referred to as slow wave sleep (SWS) or deep sleep and show an increase in slow oscillations and decreased muscle tone as sleep deepens.[9]

Alterations in REM sleep associated with pregnancy have ranged from a reduction compared to nonpregnant controls,[10,11] a reduction from early to late pregnancy,[12] through to showing no significant differences.[9,13,14] SWS changes during pregnancy vary from a decrease in comparison to prepregnancy baseline measures[13] and nonpregnant women,[11,14,15] to no consistent changes across trimesters[12] and even to an increase in

SWS.[10] Documented changes in Stage 1 sleep associated with pregnancy have also been inconsistent.[11,12,14]

Sleep efficiency (defined as time spent sleeping as a percentage of time spent in bed) is often reduced during pregnancy and declines further as pregnancy advances,[12,13] mostly as a result of increased time spent awake after sleep onset.[10-12] Earlier PSG studies found longer sleep latencies (the time taken to fall asleep) during the last month of pregnancy,[15] however more recent studies have failed to support this observation.[10,11,14] Cortical arousals from sleep are characterised by brief abrupt changes in EEG frequency (suggestive of an awake state), which results in sleep fragmentation;[16] the occurrence of these during pregnancy has yet to be reported on.

This lack of consistent findings may be due to generally small sample sizes and differences in methodology such as cross-sectional versus longitudinal design and laboratory-based versus home-based PSG. Furthermore, the effect of parity is rarely considered or reported upon.[17]

Pregnancy is accompanied by dramatic hormonal changes, which have significant potential to impact on sleep quality. One of the most responsive hormones is progesterone,[10] with previous research suggesting it has a soporific or sedative effect,[18,19] and may induce significant increases in NREM sleep.[20] However, knowledge of the effects of progesterone on human sleep mostly comes from the study of the application of exogenous hormones,[21] and clinical studies tend to limit their samples to men or post-menopausal women.[20,22] It remains uncertain how the substantial increase in progesterone during pregnancy may affect sleep.

Depressive symptomatology in the prenatal period is a significant problem with reported prevalence rates between 14% and 37%.[23-25] Pregnant women identified as being depressed report poorer sleep quality than their nondepressed counterparts,[26,27] and researchers have also begun to assess sleep deprivation as a contributor to both

prenatal[27,28] and postnatal mood changes.[29,30] There is potential that mood disturbance may account for some of the variation in altered sleep patterns during pregnancy, and vice versa.

Additionally, primary sleep disorders may be more prevalent during pregnancy and impact on sleep quality. Several studies show reported increases in snoring during pregnancy,[31-35] and although the prevalence of obstructive sleep apnoea during pregnancy is unknown there is strong suggestion that this condition may be more common during pregnancy.[34,36] Restless legs syndrome affects around a quarter of women during pregnancy,[37,38] and many people with restless legs syndrome also suffer from a distinct condition known as periodic limb movements of sleep. The prevalence of periodic limb movements of sleep during healthy singleton pregnancy is unknown, however Dzaja et al.[39] recently showed that restless legs syndrome during pregnancy is associated with increased amounts of periodic limb movements of sleep.

The potential for sleep disruption to impact on quality of life may be particularly detrimental to the pregnant woman who is preparing for the important task of child-rearing. Previous PSG studies during pregnancy have focused on changes in sleep efficiency and sleep stage architecture without attempting to account for these changes. These studies have also neglected to investigate cortical arousals during sleep and the potential causes of these. The purpose of this study was to investigate both objective and subjective changes in sleep patterns associated with early and late pregnancy as compared to the nonpregnant state, and to address limitations in previous PSG studies by investigating cortical arousals and accounting for possible influences on sleep such as hormonal change, mood state and parity.

Method

The Human Research Ethics Committees at Austin Health, Mercy Hospital for Women and La Trobe University in Melbourne, Victoria, Australia approved this study

and informed consent was obtained from all participants (see Appendix B). Four hundred and thirty pregnant women from the Outpatient Obstetrics Clinic at the Mercy Hospital for Women were consecutively approached to participate in the study, of these 58 agreed. The reasons for declining participation were typically an unwillingness to have a sleep study and inability to be away from home overnight because of family responsibilities. Ten pregnant women withdrew from the study prior to data collection due to pregnancy-related complications or inability to attend the sleep laboratory. Nonpregnant control women were recruited from advertisements in the Austin Health newsletter and from friends of the pregnant participants. The participant exclusion criteria were multiple or complicated pregnancy, significant medical, psychological or psychiatric disorder diagnosed by a health professional, a previously diagnosed sleep disorder (e.g. obstructive sleep apnoea, insomnia, hypersomnolence), or current use of anti-depressant medication. During the recruitment phase, only one pregnant woman was excluded from participation due to depression, and one nonpregnant woman was excluded due to a prior history of encephalopathy. In total, 27 women in the third trimester of pregnancy (T3; 30-38 weeks gestation), 21 women in the first trimester of pregnancy (T1; 9-14 weeks gestation) and 24 nonpregnant women (control group) participated in the study.

Polysomnography

Overnight PSG was conducted in-laboratory to control for variations in potential external disruptions in the home environment. PSG was performed using the Somté (Compumedics, Abbotsford, Australia) portable sleep-monitoring device to provide greater comfort to the participants. Portable sleep-monitoring systems are commonly used in clinical settings and have been shown to have a high level of agreement with standard laboratory-based systems.[40,41] Signals measured included EEG, EOG, nasal airflow measured via nasal cannula, arterial oxygen saturation, thoracic and abdominal respiratory effort, snore, body position, leg movements and heart rate. PSG recordings

were sleep staged by a single experienced sleep technologist who was blinded to pregnancy status, in accordance with standard criteria.[8] Variables of sleep included total sleep time (TST), sleep efficiency (defined as total sleep time/total dark time), sleep latency (defined as 3 epochs of Stage 1 sleep or 1 epoch of any other sleep stage), REM sleep latency, number of awakenings during sleep and wake after sleep onset. In addition, sleep stage 1, 2, 3, 4 and REM were expressed in minutes as well as a percentage of total sleep time. Arousals were measured in accordance with the rules set out by the American Sleep Disorders Association (ASDA) Atlas Task Force[16] and were categorised as to whether they were associated with a respiratory event, a limb movement, or were spontaneous. Participants were woken eight hours after lights out time and asked whether they had slept worse, the same, or better than usual. Morning blood was taken for serum progesterone levels. All but two of the control participants were in the follicular phase of the menstrual cycle.

Subjective Sleep Quality and Mood

Participants completed a questionnaire developed for this study (see Appendix E), rating their current (over the past fortnight) and general (or when not pregnant) sleep quality on a scale of 1-10, and answered questions pertaining to usual sleep duration, sleep latency, difficulties falling asleep and reasons for overnight awakenings. Reasons for overnight awakenings such as discomfort or back pain were rated for how frequently they occurred, on a scale of "always", "often", "rarely", or "never". For statistical analysis, "always" and "often" responses were combined and "rarely" and "never" responses were combined to create a dichotomous variable.

Current state of depression, anxiety and stress was measured with the Depression Anxiety Stress Scale – Short version (DASS21).[42] Each of the three scales has seven items that are scored on a 4-point severity/frequency scale to rate the extent to which they have experienced each state over the past week. The scores for the short version are then

doubled; the score range for each scale is 0-42. Internal consistency of the DASS21 using Cronbach's alpha has been shown to range from .88 to .94 for the Depression scale, from .82 to .87 for the Anxiety scale and from .90 to .91 for the Stress scale.[43,44] The DASS21 evidences good convergent and discriminant validity when compared with other validated measures of depression and anxiety.[44,45]

Statistical Analysis

All statistical analyses were performed with the Statistical Package for Social Sciences 15.0 (SPSS Inc., Chicago, Illinois). Data were tested for linearity and normality and non-normally distributed variables were log transformed apart from progesterone level which was subjected to inverse transformation. Chi-square tests, multivariate analysis of variance and univariate analysis of variance were conducted on the variables of interest. As progesterone is strongly linked to trimester of pregnancy, its influence on sleep needed to be investigated separately for each group with regression analyses. Effect sizes were calculated using partial eta squared (n^2). Effect sizes of .01, .09 and .25 are considered small, medium, and large in magnitude.[46] In order to determine which groups differed on ANOVA, post hoc Tukey tests were set at a significance level of $p < .05$. All values are given in means with standard deviations (M ± SD) for normally distributed variables and median (*Mdn*) and interquartile range (*IQR*) for non-normally distributed variables.

Results

Participants

Participants were approximately 30 years old and were within a healthy weight range according to pre-pregnancy Body Mass Index (BMI) and there was a high prevalence of tertiary educated women (Table 1). The three participant groups did not differ in terms of employment status or parity; however a significantly higher percentage of pregnant women were partnered compared to the control group.

Table 1

Demographic Variables

	Control (n = 24)	T1 (n = 21)	T3 (n = 27)	p
Age [a]	29.3 ± 5.9	29.6 ± 3.4	32.3 ± 3.5	.06
Pre-preg BMI [a]	23.9 ± 3.2	25.4 ± 5.4	23.4 ± 2.5	.22
Married/De Facto (%)	37.5	85.7	92.6	<.001**
Nulliparous (%)	75.0	42.9	55.6	.09
Tertiary Educated (%)	87.5	100.0	77.7	.07
Employed (%)				
Full time	50.0	42.9	40.7	.06
Part time	50.0	52.4	37.0	
Not employed	0.0	4.8	22.2	

Note. Data are M ± SD. T1 = first trimester; T3 = third trimester, BMI = body mass index.

[a] p values associated with univariate ANOVA. All other p values associated with chi-square tests.

** $p < .01$.

Objective Sleep Measurement

Multivariate analysis of variance revealed that measures of sleep fragmentation [sleep efficiency, wake after sleep onset (WASO), number of awakenings and arousals/hr] differed significantly across the groups (*Wilks*= .69, $F(8,132) = 3.43$, $p = .001$, see Table 2). In particular, women in the third trimester of pregnancy had significantly poorer sleep efficiency than the controls, and significantly more cortical arousals per hour than either the first-trimester women or controls. Wake after sleep onset was significantly less in the control group when compared to both pregnancy groups.

Table 2

Means (± SD) for Sleep Variables for Each Group

	Control (n = 24)	T1 (n = 21)	T3 (n = 27)	*partial* n^2	p
Sleep efficiency (%)	90.0 ± 6.4	84.9 ± 8.0	80.1 ± 13.5	.15	.004[†]
Sleep latency (min)	17.0 ± 19.1	19.9 ± 16.6	17.5 ± 12.8	.01	.82
REM latency (min)	133.3 ± 43.3	118.3 ± 60.9	126.1 ± 55.0	.01	.65
WASO (min)	28.0 ± 19.5	49.4 ± 35.5	62.2 ± 36.8	.18	.001[‡]
Arousals/hr [a]	8.8 (7.2-10.9)	10.6 (7.6-15.8)	14.6 (10.7-18.9)	.23	<.001[§]
Resp arousals/hr [a]	0.9 (0.5-2.3)	1.3 (0.4-2.0)	2.4 (1.3-4.7)	.13	.009[§]
Limb arousals/hr [a]	1.2 (0.5-2.4)	0.8 (0.5-2.4)	2.1 (1.3-4.8)	.13	.009[§]
Spont arousals/hr	5.9 ± 2.2	7.9 ± 3.4	8.1 ± 5.1	.07	.10
No. of awakenings	15.3 ± 4.1	16.0 ± 4.7	18.8 ± 6.8	.08	.053
Stage 1 (min)	27.8 ± 12.2	30.3 ± 15.7	35.3 ± 15.4	.05	.18
Stage 2 (min)	167.1 ± 39.4	165.7 ± 43.7	161.7 ± 40.8	.003	.89
Stage 3 (min)	77.8 ± 27.7	84.9 ± 38.1	66.9 ± 28.3	.06	.14
Stage 4 (min)	79.6 ± 20.0	61.6 ± 27.0	54.5 ± 23.8	.18	.001[†]
REM sleep (min)	75.0 ± 18.1	64.4 ± 15.5	60.1 ± 22.5	.10	.02[†]
%TST supine	33.1 ± 23.0	41.0 ± 23.6	19.1 ± 15.3	.17	.002[§]
Progesterone (nmol/L) [a]	4.2 (2.6-7.9)	68.5 (58.6-82.3)	415 (316.3-538.4)	.92	<.001[†]

Note. Effect size and probability associated with univariate ANOVA with post-hoc Tukey tests set at $p < .05$. REM = rapid eye movement, WASO = wake after sleep onset, Resp = respiratory, Spont = spontaneous, %TST = percentage of total sleep time.

[†]control vs. T3 – $p < .05$ [‡] control vs. T1 and T3 – $p < .05$ [§]control and T1 vs. T3 – $p < .05$

[a] values given as *Mdn* (*IQR)* as variable was transformed.

Further analysis of cortical arousals revealed that women in the third trimester of pregnancy had significantly more respiratory and limb movement-related arousals per hour when compared to the nonpregnant and first-trimester women, whereas spontaneous arousals did not differ across groups (see Table 2). It was subsequently found that significantly more third-trimester pregnant women had an Apnoea/Hypopnoea Index per hour >5 when compared to the first-trimester women and controls (30.8% vs. 23.8% vs. 4.2%, $p < .05$). Similarly, significantly more third-trimester women had a Periodic Leg Movement index of >5 per hour when compared to the first-trimester women and controls (29.6% vs. 9.5% vs. 4.2%, $p = .03$).

Multivariate analysis of variance on minutes spent in each stage of sleep (Stage 1, 2, 3, 4 and REM) showed that sleep architecture differed significantly across the three groups (*Wilks* = .65, $F(10,130) = 3.08$, $p = .002$; see Table 2). Women in the third trimester of pregnancy spent significantly less time in REM sleep and Stage 4 sleep as compared to the control group. Multivariate analysis of variance on the percentage of total sleep time spent in each stage of NREM sleep (Stage 1, 2, 3, and 4) also differed significantly across the groups (*Wilks* = .73, $F(8,132) = 2.86$, $p = .006$; see Figure 1). Women in the third trimester of pregnancy spent a significantly greater proportion of total sleep time in Stage 1 sleep but a significantly smaller proportion in Stage 4 sleep as compared to the first-trimester or control groups. There was no difference between groups in the percentage of total sleep time spent in REM sleep.

As shown in Table 2, sleep latency and REM sleep latency were comparable across groups. Sleeping position differed significantly, with third-trimester women spending less time in the supine position when compared to the first-trimester or control groups.

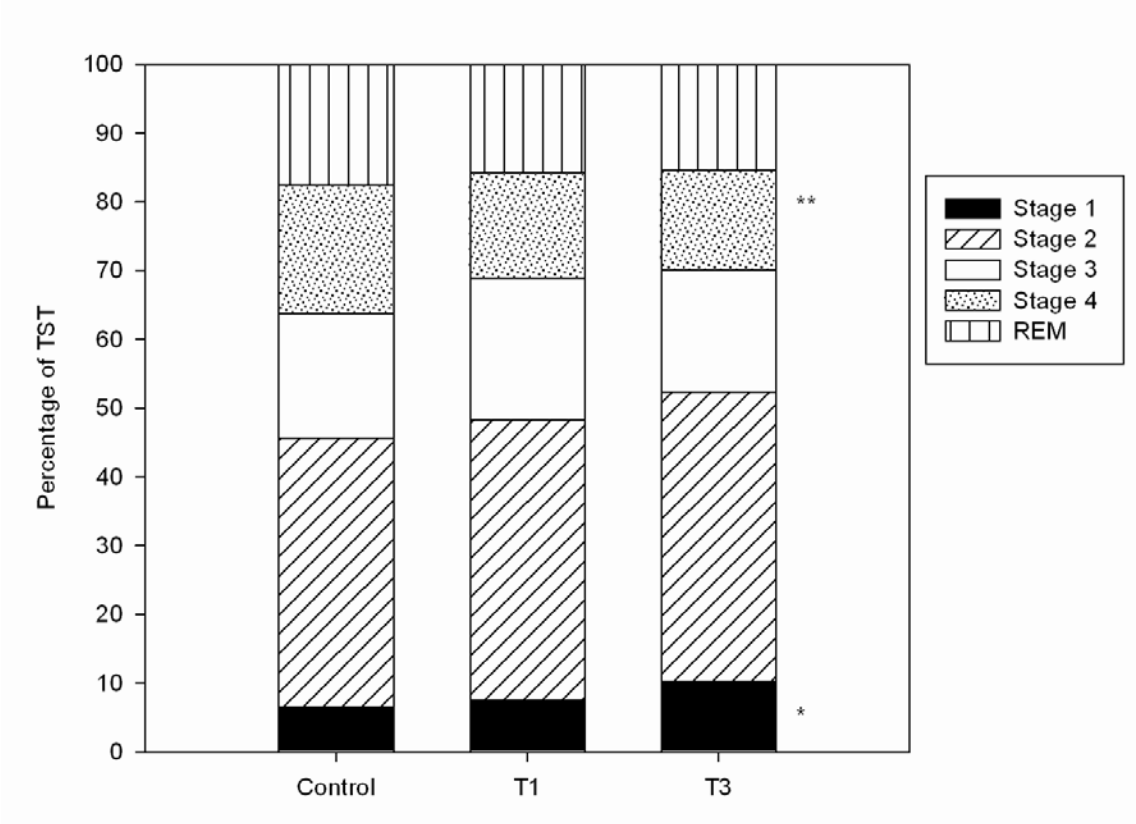

Figure 1. Mean percentage of total sleep time (TST) in each sleep stage for the control (n = 24), T1 (n = 21) and T3 (n = 27) groups. The T3 group had a significant increase in Stage 1 sleep (* p = .02) compared to the T1 and control groups, and the T3 and T1 groups had a significant reduction in Stage 4 sleep (**p = .02) compared to the control group. T1 = first trimester of pregnancy, T3 = third trimester of pregnancy.

In terms of perceived sleep quality for the PSG study, 71% of the third-trimester group said they slept similar to usual, compared to 43% of the first-trimester group and only 25% of the control group. Alternately, 70% of the control group said they slept worse than usual, compared to 57% of the first-trimester group and 29% of the third-trimester group. This difference in perceived sleep quality was significant (p = .03).

Nulliparas versus Multiparas

As shown in Table 3, nulliparous women in the third trimester had significantly poorer sleep efficiency than multiparous women in the third trimester of pregnancy. This appears mostly due to more time in Stage 2 sleep in the multiparous women. No other measures of sleep differed across the groups.

Table 3

Means (± SD) for Sleep Variables by Pregnancy Trimester and Parity

	First Trimester (T1)		Third Trimester (T3)			
	Nulliparous (n = 9)	Multiparous (n = 12)	Nulliparous (n = 15)	Multiparous (n = 12)	*partial* n^2	*p*
Sleep effic. (%)	83.8 ± 7.2	85.7 ± 8.9	75.2 ± 15.2	86.4 ± 7.6	.18	.03[†]
WASO (min)	55.4 ± 36.3	44.9 ± 35.8	77.1 ± 37.9	43.7 ± 26.5	.16	.052
No. of awake.	15.4 ± 2.2	16.4 ± 6.0	19.3 ± 6.0	18.2 ± 8.0	.06	.42
Arousals/hr [a]	10.6 (6.1-15.8)	11.0 (8.8-16.2)	15.0 (12.7-18.9)	13.2 (9.2-19.0)	.14	.08
Stage 1 (min)	33.1 ± 15.6	28.2 ± 16.2	32.0 ± 15.4	39.5 ± 14.9	.07	.36
Stage 2 (min)	149.6 ± 30.6	177.8 ± 49.1	145.4 ± 43.1	182.2 ± 27.3	.16	.04[‡]
Stage 3 (min)	88.2 ± 42.6	82.5 ± 36.0	66.3 ± 26.8	67.7 ± 31.1	.08	.33
Stage 4 (min)	68.8 ± 20.4	56.2 ± 30.8	57.9 ± 25.6	50.3 ± 21.7	.06	.43
REM (min)	63.4 ± 13.9	65.0 ± 17.1	53.8 ± 21.1	68.0 ± 22.4	.09	.26

Note. Effect size and probability associated with univariate ANOVA with post-hoc Tukey tests set at $p < .05$. effic. = efficiency; WASO = wake after sleep onset; awake. = awakenings, REM = rapid eye movement.

[†]T3 nulliparous vs. T3 multiparous – $p < .05$ [‡] T3 nulliparous vs. T3 multiparous – $p < .09$.

[a] values given as *Mdn* (*IQR)* as variable was transformed.

Progesterone

Progesterone level differed across the groups in accordance with pregnancy state (see Table 2). Within the control group, higher progesterone levels were associated with fewer awakenings during sleep (r = -.51, $F(1,21)$ = 7.48, p = .01). Progesterone was unrelated to sleep quality within the first-trimester group. Within the third-trimester group and after accounting for gestational age, progesterone significantly explained an additional 18.3% of the variance in the percentage of time in Stage 2 sleep (r = -.50,

$F(1,23)=5.63$, $p = .03$), 17.1% in number of awakenings ($r = .34$, $F(1,23)=4.77$, $p = .04$) and 15.9% in wake after sleep onset ($r = .40$, $F(1,23)=4.43$, $p = .046$).

Mood State

On average, all groups scored within the normal range for depression (control – *Mdn(IQR)* = 2.0 (0.0 - 4.0), T1 = 2.0 (2.0 – 5.5), T3 = 2.0 (0.0-3.5), anxiety (control - *Mdn(IQR)* = 1.0 (0.0 - 4.0), T1 = 2.0 (0.0 – 4.0), T3 = 4.0 (0.0-6.0), and stress (control - *Mdn(IQR)* = 9.0 (6.0 - 12.0), T1 = 7.0 (2.0 – 13.0), T3 = 6.0 (4.0-12.0). A multivariate analysis of variance showed no differences in mood status across the groups (*Wilks* = .86, $F(6,126) = 1.67$, $p>.1$) and depression and stress were not associated with any sleep variables. Anxiety showed a significant but weak negative correlation with minutes spent in Stage 1 sleep ($r = -.26$, $p = .03$).

Subjective Sleep Quality

Women in the third trimester of pregnancy reported a significantly greater reduction in sleep quality over the past six months as compared to the control group (T3: 2.6 ± 1.7; control: 1.0 ± 1.0; $F(2,69) = 7.02$, $p = .002$). As shown in Table 4, reported average sleep duration, sleep latency, and daytime tiredness did not differ between the groups. There was a trend for more third-trimester women to report difficulty falling asleep when compared to first-trimester women or controls. Pregnant women reported significantly more overnight awakenings compared to the controls, and were more likely to report difficulty falling back asleep. Third-trimester pregnant women were more likely to report frequently waking during the night due to discomfort, back pain and leg cramps when compared to controls or first-trimester women. Awakening due to urinary frequency was reported often for both pregnant groups.

Table 4

Percentage of Participants Reporting Sleep-Related Problems and Reported Frequency of Causes of Night Awakenings in Each Group

Complaint (%)	Control (n = 24)	T1 (n = 21)	T3 (n = 27)	p
Sleep-Related Problems				
< 8 hours sleep per night	79.2	71.4	74.1	.83
Sleep latency >20 mins	25.0	28.6	44.4	.29
Difficulty falling asleep	12.5	9.5	37.0	.06
Tiredness	70.8	95.2	92.6	.11
Difficulty falling asleep after waking	8.3	47.6	63.0	.001**
No. of awakenings				
None	25.0	4.8	3.7	.001**
1-2	66.7	57.1	29.6	
3-4	8.3	28.6	44.4	
5+	0.0	9.5	22.2	
Cause of Night Awakenings				
Uncomfortable	29.2	23.8	66.6	.009**
Need to urinate	16.7	76.2	70.3	.001**
Back pain/leg cramps	4.2	10.0	37.0	.005**
Body temperature	20.8	20.0	18.5	.98
Shortness of breath	0.0	5.0	3.7	.28
Children/partner	26.0	45.0	18.5	.07

Note. chi-square test, $p < .05$. Values for causes of night awakenings given as the percentage of participants responding with "often" or "always".

** $p < .01$

Discussion

The results of our study show that sleep in the third trimester of pregnancy is characterised by decreased sleep efficiency, increased wake after sleep onset and increased cortical arousals. The deepest stage of sleep, Stage 4, is reduced and a higher proportion of sleep time is spent in Stage 1 sleep as compared to the first-trimester or the nonpregnant state. Furthermore, this study found that third-trimester pregnant women spend less time in REM sleep compared to nonpregnant women, generally as a consequence of their reduced overall sleep efficiency rather than an alteration in the structure of their sleep stages. No differences in sleep latency or REM sleep latency were found. Women in the first trimester of pregnancy also spend more time awake after sleep onset and spend a lesser proportion of their sleep in Stage 4 sleep as compared to nonpregnant women. Sleep efficiency and time in REM sleep showed a trend towards the pattern seen in the third trimester of pregnancy.

Reports of frequent awakenings and difficulty returning to sleep, mostly due to discomfort and bodily aches, were regularly made by the pregnant women in this study. The fact that third-trimester pregnant women spent substantially less time sleeping supinely as compared to the other groups also indicates compromised sleeping comfort. Unfortunately, PSG only allows attribution of a specific cause to an awakening if it has a physical source. By examining cortical arousals during sleep we found that third-trimester women experienced more cortical arousals, especially as a consequence of limb movements or respiratory events, compared to either first-trimester or nonpregnant women. Cortical arousal often results in disrupted sleep with reduced restorative power,[47] as the individual returns to light sleep rather than deep sleep following arousal. This trade-off of more Stage 1 sleep for less Stage 4 sleep was a key feature of our findings in the late pregnancy group.

Investigation of sleep quality according to parity revealed that in the third trimester of pregnancy, nulliparous women have significantly poorer sleep efficiency than multiparous women, mostly as a result of multiparas spending more time in Stage 2 sleep which is considered to be a lighter stage of sleep. Sleep in the first trimester of pregnancy was not affected by parity.

In contrast to the suggestion that progesterone may have sedating properties,[18,19] we found that higher progesterone levels in the third trimester of pregnancy were associated with increased awakenings and more time awake after sleep onset. This finding is unexpected given previous work indicating a positive relationship between progesterone and improved sleep measures, such as improved sleep quality in postmenopausal women following hormone replacement therapy,[48] and the suggestion that progesterone may play a role in protecting premenopausal women from sleep-disordered breathing by stimulating upper airway musculature.[49] However, hormonal influences such as progesterone have been hypothesised to be a cause of restless legs syndrome during pregnancy,[50] which can result in disrupted sleep. In our study, the association between the number of periodic limb movements during sleep and progesterone level in the third trimester was almost significant ($r = .39$, $p = .056$).

In our sample, current state of depression, anxiety and stress did not differ across the groups and did not show any significant association with sleep disruption. The women in this study were typically in the normal to mildly affected range, so we can conclude that the differences in sleep quality across the pregnant groups were not the result of differences in mood state.

Our findings of decreased sleep efficiency and increased wake after sleep onset during pregnancy are supported by most previous studies,[10-13,15] as is the reduction in Stage 4 sleep during pregnancy.[13-15] Our finding that minutes spent in REM sleep was reduced in the third-trimester pregnant group has previous support,[10-12] as well as

opposition.[13,14] Lee and colleagues[13] expressed their results as the percentage of total sleep time in REM rather than total minutes and had a result close to significance, and the study by Schorr et al.[14] was limited by its very small sample size. Past findings surrounding Stage 1 sleep have so far been discrepant. As with the current study, an increased level of Stage 1 sleep has been previously found,[11-14],whereas others find no evidence for this marker of sleep fragmentation.[10-12] Again, many possibilities exist for this and other disparities, including sample sizes of less than 10 per group, [10,12] laboratory-based sleep studies or home sleep studies, variations in how much time the women were allowed to sleep for and the amount of sleep time included in data analyses. Parity has rarely been considered in past PSG studies, with existing literature suggesting that multiparas have a slightly lower sleep efficiency than nulliparas without a change in REM or SWS.[13,51] In contrast, the current study lends support to previous actigraphy research[52] which found that nulliparous women had lower sleep efficiency than multiparous women. We may speculate that multiparous women were able to sleep better due to previous experience sleeping through the discomforts of pregnancy, or that sleeping away from home allowed them to catch up on sleep away from usual disruptions caused by their other children.

The high frequency of cortical arousals from sleep during pregnancy has not been previously reported. Frequent cortical arousal typically results in the person continually waking fully or returning to light sleep, leading to sleep fragmentation. Studies of sleep fragmentation commonly find increased objective and subjective sleepiness, decreased psychomotor performance and negative mood changes.[53] More specifically, measures of arousal from sleep have been significantly correlated with objective measures of daytime alertness[54,55] and increases in blood pressure.[56,57] The fact that arousals were also secondary to respiratory events or limb movements suggests that conditions such as sleep-disordered breathing and periodic limb movements of sleep should be considered as a

cause of sleep disruption, given that current literature is building to suggest that these conditions may be more common during pregnancy.[34,36,39,58]

Sleep efficiency during the later stages of pregnancy in some studies has been found to be as high as 90%,[10,13,51] similar to that of our control group. The third-trimester pregnant women in this study spent 10% less time asleep on average, and almost a quarter slept for less than six hours in total. Since pregnancy stretches over many months, partial sleep deprivation may become chronic and can result in seriously impaired neurobehavioural function.[59] Reduced sleep time in the last month of pregnancy has also been associated with longer labours and a higher likelihood of caesarean delivery.[60] Additionally, the cognitive impact of sleep restriction is frequently underestimated,[59] which may have potentially dangerous implications for activities of daily living, such as driving.

Limitations

This study is limited by the use of a single night of PSG to characterise sleep patterns, and its cross-sectional rather than longitudinal nature. However, previous polysomnographic research during pregnancy found no differences in sleep characteristics when including an adaptation night.[13] Undertaking multiple sleep studies at appropriate time points can be a major problem with the study of pregnant women and they are often unwilling to undergo additional measurements and procedures. This was reflected in the low response rate during recruitment and the high dropout rate due to complications of pregnancy. Although limited by our sample size, it was at least comparable to or larger than many existing PSG studies.[10-12,14,15]

Although recruitment for this study was targeted at consecutive patients at a large public hospital, the nature of the study may have resulted in biased sampling (i.e. those who believe they have a sleeping problem) and restrict generalisation of results. However, this works both ways, in that some pregnant women declined participation

citing poor sleep and not wanting to spend a night away from home. Measuring sleep in an unfamiliar laboratory setting may affect sleep outcomes for some women, but this allows participants in each group to undergo the same sleep-monitoring conditions and any associated discomfort is equivalent across groups. We actually found in this study that pregnant women tended to report sleeping similarly to normal whilst in the laboratory, whereas the control group tended to report poorer sleep quality than usual.

Participants in this study were limited to an eight-hour period for time in bed. Although restricting potential sleep time may appear to limit the generalisability of our findings, it is common for women to continue in the work force until very late into pregnancy (as evidenced by 78% of the third-trimester women in this study who were still working), and daily responsibilities such as child-rearing or home duties may exist regardless of pregnancy status. The ability of the pregnant woman to sleep within certain time constraints therefore remains relevant.

Conclusions

In summary, pregnancy is characterised by decreased sleep efficiency and increased awakenings, with a trade-off of less deep sleep in exchange for increased light sleep and less time in REM sleep. In addition to existing literature, this study provides greater depth by revealing a higher number of cortical arousals during the later stages of pregnancy, particularly in response to respiratory events and limb movements.

Given the impact sleep has on physical and mental well-being, assessing sleep quality throughout pregnant is important. The creation of a screening tool that can be administered quickly by a health professional during consultation should be considered. However, as self-report measures can only reveal so much about an individual's sleeping habits, it is important to understand the characteristics of sleep during pregnancy in order to recognise when referral to a sleep specialist may be required, such as the possible presence of a primary sleep disorder (such as obstructive sleep apnoea or periodic leg

movement disorder) or significant sleep deprivation, which would require confirmation via PSG. Only once the cause of sleep disruption is identified can appropriate treatment options be explored.

Acknowledgments

The authors would like to thank the staff at the Austin Health Sleep Laboratory for their support of this project and we appreciate the valuable contribution made by each of the research participants.

This research was funded by La Trobe University and the Austin Health Medical Research Foundation. The authors indicate no conflicts of interest.

References

1. Lopes EA, Carvalho LB, Seguro PB, et al. Sleep disorders in pregnancy. *Arq Neuropsiquiatr*. 2004; **62**: 217-21.
2. Baratte-Beebe K, Lee KA. Sources of midsleep awakenings in childbearing women. *Clin Nurs Res*. 1999; **8**: 386-97.
3. Mindell JA, Jacobson BJ. Sleep disturbances during pregnancy. *JOGNN*. 2000; **29**: 590-7.
4. Naud K, Ouellet A, Brown C, Pasquier JC, Moutquin JM. Is sleep disturbed in pregnancy? *J Obstet Gynaecol Can*. 2010; 32: 28-34.
5. Facco FL, Kramer J, Ho KH, Zee PC, Grobman WA. Sleep disturbances in pregnancy. *Obstet Gynecol*. 2010; 115: 77-83.
6. Means M, Edinger J, Glenn D, Fins A. Accuracy of sleep perceptions among insomnia sufferers and normal sleepers. *Sleep Med*. 2003; **4**: 285-96.
7. Pinto Jr L, Pinto M, Goulart L, et al. Sleep perception in insomniacs, sleep-disordered breathing patients, and healthy volunteers-an important biologic parameter of sleep. *Sleep Med*. 2009; **10**: 865-8.
8. Rechtschaffen A, Kales A. A manual of standardized terminology, techniques, and scoring system for sleep stages of human subjects. Los Angeles: Brain Information Service; 1968.
9. Carskadon MA, Dement WC. Normal human sleep: an overview. In: Kryger M, Roth T, Dement WC (eds.). Principles and practice of sleep medicine, 4th edn. Philadelphia, Pennsylvania: W.B. Saunders Company; 2005; pg 13-23.
10. Driver HS, Shapiro CM. A longitudinal study of sleep stages in young women during pregnancy and postpartum. *Sleep*. 1992; **15**: 449-53.
11. Hertz G, Fast A, Feinsilver SH, Albertario CL, Schulman H, Fein AM. Sleep in normal late pregnancy. *Sleep*. 1992; **15**: 246-51.
12. Brunner DP, Münch M, Biedermann K, Huch R, Huch A, Borbély AA. Changes in sleep and sleep electroencephalogram during pregnancy. *Sleep*. 1994; **17**: 576-82.
13. Lee KA, Zaffke ME, McEnany G. Parity and sleep patterns during and after pregnancy. *Obstet Gynecol*. 2000; **95**: 14-8.

14. Schorr SJ, Chawla A, Devidas M, Sullivan CA, Naef RW, Morrison JC. Sleep patterns in pregnancy: a longitudinal study of polysomnography recordings during pregnancy. *J Perinatol*. 1998; **18**: 427-30.
15. Karacan I, Heine W, Agnew HW, Williams RL, Webb WB, Ross JJ. Characteristics of sleep patterns during late pregnancy and the postpartum periods. *Am J Obstet Gynecol*. 1968; **101**: 579-86.
16. Bonnet MH, Carley D, Carskadon MA, et al. EEG arousals: scoring rules and examples: a preliminary report from the Sleep Disorders Atlas Task Force of the American Sleep Disorders Association. *Sleep*. 1992; **15**: 173-84.
17. Lee K. Alterations in sleep during pregnancy and postpartum: a review of 30 years of research. *Sleep Med Rev*. 1998; **2**: 231-42.
18. Herrmann WM, Beach RC. Experimental and clinical data indicating the psychotropic properties of progestogens. *Postgrad Med J*. 1978; **54**: 82-7.
19. Söderpalm AH, Lindsey S, Purdy RH, Hauger R, de Wit H. Administration of progesterone produces mild sedative-like effects in men and women. *Psychoneuroendocrinology*. 2004; **29**: 339-54.
20. Friess E, Tagaya H, Trachsel L, Holsboer F, Rupprecht R. Progesterone-induced changes in sleep in male subjects. *Am J Physiol*. 1997; **272**: E885-91.
21. Manber R, Armitage R. Sex, steroids, and sleep: a review. *Sleep*. 1999; **22**: 540-55.
22. Schüssler P, Kluge M, Yassouridis A, et al. Progesterone reduces wakefulness in sleep EEG and has no effect on cognition in healthy postmenopausal women. *Psychoneuroendocrinology*. 2008; **33**: 1124-31.
23. Andersson L, Sundström-Poromaa I, Bixo M, Wulff M, Bondestam K, åström M. Point prevalence of psychiatric disorders during the second trimester of pregnancy: a population-based study. *Am J Obstet Gynecol*. 2003; **189**: 148-54.
24. Lee AM, Lam SK, Sze Mun Lau SM, Chong CS, Chui HW, Fong DY. Prevalence, course and risk factors for antenatal anxiety and depression. *Obstet Gynecol*. 2007; **110**: 1102-12.
25. Priest SR, Austin MP, Barnett BB, Buist A. A psychosocial risk assessment model (PRAM) for use with pregnant and postpartum women in primary care settings. *Arch Womens Ment Health*. 2008; **11**: 307-17.
26. Jomeen J, Martin CR. Assessment and relationship of sleep quality to depression in early pregnancy. *J Reprod Infant Psychol*. 2007; **25**: 87-9

27. Field T, Diego M, Hernandez-Reif M, Figueiredo B, Schanberg S, Kuhn C. Sleep disturbances in depressed pregnant women and their newborns. *Infant Behav Dev*. 2007; **30**: 127-133.
28. Skouteris H, Germano C, Wertheim EH, Paxton SJ, Milgrom J. Sleep quality and depression during pregnancy: a prospective study. *J Sleep Res*. 2008; **17**: 217-20.
29. Wilkie G, Shapiro CM. Sleep deprivation and the postnatal blues. *J Psychosom Res*. 1992; **36**: 309-16.
30. Wolfson AR, Crowley SJ, Anwer U, Bassett JL. Changes in sleep patterns and depressive symptoms in first-time mothers: Last trimester to 1-year postpartum. *Behav Sleep Med*. 2003; **1**: 54-67.
31. Izci B, Riha RL, Martin SE, et al. The upper airway in pregnancy and pre-eclampsia. *Am J Respir Crit Care Med*. 2003; **167**: 137-40.
32. Izci B, Vennelle M, Liston WA, Dundas KC, Calder AA, Douglas NJ. Sleep-disordered breathing and upper airway size in pregnancy and post-partum. *Eur Respir J*. 2006; **27**: 321-7.
33. Perez-Chada D, Videla AJ, O'Flaherty ME, et al. Snoring, witnessed sleep apnoeas and pregnancy-induced hypertension. *Acta Obstet Gynecol Scand*. 2007; **86**: 788-92.
34. Pien GW, Fife D, Pack AI, Nkwuo JE, Schwab RJ. Changes in symptoms of sleep-disordered breathing during pregnancy. *Sleep*. 2005; **28**: 1299-305.
35. Ursavas A, Karadag M, Nalci N, Ercan I, Gozu RO. Self-reported snoring, maternal obesity and neck circumference as risk factors for pregnancy-induced hypertension and preeclampsia. *Respiration.* 2008; **76**: 33-9.
36. Edwards N, Blyton DM, Hennessy A, Sullivan CE. Severity of sleep-disordered breathing improves following parturition. *Sleep*. 2005; **28**: 737-41.
37. Manconi M, Govoni V, De Vito A, et al. Restless legs syndrome and pregnancy. *Neurology*. 2004; **63**: 1065-9.
38. Tunç T, Karadag YS, Dogulu F, Inan LE. Predisposing factors of restless legs syndrome in pregnancy. *Mov Disord*. 2007; **22**: 627-31.
39. Dzaja A, Wehrle R, Lancel M, Pollmacher T. Elevated estradiol plasma levels in women with restless legs during pregnancy. *Sleep*. 2009; **32**: 169-74.
40. Churchward T, O'Donoghue F, Rochford D, Pierce R, Barnes M, Higgins S. Diagnostic accuracy and cost effectiveness of home based PSG in OSA. (Abstract). *Sleep Biol Rhythms*. 2006; **4**(s1): A11.

41. Mykytyn I, Sajkov D, Neill A, McEvoy R. Portable computerized polysomnography in attended and unattended settings. *Chest*. 1999; **115**: 114-22.
42. Lovibond SH, Lovibond PF. Manual for the Depression Anxiety Stress Scales, 2nd edn. Sydney: Psychology Foundation; 1995.
43. Henry J, Crawford J. The 21-item version of the Depression Anxiety Stress Scales (DASS–21): Normative data and psychometric evaluation in a large non-clinical sample. *Br J Clin Psychol*. 2005; **44**: 227-39.
44. Antony M, Bieling P, Cox B, Enns M, Swinson R. Psychometric properties of the 42-item and 21-item versions of the Depression Anxiety Stress Scales (DASS) in clinical groups and a community sample. *Psychol Assess*. 1998; **10**: 176-81.
45. Crawford J, Henry J. The Depression Anxiety Stress Scales (DASS): Normative data and latent structure in a large non-clinical sample. *Br J Clin Psychol*. 2003; **42**: 111-31.
46. Cohen J. Statistical power analysis for the behavioral sciences. 2nd ed. Mahwah, NJ: Lawrence Erlbaum Associates; 1988.
47. Bonnet MH. Acute sleep deprivation. In: Kryger M, Roth T, Dement WC (eds.). Principles and practice of sleep medicine, 4th edn. Philadelphia, Pennsylvania: W.B. Saunders Company; 2005; pg 51-66.
48. Montplaisir J, Lorrain J, Denesle R, Petit D. Sleep in menopause: Differential effects of two forms of hormone replacement therapy. *Menopause*. 2001; **8**: 10-16.
49. Driver HS, McLean H, Kumar DV, Farr N, Day AG, Fitzpatrick MF. The influence of the menstrual cycle on upper airway resistance and breathing during sleep. *Sleep*. 2005; **28**: 449-456.
50. Manconi M, Govoni V, De Vito A, et al. Pregnancy as a risk factor for restless legs syndrome. *Sleep Med*. 2004; **5**: 305-308.
51. Waters MA, Lee KA. Differences between primigravidae and multigravidae mothers in sleep disturbances, fatigue, and functional status. *J Nurse Midwifery*. 1996; **41**: 364-7.
52. Signal TL, Gander PH, Sangalli MR, Travier N, Firestone RT, Tuohy JF. Sleep duration and quality in healthy nulliparous and multiparous women across pregnancy and post-partum. *Aust N Z J Obstet Gynaecol*. 2007; **47**: 16-22.
53. Bonnet MH, Arand DL. Clinical effects of sleep fragmentation versus sleep deprivation. *Sleep Med Rev*. 2003; **7**: 297-310.

54. Carskadon MA, Brown ED, Dement WC. Sleep fragmentation in the elderly: Relationship to daytime sleep tendency. *Neurobiol Aging*. 1982; **3**: 321-7.
55. Martin SE, Engleman HM, Kingshott RN, Douglas NJ. Microarousals in patients with sleep apnoea/hypopnoea syndrome. *J Sleep Res*. 1997; **6**: 276-80.
56. Davies RJ, Belt PJ, Roberts SJ, Ali NJ, Stradling JR. Arterial blood pressure responses to graded transient arousal from sleep in normal humans. *J Appl Physiol*. 1993; **74**: 1123-30.
57. Morrell MJ, Finn L, Kim H, Peppard PE, Badr MS, Young T. Sleep fragmentation, awake blood pressure, and sleep-disordered breathing in a population-based study. *Am J Respir Crit Care Med*. 2000; **162**: 2091-6
58. Nikkola E, Ekblad U, Ekholm E, Mikola H, Polo O. Sleep in multiple pregnancy: breathing patterns, oxygenation, and periodic leg movements. *Am J Obstet Gynecol*. 1996; **174**: 1622-5.
59. Van Dongen HP, Maislin G, Mullington JM, Dinges DF. The cumulative cost of additional wakefulness: dose-response effects on neurobehavioral functions and sleep physiology from chronic sleep restriction and total sleep deprivation. *Sleep*. 2003; **26**: 117-26.
60. Lee KA, Gay CL. Sleep in late pregnancy predicts length of labor and type of delivery. *Am J Obstet Gynecol*. 2004; **191**: 2041-6.

Chapter 4

Sleep-Disordered Breathing and Periodic Limb Movements of Sleep in Normal Pregnancy

Manuscript in preparation to be submitted for publication in

Journal of Sleep Research.

Preface

In the course of investigating sleep patterns during pregnancy in Chapter 3, another pregnancy-related phenomenon became apparent. Recent research suggests that sleep-disordered breathing becomes more common during pregnancy. Sleep-disordered breathing encompasses a spectrum of disorders characterised by upper airway resistance during sleep, ranging from snoring through to obstructive sleep apnoea (OSA). OSA is characterised by repeated episodes of partial or complete upper airway obstruction during sleep, which leads to hypoxaemia and frequent cortical arousals. Episodes of upper airway collapse are categorised as apnoeas (cessation of airflow ≥ 10 seconds) or hypopnoeas (discernable reduction in airflow ≥ 10 seconds associated with either an oxyhaemoglobin desaturation of ≥ 3% or a cortical arousal). OSA is then classified according to the apnoea-hypopnoea index (AHI), which is calculated as the number of apnoeas and hypopnoeas per hour of sleep. Although different classifications of OSA severity exist, mild OSA is commonly considered as an AHI of 5 – 15, moderate OSA as an AHI of 15 – 30, with severe OSA as an AHI of greater than 30. Recent estimates report that OSA occurs in at least 2% of the female and 4% of the male adult population.

In the present study, visual inspection of the raw sleep study data for the pregnant women appeared to reveal signs of sleep-disordered breathing that would not be expected in healthy young women. This led to the development of Chapter 4, the primary purpose of which was to investigate both objective and subjective changes in respiration during sleep in healthy pregnancy. Secondly, this chapter addressed periodic limb movements of sleep, following on from literature suggesting an increased prevalence of movement disorders during pregnancy.

Sleep-Disordered Breathing and Periodic Limb Movements of Sleep in Normal Pregnancy

Running head – SDB and PLMS in Pregnancy

Danielle L. Wilson, BA (Hons.)[1,2]; Maree Barnes, MBBS[2,3]; Lenore Ellett, MBBS[4]; Michael Permezel MD FRANZCOG[4,5]; Martin Jackson, MSc[1]; Simon F. Crowe*, PhD[1]

[1]School of Psychological Science, La Trobe University, Bundoora, Victoria, Australia; [2]Institute for Breathing and Sleep, Austin Health, Heidelberg, Victoria, Australia; [3]Department of Medicine, University of Melbourne, Parkville, Victoria, Australia, [4] Department of Obstetrics and Gynaecology, Mercy Hospital for Women, Heidelberg, Victoria, Australia; [5]Department of Obstetrics and Gynaecology, University of Melbourne, Parkville, Victoria, Australia.

Address correspondence to: Simon F. Crowe, School of Psychological Science, La Trobe University, Bundoora, VIC, 3086, Australia. Tel: 613 9479 1380; Fax: 613 9479 1956; E-mail: s.crowe@latrobe.edu.au

The authors declare that they have no conflict of interests.

Number of words – 3,560

Number of references - 47

Summary

This study aims to objectively investigate sleep-disordered breathing (SDB) and periodic limb movements of sleep (PLMS) in the first and third trimester of uncomplicated pregnancy as compared to the nonpregnant state. Twenty-seven women in the third trimester of pregnancy, 21 women in the first trimester of pregnancy and 24 nonpregnant control women underwent overnight polysomnography and completed a questionnaire regarding symptoms of sleep-disordered breathing. Significantly more women in the third trimester of pregnancy had an apnoea/hypopnoea index per hour (AHI/hr) of greater than 5 than did the nonpregnant women. On average, women in the third trimester of pregnancy snored for a significantly greater proportion of total sleep time as compared to the nonpregnant women, and they were more likely to show indicators of airflow limitation on polysomnography. Women in the first trimester of pregnancy showed a trend towards the patterns seen in the third trimester. Compared to the nonpregnant women, the pregnant women tended to report symptoms of snorting and gasping more frequently but not loud snoring, suggesting that self-report measures of SDB may be unreliable. A PLMS index of greater than 5 per hour was significantly more common in the third-trimester when compared to the first-trimester and nonpregnant state. This research shows a small but clinically important difference in SDB symptoms and PLMS exists between healthy non-obese pregnant and nonpregnant women. Further research into sleep-related breathing disorders during pregnancy is indicated, and an assessment of sleep health should be an important addition to routine antenatal care.

Keywords: Pregnancy, polysomnography, sleep-disordered breathing, snoring, airflow limitation.

Sleeping problems are frequently reported during pregnancy and are attributed to a wide variety of physical and psychological causes (Baratte-Beebe and Lee, 1999, Mindell and Jacobson, 2000, Schweiger, 1972). Sleep patterns during pregnancy have been explored with the use of polysomnography (PSG), with results generally confirming reports of disturbed sleep (Brunner et al., 1994, Driver and Shapiro, 1992, Hertz et al., 1992, Lee et al., 2000).

The term sleep-disordered breathing (SDB) encapsulates a spectrum of sleep-related breathing disorders including upper airway resistance syndrome and obstructive sleep apnoea (OSA), and is typically associated with physical symptoms such as snoring, snorting, gasping and choking episodes during sleep. The prevalence of snoring during pregnancy has primarily been studied using self-report techniques, and has been estimated at 12% to 41% by the third trimester of uncomplicated pregnancy (Franklin et al., 2000, Izci et al., 2003, Izci et al., 2006, Loube et al., 1996, Perez-Chada et al., 2007, Ursavas et al., 2008) compared to approximately 4% to 17% in the nonpregnant female population (Izci et al., 2003, Izci et al., 2006, Loube et al., 1996, Ursavas et al., 2008). The rate of snoring in pre-eclampic pregnancy has been reported to be as high as 75% (Izci et al., 2003). Breathing pauses and choking episodes during sleep have been reported in 14% to 30.6% of women in the third trimester of pregnancy (Izci et al., 2006, Mindell and Jacobson, 2000), and cumulative increases in apnoea symptoms have been reported from 14 weeks gestation until delivery (Pien et al., 2005).

It is unclear why SDB may be more common during pregnancy, but changes in respiratory physiology during pregnancy may predispose women to apnoeic respiratory events during sleep. During pregnancy, functional residual capacity is often reduced (McAuliffe et al., 2002), due to elevation of the diaphragm from the expanding uterus. It has also been suggested that the increase in the hormone relaxin culminates in increased upper airway collapsibility and decreased upper airway calibre (Edwards and Sullivan,

2008, Izci et al., 2006), and changes in the airway mucosa results in nasopharyngeal oedema (Elkus and Popovich, 1992). Increased progesterone during pregnancy may in fact be protective against apnoeic respiratory events due to its impact on heightened respiratory drive (Contreras et al., 1991), which protects against upper airway occlusion by enhancing responsiveness of upper airway dilator muscles to stimuli during sleep (Popovic and White, 1998). However, progesterone also increases diaphragmatic effort leading to greater negative inspiratory pressures at the level of the upper airway which may lead to an increased tendency for the upper airway to collapse during sleep (Edwards et al., 2002). As pregnancy progresses, episodes of partial or complete upper airway obstruction may cumulate and progress to OSA.

There is little research on the prevalence of OSA in pre-menopausal women generally (Bixler et al., 2001), and even less in pregnancy. Previous research objectively measuring SDB in pregnancy has largely focused on specific subgroups such as those with risk factors for pre-eclampsia (Guilleminault et al., 2007, Blyton et al., 2004) or pregnant women already suspected of having OSA (Sahin et al., 2008, Edwards et al., 2005).

Another common physiological condition which has potential to cause sleep disruption is restless legs syndrome (RLS), which affects approximately 25% of pregnant women (Manconi et al., 2004, Tunç et al., 2007). The majority of people with RLS have stereotyped repetitive movements during sleep, a distinct condition known as periodic limb movements of sleep (PLMS) which requires confirmation with PSG. Intense movements may cause arousals, which if numerous may lead to non-restorative sleep (Montplaisir et al., 2000). Very few studies have reported on PLMS during pregnancy (Hertz et al., 1992, Nikkola et al., 1996) and no study has specifically investigated the occurrence of PLMS during healthy singleton pregnancy.

Current knowledge on the implications of SDB during pregnancy is limited, but recent data suggest that it may have an impact on pregnancy-induced hypertension (Poyares et al., 2007, Perez-Chada et al., 2007, Franklin et al., 2000) and preeclampsia (Ursavas et al., 2008), and case study data suggests a link between OSA and growth restriction of the foetus (Charbonneau et al., 1991, Roush and Bell, 2004, Sahin et al., 2008). The purpose of this study is to investigate both objective and subjective changes in respiration during sleep, in healthy pregnancy at both the early and later stages. The occurrence of PLMS and the impact on sleep will also be investigated. It is hypothesised that the frequency of symptoms of SDB such as snoring and apnoeic respiratory events and the frequency of PLMS will increase in line with the progression of pregnancy.

Method

The Human Research Ethics Committees at Austin Health, Mercy Hospital for Women and La Trobe University approved this study and informed consent was obtained from all participants (see Appendix B). Four hundred and thirty pregnant women from the Outpatient Obstetrics Clinic at the Mercy Hospital for Women in Heidelberg, Victoria, Australia were consecutively approached to participate in the study, and of these 58 agreed to participate. Declining to participate was generally due to the time commitment involved, unwillingness to have a sleep study or an inability to be away from home overnight due to family responsibilities. After volunteering to participate in the study, 10 pregnant women withdrew prior to data collection due to pregnancy-related complications or inability to schedule an appropriate time to attend the sleep laboratory. Nonpregnant women were recruited from advertisements in the Austin Health newsletter and from friends of the pregnant participants. Following initial expressions of interest in the study, a total of seven nonpregnant women did not participate; one woman was excluded due to her medical history, one could not arrange a suitable date to undergo a sleep study, and the others were lost to follow-up. Participants were excluded from the

study if they had a multiple or complicated pregnancy (including hypertension, gestational diabetes mellitus and preeclampsia), significant medical, psychological or psychiatric co-morbidity, or a previously diagnosed sleep disorder. No other sleep-related information was gathered during the recruitment process. In total, 27 women in the third trimester of pregnancy (T3; 30-38 weeks gestation), 21 women in the first trimester of pregnancy (T1; 9-14 weeks gestation) and 24 nonpregnant women (control group) participated in the study.

Polysomnography

Overnight PSG was performed in-laboratory to control for variations in potential external disruptions in the home environment. PSG was performed using the Somté (Compumedics, Abbotsford, Australia) portable sleep-monitoring device. Signals measured included single channel electroencephalogram (EEG; C3-A2), electrooculogram (EOG), nasal airflow measured via nasal oxygen cannula, arterial oxygen saturation measured via finger oximetry, thoracic and abdominal respiratory effort, snore, body position, leg movements and heart rate. PSG recordings were de-identified and sleep staged by a single experienced sleep technologist in accordance with standard criteria (Rechtschaffen and Kales, 1968). Respiratory events were scored as defined by the Chicago criteria (1999), and calculated parameters included the Apnoea/Hypopnoea Index per hour of sleep (AHI/hr) for rapid eye movement (REM) and non-REM (NREM) sleep in the supine and nonsupine positions. The percentage of total sleep time (TST) with oxygen saturation less than 95% and number of oxygen desaturations of $\geq$ 4% per hour (Oxygen Desaturation Index; ODI/hr) were calculated. PLMS were measured in accordance with the rules set out by the ASDA Atlas Task Force (1993).

Measurement of Snoring

Snoring on PSG was firstly analysed automatically by the Compumedics Profusion PSG 3 software with the threshold set to 4, minimum time between snores as 0.8 seconds, and minimum snore duration as 0.4 seconds. Snore analysis was then verified visually by the sleep technologist to reduce error, with snoring threshold for each participant determined to be at least 25% of the calibration signal given at the start of the night when they were asked to make a snore as loud as they could. Snoring was then expressed as the percentage of breaths with associated snores during sleep.

Snoring symptoms

Participants completed the Multivariate Apnea Risk Index (MAP Index; Maislin et al., 1995) at the time of the sleep study (see Appendix F). The MAP Index is a brief screening tool for OSA based on the reported frequency (nights per week) of various symptoms such as loud snoring, snorting, gasping and breathing pauses. Responses were then condensed into three categories; "never", "less than 3 nights per week" and "at least 3 nights per week". Habitual snorers were those who reported snoring at least 3 times per week.

Statistical Analysis

All statistical analyses were performed with the Statistical Package for Social Sciences 15.0 (SPSS Inc., Chicago, Illinois). Data were checked for linearity and normality. Many of the SDB measures were positively skewed as would be expected in the general population, and hence for statistical purposes non-normally distributed variables were transformed as appropriate. One third-trimester participant was excluded from analysis due to PSG signal failure and supine AHI/hr could not be calculated for one control and one third-trimester participant due to absence of supine sleep. Chi-square tests, multivariate analysis of variance and univariate analysis of variance were conducted on the variables of interest, with Newman-Keuls post hoc tests at a significance level of *p*

< .05. All values are given in mean ± SD for normally distributed variables or median and interquartile (IQR) range for non-normally distributed variables.

Results

Participants

Participants were approximately 30 years old, were within a healthy weight range according to pre-pregnant Body Mass Index (BMI) and there was a high prevalence of tertiary educated women (Table 1).

Table 1

Demographic Variables

	Control (n = 24)	T1 (n = 21)	T3 (n = 26)	p
Age[a]	29.3 ± 5.9	29.6 ± 3.4	32.1 ± 3.6	.051
Current BMI[a]	23.9 ± 3.2	26.3 ± 5.9	29.5 ± 3.3	<.001
Prepreg BMI[a]	23.9 ± 3.2	25.4 ± 5.4	23.4 ± 2.5	.24
Married/De Facto (%)	38	86	92	<.001
Nulliparous (%)	75	43	54	.08
Tertiary educated (%)	88	100	77	.06
Employed (%)				
Full time	50	43	39	.08
Part time	50	52	39	
Not employed	0	5	23	

Note. Data are M ± SD. T1 = first trimester; T3 = third trimester, BMI = body mass index

[a] p values associated with univariate ANOVA. All other p values associated with chi-square tests.

The three participant groups did not differ significantly in terms of employment status or parity, however a significantly higher percentage of the pregnant women were in a stable relationship as compared to the control group. BMI at the time of testing differed significantly between groups in accordance with stage of pregnancy.

Sleep-Disordered Breathing

Significantly more women in the third trimester of pregnancy scored an overall AHI/hr of greater than 5, as compared to the control group (30.8% vs. 4.2%, $\chi^2 = 5.98$, $p = .014$). The proportion of women with an AHI/hr of greater than 5 in the first-trimester group (23.8%) did not differ from the other groups. However as can be seen in Table 2, the AHI/hr by sleep stage and position were not different across the three groups (*Wilks* = .91, $F(8,126) = .75$, $p = .65$), and the overall average AHI/hr did not differ.

What did differ across the groups was the variability in AHI/hr scores, such that the third-trimester women had a much wider spread of AHI/hr values than the controls. Although difficult to objectively measure and quantify, visual inspection of the raw data showed that upper airway resistance and flow limitation was common on many of the third-trimester pregnant women's polysomnograms (see Figure 1 and Figure 2 for examples).

Table 2

Sleep-Disordered Breathing Measures for Each Group

Parameter	Control (n = 24)	T1 (n = 21)	T3 (n = 26)	Partial n^2	p
AHI/hr NREM	0.5 (0.2-0.7)	0.5 (0.2-1.4)	0.9 (0.4-2.2)	.06	.15
AHI/hr REM	8.2 (3.6-15.2)	11.9 (7.1-21.8)	13.0 (7.0-21.6)	.04	.25
AHI/hr supine[a]	1.7 (0.7-3.9)	2.6 (1.3-5.2)	4.7 (0.4-8.3)	.02	.56
AHI/hr nonsupine	1.5 (0.8-4.0)	2.1 (0.8-3.6)	2.1 (1.3-4.4)	.03	.39
AHI/hr overall	1.9 (1.0-3.5)	2.4 (1.6-4.8)	2.9 (1.4-5.5)	.04	.30
Minimum O_2 (%)[b]	92.0 ± 1.5	92.6 ± 1.9	92.3 ± 1.8	.02	.49
O_2<95% %TST	1.2 (0.5-5.9)	1.5 (0.3-21.1)	4.3 (0.4-32.4)	.03	.37
ODI/hr	0.5 (0.1-1.2)	0.3 (0-0.5)	0.3 (0-1.2)	.03	.36

Note. Data are Mdn (IQR) as variables were transformed. Effect size and probability associated with univariate ANOVA. AHI/hr = apnoea/hypopnoea index per hour; O2 = oxygen saturation; %TST = percentage of total sleep time; ODI/hr = oxygen desaturation index; T1 = first trimester; T3 = third trimester.

[a] Control n=23 and T3 n=25. [b] M ± SD.

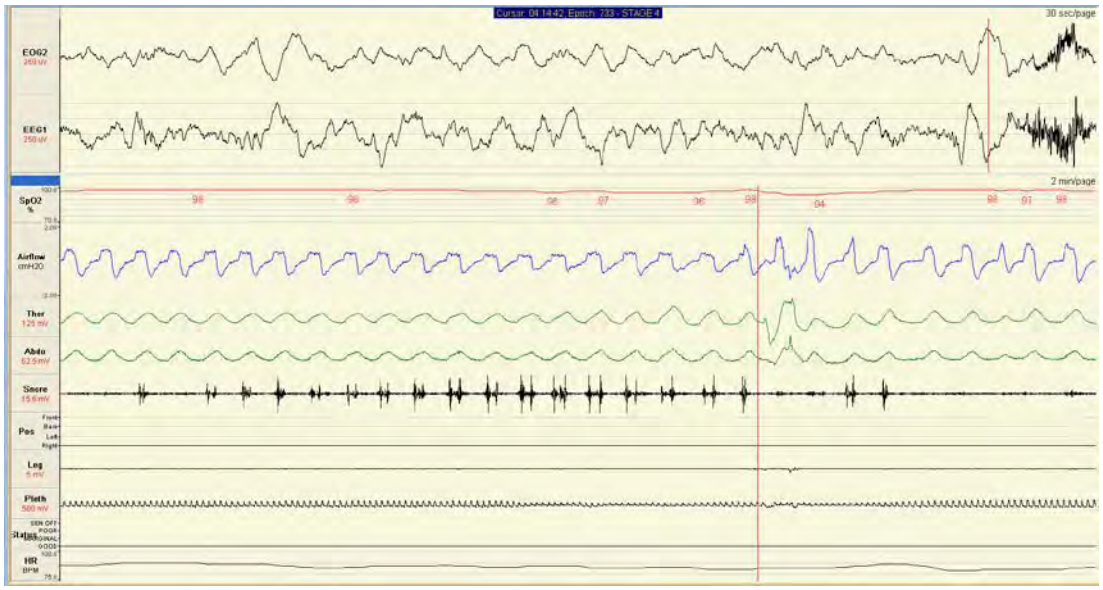

Figure 1. An example of snoring and airflow limitation in a third-trimester pregnant participant with an overall AHI/hr of 1.4. The top pane shows a 30-sec epoch of Stage 4 NREM sleep, and the bottom pane is set at 2-min. As can be seen, flow limitation resulted in cortical arousal and a mild drop in arterial oxygen saturation. At the time the participant was positioned on her right side. Her BMI at the time of the sleep study was 24.3.

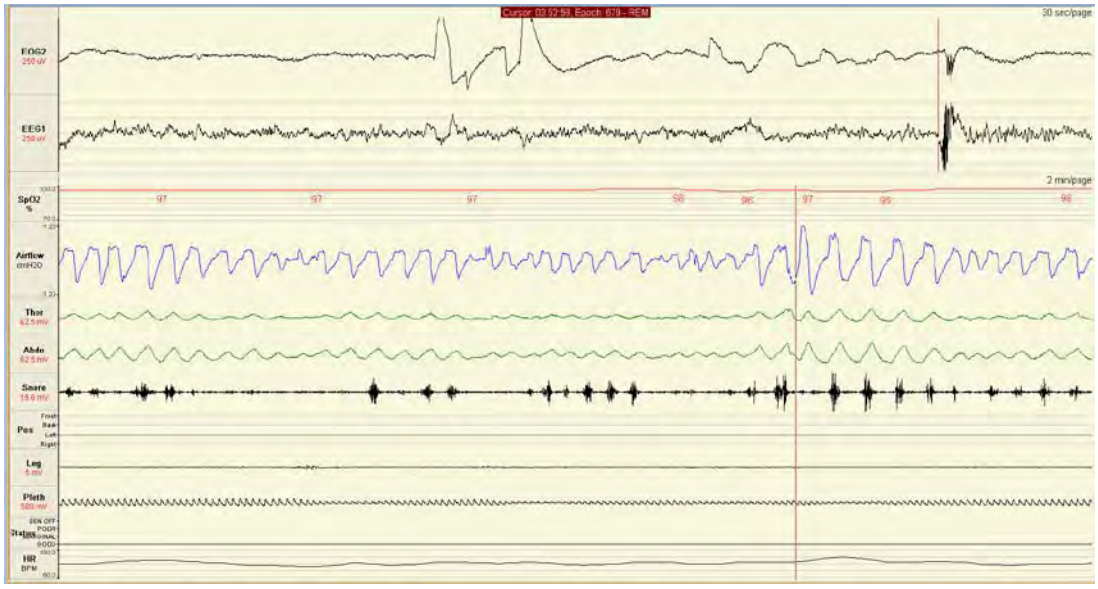

Figure 2. An example of snoring and airflow limitation in a third-trimester pregnant participant during REM sleep. As can be seen, flow limitation resulted in cortical arousal. At the time the participant was positioned on her left side. This participant had an overall AHI/hr of 1.8. Her BMI at the time of the sleep study was 29.1.

Women in the third trimester of pregnancy spent significantly more of their TST snoring than did the control group (see Figure 3). Snoring frequency increased significantly with BMI in the control (r = .76, p <.001) and first-trimester (r = .70, p = .003) groups, however snoring frequency was not significantly associated with BMI during the third trimester of pregnancy (r = .17, p = .44).

Measures of nocturnal arterial oxygen saturation (minimum oxygen saturation, percentage of TST with O_2 saturation < 95%, ODI/hr) did not differ across the groups (*Wilks* = .89, $F(6,132) = 1.34$, p = .24). However as shown in Table 2, the interquartile range values for percentage of TST with O_2 saturation less than 95% was much more variable in the third-trimester pregnancy group as compared to the control group.

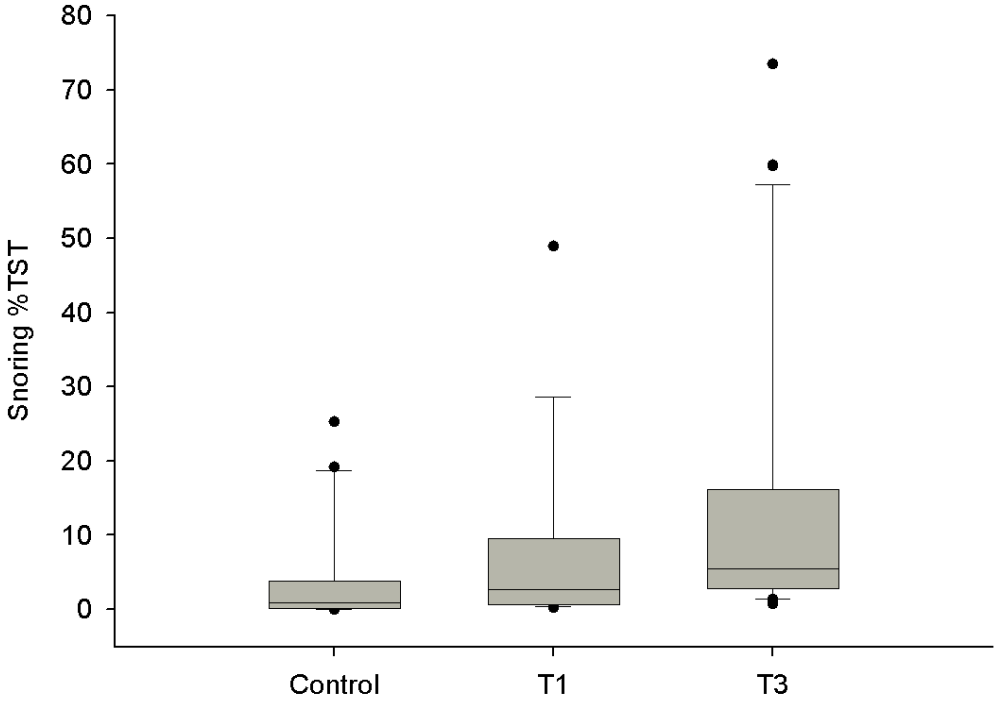

Figure 3. Box plots displaying median and interquartile range for snoring frequency as a percentage of total sleep time (TST) for each group. On average, T3 women spent a significantly higher percentage of TST snoring (Mdn = 5.5, IQR = 2.7 - 16.2) compared to the control group (Mdn = 0.9, IQR = 0.1 - 3.8; p = .001). T1 women did not differ from the other groups (Mdn = 2.7, IQR = 0.6 – 9.6). T1 = first trimester of pregnancy. T3 = third trimester of pregnancy.

Subjective Snoring

The reported frequency of SDB symptoms for participants who were either themselves aware or had been told of their symptoms is presented in Table 3. The difference in the reported frequency of snorting and gasping during sleep across the three groups was nearing significance ($\chi^2 = 9.10$, $p = .06$), with more third-trimester pregnant women reporting occasional (< 3 nights per week) or frequent (≥ 3 nights per week) symptoms of snorting and gasping. There was no significant difference across groups on reported frequency of loud snoring or breathing pauses and choking.

Table 3

Reported Symptoms of Sleep-Disordered Breathing on the MAP Index

%	Control	T1	T3	*p*
Snorting/Gasping				
Never	86.4	87.5	52.6	.06
< 3 nights per week	13.6	6.3	31.6	
≥ 3 nights per week	0	6.3	15.8	
Loud Snoring				
Never	69.6	66.7	41.7	.15
< 3 nights per week	30.4	22.2	41.7	
≥ 3 nights per week	0	11.1	16.7	
Choking/Apnoeas				
Never	100	93.8	89.5	.32
< 3 nights per week	0	6.3	10.5	
≥ 3 nights per week	0	0	0	

Note. Chi-square test, $p < .05$. T1 = first trimester; T3 = third trimester.

However, further analyses show that reported symptom frequency may not always be indicative of objective measures. As shown in Figure 4, there is large variation in objectively measured snoring for reported non-snorers, infrequent snorers and habitual snorers. For example, one third-trimester pregnant participant reported never snoring, but snored for 23% of her TST, whereas another reported infrequent snoring (actual response on the MAP Index was less than once per week) but snored for 60% of her total sleep time. In the first-trimester pregnant group, two participants reported never snoring but they snored for 49% and 20% of their TST and were in fact the heaviest snorers within the first-trimester group.

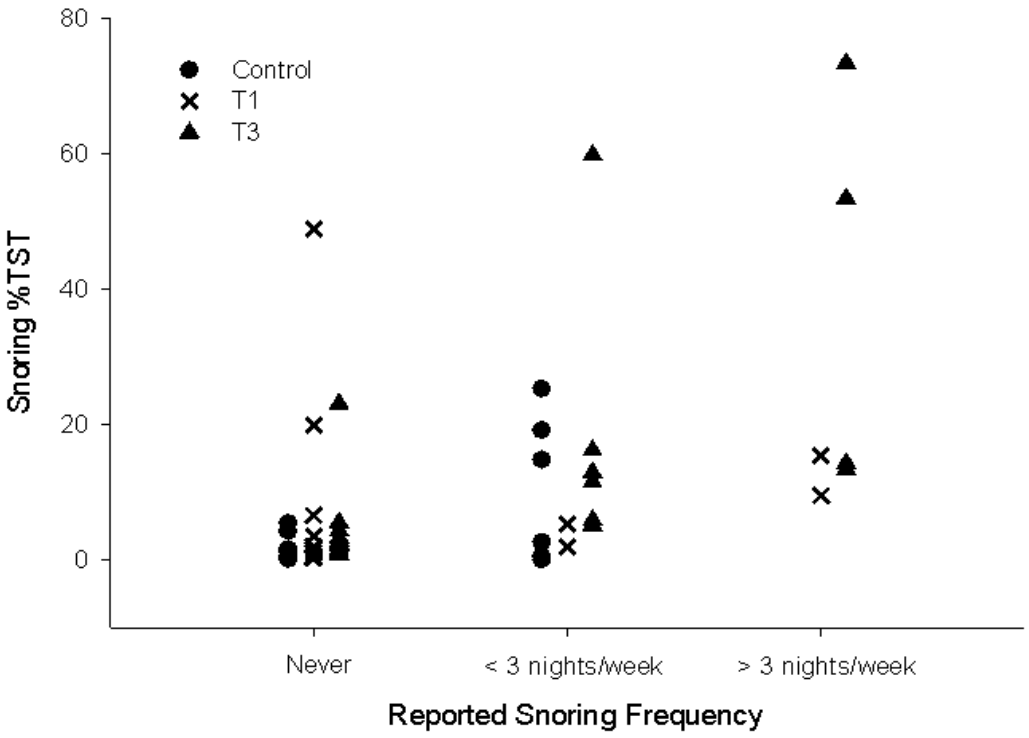

Figure 4. Percentage of breaths with snores present during sleep as measured on PSG for participants who reported never snoring, snoring < 3 nights per week, or snoring ≥ 3 nights per week. Data is shown separately for the control group, first-trimester pregnant group (T1) and third-trimester pregnant group (T3).

Periodic Limb Movements of Sleep

On average, PLMS were seen more frequently in the third-trimester group (*Mdn* = 1.8/hr, *IQR* = 0-5.7) when compared to the first-trimester (0, 0-2.8) and control group (0, 0-1; $F(2,69) = 4.59$, $p = .01$; see Figure 5). Significantly more third-trimester women had a PLMS index of >5 as compared to the controls (29.6% vs. 4.2%, $p = .03$), but not >15 in accordance with the International Classification of Sleep Disorders, Second Edition (ICSD-2; AASM, 2005) criteria for an abnormal PLMS index (11.1% vs. 0%, $p = .22$). Although PLMS were more common in the third trimester of pregnancy, there was no correlation between PLMS and sleep efficiency in this group ($r = .09$, $p = .64$) or overall ($r = -.02$, $p = .88$). PLMS index within each group or overall did not correlate with any stage of sleep or measure of overnight awakenings.

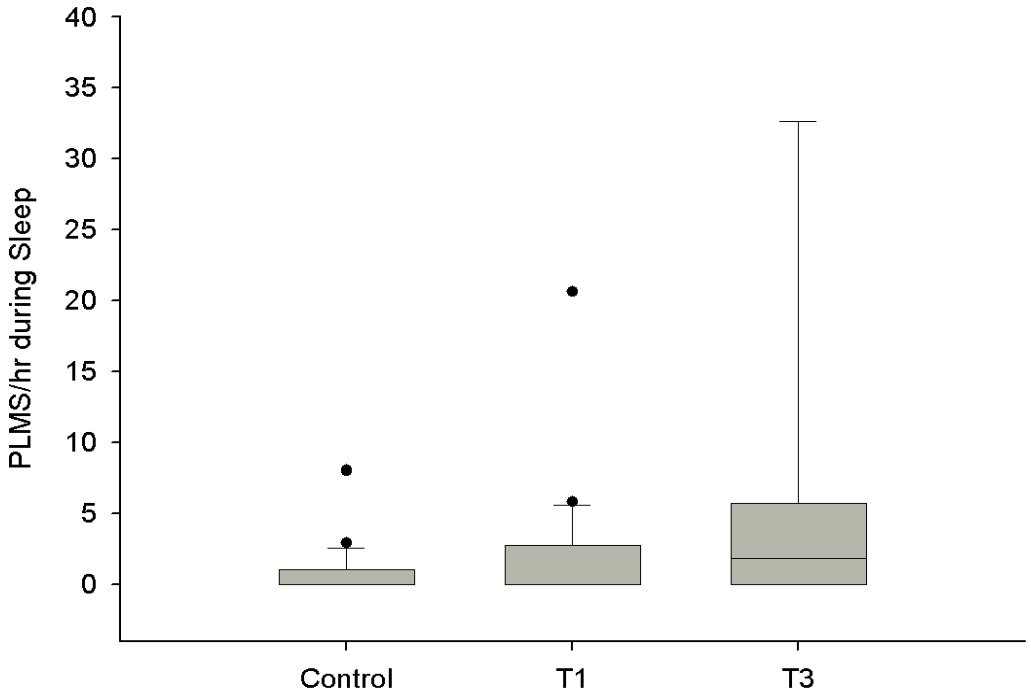

Figure 5. Box plots displaying median and interquartile range for PLMS index for each group. On average, PLMS were seen more frequently in the T3 women compared to the T1 and control women ($p = .01$). Note: two outliers for T3 group are not displayed. T1 = first trimester of pregnancy. T3 = third trimester of pregnancy.

Sleep Efficiency

Sleep efficiency was significantly higher in the control group (M = 90.0, SD = 6.4) compared to the third-trimester pregnant group (M = 81.7, SD = 10.8) and first-trimester pregnant group (M = 84.9, SD = 8.0; $F(2,68 = 5.68$, $p = .005$, $n^2 = .14$). Sleep position also differed significantly, with women in the third trimester of pregnancy spending a lesser percentage of TST in the supine position (M = 19.4, SD = 15.4) compared to the first-trimester (M = 41.0, SD = 23.6) and control group (M = 33.1, SD = 23.0; $F(2,67) = 6.55$, $p = .003$, $n^2 = .16$).

Discussion

The aim of this study was to objectively investigate SDB and PLMS in a sample of otherwise healthy non-obese pregnant women. Within this sample, 31% of the third-trimester pregnant women scored an overall AHI/hr of greater than 5, compared with 24% of the first-trimester pregnant women and only 4% of the nonpregnant women. Furthermore, visual inspection of the raw data revealed that upper airway resistance and flow limitation was apparent in the respiratory profiles of many of the third-trimester pregnant women. This observation supports previous work measuring oesophageal pressure during sleep in healthy young pregnant women, which identified two abnormal breathing patterns during sleep that were often associated with loud chronic snoring (Guilleminault et al., 2000).

Snoring was also most prevalent amongst the third-trimester pregnant women with a quarter of the sample snoring for over 16% of the night. This finding was despite the fact that third-trimester pregnant women spent a significantly lesser proportion of their sleep time supine, a position which typically increases snoring (Oksenberg and Silverberg, 1998). Women in the first trimester of pregnancy also tended to spend a higher proportion of their sleep time snoring as compared to the controls, but not significantly so. Although objectively measured in this study, snoring can be difficult to

quantify and subsequently compare to previous research studies. Our study gives objective support to previous questionnaire-based studies which found that snoring was more commonly reported during pregnancy (Izci et al., 2006, Perez-Chada et al., 2007, Pien et al., 2005, Loube et al., 1996, Ursavas et al., 2008). However, from our study it was apparent that some women under-report their snoring habits, potentially due to the perceived negative stigma attached to snoring. This discrepancy between reported and actual snoring brings into question the accuracy of self-reported measures as a means of assessing this important parameter. Furthermore, it casts uncertainty over the validity of conclusions made by studies linking self-reported snoring during pregnancy to negative outcomes such as pregnancy-induced hypertension and pre-eclampsia (Bourjeily et al., 2010, Franklin et al., 2000, Perez-Chada et al., 2007).

Although the difference in AHI/hr across the groups was mostly a wider variation in AHI/hr scores amongst the third-trimester pregnant women rather than significantly different median values, the significantly increased prevalence of snoring in this group of women may be of clinical significance. This pattern of SDB is more likely to resemble a syndrome referred to as upper airway resistance syndrome (UARS), which does not feature the classical repetitive episodes of complete obstruction often seen in males who have OSA (Edwards and Sullivan, 2008). Our finding that a quarter of the third-trimester pregnant women spent almost a third of their TST with their arterial oxygen saturation at less than 95% further hints that pregnancy is associated with prolonged flow limitation rather than discrete respiratory events. Studies have shown that even seemingly low levels of disease such as UARS in women is still associated with marked impairment of daytime function (Guilleminault et al., 1993), symptoms of insomnia, fatigue and depressive mood (Guilleminault et al., 2006), and the development of hypertension (Guilleminault et al., 1996). Consequently, a relatively low AHI/hr value should not automatically exclude diagnosis of a significant sleep-related breathing disorder. Given

the potential for healthy pregnant women to develop even a mild degree of SDB, further research is required to ascertain possible adverse maternal and foetal outcomes of milder forms of SDB.

Given that SDB in women may not typically feature discrete episodes of upper airway obstruction often seen in males with OSA, using only AHI/hr calculated via PSG may not be the optimal measure when investigating upper airway function in pregnant women. Unfortunately, other methods used to quantify limited airflow, such as oesophageal manometry, are invasive and uncomfortable for the patient and therefore other means of investigating SDB or even the development of a different diagnostic criterion for this population is warranted.

Research into SDB during pregnancy is still in the early stages, and as yet it is unknown whether pregnancy only exacerbates pre-existing SDB or whether SDB can develop in previously unaffected pregnant women. A large prospective study is needed to reveal how the many proposed mechanisms such as narrowed upper airway size (Izci et al., 2006), nasopharyngeal oedema (Pilkington et al., 1995, Elkus and Popovich, 1992), rhinitis (Gani et al., 2003), hormonal influences on upper airway and diaphragmatic drive (Edwards and Sullivan, 2008), obesity (Richman et al., 1994) and gestational weight gain contribute to this condition. In the case that the link between SDB and negative pregnancy outcomes is strengthened, the development of a predictive tool to determine which women are likely to develop SDB during pregnancy is important, particularly one that could be incorporated into antenatal health assessments.

Women in the third trimester of pregnancy also featured a higher rate of PLMS, although the PLMS index did not influence overall sleep quality. A PLMS index of > 5 for the entire night of sleep is considered pathological (Montplaisir et al., 2000), and within our sample 29% of the third-trimester pregnant women met this criterion compared to only 4% of the nonpregnant women. Given the apparent commonness of this

condition, there is a distinct lack of data on PLMS during pregnancy. RLS during pregnancy has been associated with increased amounts of PLMS (Dzaja et al., 2009), however the pregnancy literature appears to focus on RLS which is considered as distinct from PLMS.

The main limitation of this study is its cross-sectional, rather than longitudinal nature. Ideally, pregnant women would have had multiple sleep studies over the course of their pregnancy. However, pregnant women are often unwilling to undergo additional tests and procedures above and beyond those already associated with their pregnancy, especially when it involves multiple nights away from home. This was reflected in the low response rate during recruitment and the high dropout rate after interest in the study was initially expressed. Consequently, the investigation of sleep-related breathing disorders during pregnancy has typically been based on the much less reliable self-report methodologies. The low response rate was unlikely to lead to sample bias, as women approached to participate in this study were not informed of the study hypotheses and were blinded to the fact that SDB was a particular focus of the study.

This study has shown a clinically relevant difference in SDB symptoms and PLMS between healthy pregnant and nonpregnant women. In particular, women in the third trimester of pregnancy were more likely to demonstrate at least a mild degree of OSA, and on average they spent a significantly greater proportion of sleep time snoring as compared to nonpregnant women. Almost a third of the women in the third trimester of pregnancy were found to have a PLMS index considered to be pathological. Further research into the aetiology and evolution of sleep disorders during pregnancy is indicated, as well as investigation of potential adverse maternal and foetal effects of milder forms of SDB. An assessment of sleep health should be considered as an important addition to routine antenatal care.

Acknowledgments

The authors would like to thank the staff at the Austin Health Sleep Laboratory for their support of this project and we appreciate the valuable contribution made by each of the research participants.

This research was funded by La Trobe University and the Austin Health Medical Research Foundation. The authors declare that they have no conflict of interest.

References

American Academy of Sleep Medicine. *International Classification of Sleep Disorders, 2nd ed.: Diagnostic and coding manual*. American Academy of Sleep Medicine, Westchester, IL, 2005.

Baratte-Beebe, K. and Lee, K. A. Sources of midsleep awakenings in childbearing women. *Clinical Nursing Research*, 1999, 8: 386-97.

Bixler, E. O., Vgontzas, A. N., Lin, H. M., Ten Have, T., Rein, J., Vela-Bueno, A. and Kales, A. Prevalence of sleep-disordered breathing in women: Effects of gender. *Am J Respir Crit Care Med*, 2001, 163: 608-13.

Blyton, D. M., Sullivan, C. E. and Edwards, N. Reduced nocturnal cardiac output associated with preeclampsia is minimized with the use of nocturnal nasal CPAP. *Sleep*, 2004, 27: 79-84.

Bourjeily, G., Raker, C. A., Chalhoub, M. and Miller, M. A. Pregnancy and fetal outcomes of symptoms of sleep-disordered breathing. *European Respiratory Journal*, 2010, 36: 849-55.

Brunner, D. P., Münch, M., Biedermann, K., Huch, R., Huch, A. and Borbély, A. A. Changes in sleep and sleep electroencephalogram during pregnancy. *Sleep*, 1994, 17: 576-82.

Charbonneau, M., Falcone, T., Cosio, M. and Levy, R. Obstructive sleep apnea during pregnancy. Therapy and implications for fetal health. *Am Rev Respir Dis*, 1991, 144: 461-3.

Contreras, G., Gutiérrez, M., Beroíze, T., Fantín, A., Oddó, H., Villarroel, L., Cruz, E. and Lisboa, C. Ventilatory drive and respiratory muscle function in pregnancy. *Am Rev Respir Dis*, 1991, 144: 837-41.

Driver, H. S. and Shapiro, C. M. A longitudinal study of sleep stages in young women during pregnancy and postpartum. *Sleep*, 1992, 15: 449-53.

Dzaja, A., Wehrle, R., Lancel, M. and Pollmacher, T. Elevated estradiol plasma levels in women with restless legs during pregnancy. *Sleep*, 2009, 32: 169-74.

Edwards, N., Blyton, D. M., Hennessy, A. and Sullivan, C. E. Severity of sleep-disordered breathing improves following parturition. *Sleep*, 2005, 28: 737-41.

Edwards, N., Middleton, P. G., Blyton, D. M. and Sullivan, C. E. Sleep disordered breathing and pregnancy. *Thorax*, 2002, 57: 555-58.

Edwards, N. and Sullivan, C. A. Sleep-disordered breathing in pregnancy. *Sleep Med Clin*, 2008, 3: 81-95.

Elkus, R. and Popovich, J. Respiratory physiology in pregnancy. *Clin Chest Med*, 1992, 13: 555-65.

Franklin, K. A., Holmgren, P., Jonsson, F., Poromaa, N., Stenlund, H. and Svanborg, E. Snoring, pregnancy-induced hypertension, and growth retardation of the fetus. *Chest*, 2000, 117: 137-41.

Gani, F., Braida, A., Lombardi, C., Del Giudice, A., Senna, G. and Passalacqua, G. Rhinitis in pregnancy. *Eur Ann Allergy Clin Immunol*, 2003, 35: 306-13.

Guilleminault, C., Kirisoglu, C., Poyares, D., Palombini, L., Leger, D., Farid-Moayer, M. and Ohayon, M. M. Upper airway resistance syndrome: a long-term outcome study. *J Psychiatr Res*, 2006, 40: 273-79.

Guilleminault, C., Palombini, L., Poyares, D., Takaoka, S., Huynh, N. and El-Sayed, Y. Pre-eclampsia and nasal CPAP: Part 1. Early intervention with nasal CPAP in pregnant women with risk-factors for pre-eclampsia: Preliminary findings. *Sleep Medicine*, 2007, 9: 9-14.

Guilleminault, C., Querra-Salva, M., Chowdhuri, S. and Poyares, D. Normal pregnancy, daytime sleeping, snoring and blood pressure. *Sleep Med*, 2000, 1: 289-97.

Guilleminault, C., Stoohs, R. A., Clerk, A., Cetel, M. and Maistros, P. A cause of excessive daytime sleepiness. The upper airway resistance syndrome. *Chest*, 1993, 104: 781-87.

Guilleminault, C., Stoohs, R. A., Shiomi, T., Kushida, C. and Schnittger, I. Upper airway resistance syndrome, nocturnal blood pressure monitoring, and borderline hypertension. *Chest*, 1996, 109: 901-08.

Hertz, G., Fast, A., Feinsilver, S. H., Albertario, C. L., Schulman, H. and Fein, A. M. Sleep in normal late pregnancy. *Sleep*, 1992, 15: 246-51.

Izci, B., Riha, R. L., Martin, S. E., Vennelle, M., Liston, W. A., Dundas, K. C., Calder, A. A. and Douglas, N. J. The upper airway in pregnancy and pre-eclampsia. *American Journal of Respiratory and Critical Care Medicine*, 2003, 167: 137-40.

Izci, B., Vennelle, M., Liston, W. A., Dundas, K. C., Calder, A. A. and Douglas, N. J. Sleep-disordered breathing and upper airway size in pregnancy and post-partum. *The European Respiratory Journal*, 2006, 27: 321-27.

Lee, K. A., Zaffke, M. E. and Mcenany, G. Parity and sleep patterns during and after pregnancy. *Obstetrics and Gynecology*, 2000, 95: 14-18.

Loube, D. I., Poceta, J. S., Morales, M. C., Peacock, M. D. and Mitler, M. M. Self-reported snoring in pregnancy: Association with fetal outcome. *Chest*, 1996, 109: 885-89.

Maislin, G., Pack, A. I., Kribbs, N. B., Smith, P. L., Schwartz, A. R., Kline, L. R., Schwab, R. J. and Dinges, D. F. A survey screen for prediction of apnea. *Sleep*, 1995, 18: 158-66.

Manconi, M., Govoni, V., De Vito, A., Economou, N. T., Cesnik, E., Casetta, I., Mollica, G., Ferini-Strambi, L. and Granieri, E. Restless legs syndrome and pregnancy. *Neurology*, 2004, 63: 1065-69.

Mcauliffe, F., Kametas, N., Costello, J., Rafferty, G. F., Greenough, A. and Nicolaides, K. Respiratory function in singleton and twin pregnancy. *BJOG: an International Journal of Obstetrics and Gynaecology*, 2002, 109: 765-69.

Mindell, J. A. and Jacobson, B. J. Sleep disturbances during pregnancy. *Journal of Obstetric, Gynecologic, and Neonatal Nursing*, 2000, 29: 590-97.

Montplaisir, J., Nicolas, A., Godbout, R. and Walters, A. S. Restless legs syndrome and periodic limb movement disorder. In: M. Kryger, T. Roth and W. C. Dement (Eds), *Principles and practice of sleep medicine 3rd edition*. W. B. Saunders Company, Philadelphia, Pennsylvania, 2000.

Nikkola, E., Ekblad, U., Ekholm, E., Mikola, H. and Polo, O. Sleep in multiple pregnancy: breathing patterns, oxygenation, and periodic leg movements. *Am J Obstet Gynecol*, 1996, 174: 1622-25.

Oksenberg, A. and Silverberg, D. The effect of body posture on sleep-related breathing disorders: facts and therapeutic implications. *Sleep Med Rev*, 1998, 2: 139-62.

Perez-Chada, D., Videla, A. J., O'flaherty, M. E., Majul, C., Catalini, A. M., Caballer, C. A. and Franklin, K. A. Snoring, witnessed sleep apnoeas and pregnancy-induced hypertension. *Acta Obstetricia et Gynecologica Scandinavica*, 2007, 86: 788-92.

Pien, G. W., Fife, D., Pack, A. I., Nkwuo, J. E. and Schwab, R. J. Changes in symptoms of sleep-disordered breathing during pregnancy. *Sleep*, 2005, 28: 1299-305.

Pilkington, S., Carli, F., Dakin, M., Romney, M., De Witt, K., Doré, C. and Cormack, R. Increase in Mallampati score during pregnancy. *Br J Anaesth*, 1995, 74: 638-42.

Popovic, R. and White, D. Upper airway muscle activity in normal women: influence of hormonal status. *J Appl Physiol*, 1998, 84: 1055-62.

Poyares, D., Guilleminault, C., Hachul, H., Fujita, L., Takaoka, S., Tufik, S. and Sass, N. Pre-eclampsia and nasal CPAP: Part 2. Hypertension during pregnancy, chronic snoring, and early nasal CPAP intervention. *Sleep Medicine*, 2007, 9: 15-21.

Rechtschaffen, A. and Kales, A. *A manual of standardized terminology, techniques, and scoring system for sleep stages of human subjects*. Brain Information Service, Los Angeles, 1968 (

Richman, R. M., Elliot, L. M., Burns, C. M., Bearpark, H. M., Steinbeck, K. S. and Caterson, I. D. The prevalence of obstructive sleep apnoea in an obese female population. *Int J Obes Relat Metab Disord*, 1994, 18: 173-77.

Roush, S. F. and Bell, L. Obstructive sleep apnea in pregnancy. *The Journal of the American Board of Family Practice*, 2004, 17: 292-94.

Sahin, F. K., Koken, G., Cosar, E., Saylan, F., Fidan, F., Yilmazer, M. and Unlu, M. Obstructive sleep apnea in pregnancy and fetal outcome. *International Journal of Gynecology and Obstetrics*, 2008, 100: 141-46.

Schweiger, M. S. Sleep disturbance in pregnancy: A subjective survey. *Am J Obstetr Gynecol*, 1972, 114: 879-82.

Sleep-related breathing disorders in adults: recommendations for syndrome definition and measurement techniques in clinical research. The Report of an American Academy of Sleep Medicine Task Force. *Sleep*, 1999, 22: 667-89.

The ASDA Atlas Task Force. Recording and scoring leg movements. *Sleep*, 1993, 16: 748-59.

Tunç, T., Karadag, Y. S., Dogulu, F. and Inan, L. E. Predisposing factors of restless legs syndrome in pregnancy. *Movement Disorders*, 2007, 22: 627-31.

Ursavas, A., Karadag, M., Nalci, N., Ercan, I. and Gozu, R. O. Self-reported snoring, maternal obesity and neck circumference as risk factors for pregnancy-induced hypertension and preeclampsia. *Respiration*, 2008, 76: 33-39.

Chapter 5

Reduced Verbal Memory Retention is unrelated to Sleep Disturbance during Pregnancy

Manuscript submitted in April 2011 for publication in

Australian Psychologist.

Preface

So far, Chapters 2 and 3 have shown that pregnancy is associated with reduced verbal episodic memory and that sleep is disrupted in a number of ways. As yet the cause of memory problems during pregnancy is unknown. This study hypothesises that the popular theory that memory consolidation occurs during sleep may be applicable to the pregnant population and may help to explain why memory difficulties occur. No study to date has objectively measured both memory performance and sleep in the attempt to explain memory difficulties during pregnancy.

The purpose of Chapter 5 is to bring together the results from previous chapters, to examine whether memory impairments during pregnancy can be attributed to sleep disturbance, whilst accounting for potential confounders to this relationship. The present study also aims to test two common theories of memory consolidation during sleep by investigating the relationships between different types of memory and sleep stages.

Reduced Verbal Memory Retention is unrelated to Sleep Disturbance during Pregnancy

Danielle L. Wilson

School of Psychological Science, La Trobe University, Bundoora, Victoria, Australia

Institute for Breathing and Sleep, Austin Health, Heidelberg, Victoria, Australia

Maree Barnes

Institute for Breathing and Sleep, Austin Health, Heidelberg, Victoria, Australia

Department of Medicine, University of Melbourne, Parkville, Victoria, Australia

Lenore Ellett and Michael Permezel

Department of Obstetrics and Gynaecology, Mercy Hospital for Women, Heidelberg, Victoria, Australia

Martin Jackson and Simon F. Crowe

School of Psychological Science, La Trobe University, Bundoora, Victoria, Australia

This research was funded by La Trobe University and the Austin Health Medical Research Foundation. The authors have indicated no financial conflicts of interest.

Address correspondence to: Simon F. Crowe, School of Psychological Science, La Trobe University, Bundoora, VIC, 3086, Australia. Tel: 613 9479 1380; Fax: 613 9479 1956; E-mail: s.crowe@latrobe.edu.au

Abstract

This study investigated episodic and procedural memory retention in early and late pregnancy and whether memory retention was related to sleep disruption. Twenty-six women in the third trimester of pregnancy, 20 women in the first trimester of pregnancy and 24 nonpregnant controls were administered a series of verbal and visual episodic memory tasks and two procedural memory tasks, and underwent an overnight sleep study. Results indicated that when compared to controls, both pregnant groups had reduced retention in verbal episodic memory but were unimpaired on visual and procedural memory tasks. The pregnant women also demonstrated significant disruption of sleep patterns. Contrary to prevailing theories regarding memory consolidation during sleep, reduced memory retention was not related to any measure of sleep.

Keywords: Attention, Consolidation, Episodic, Pregnant, Procedural, Progesterone

Word count: 6,591 (excluding references)

Memory complaints are commonly reported during pregnancy (Brindle, Brown, Brown, Griffith, & Turner, 1991; Janes, Casey, Huntsdale, & Angus, 1999; Parsons & Redman, 1991), with deficits demonstrated on word list learning (Buckwalter, et al., 1999; de Groot, Vuurman, Hornstra, & Jolles, 2006; Sharp, Brindle, Brown, & Turner, 1993), paragraph recall (Keenan, Yaldoo, Stress, Fuerst, & Ginsburg, 1998) semantic fluency (de Groot, Hornstra, Roozendaal, & Jolles, 2003) and priming (Brindle, et al., 1991; Sharp, et al., 1993). However, this effect is not consistently observed (Casey, 2000; Casey, Huntsdale, Angus, & Janes, 1999; Christensen, Poyser, Pollitt, & Cubis, 1999).

The cause of memory complaints during pregnancy is yet to be determined, but is likely to be multi-factorial. One common explanation for memory impairments in pregnancy relates to hormonal change, but no consistent associations between these factors has been noted (Buckwalter, et al., 1999; Silber, Almkvist, Larsson, & Uvnas-Moberg, 1990). A frequent complaint made during pregnancy is that of sleep disruption. While correlations between crude measures of self-reported sleep disturbance and verbal memory (Christensen, Leach, & Mackinnon, 2010; Keenan, et al., 1998) have been noted, as yet no study has objectively measured both memory performance and sleep in the attempt to explain memory difficulties during pregnancy.

Polysomnography (PSG) studies undertaken during pregnancy have consistently shown that sleep efficiency (defined as time spent sleeping as a percentage of time spent in bed) is reduced in the pregnant state and deteriorates as pregnancy advances (Brunner, et al., 1994; K. A. Lee, Zaffke, & McEnany, 2000), mostly as a result of increased time spent awake after sleep onset (Brunner, et al., 1994; Driver & Shapiro, 1992; Hertz, et al., 1992). The alterations in rapid eye movement (REM) sleep associated with pregnancy have ranged from a reduction in comparison to nonpregnant controls (Driver & Shapiro, 1992; Hertz, et al., 1992), a reduction from early to late pregnancy (Brunner, et al., 1994),

through to showing no significant differences (K. A. Lee, et al., 2000; Schorr, et al., 1998). Slow wave sleep (SWS) is often decreased compared to prepregnancy baseline measures (K. A. Lee, et al., 2000) and nonpregnant women (Hertz, et al., 1992; Schorr, et al., 1998), however no changes across trimesters (Brunner, et al., 1994) and even an increase in SWS in pregnancy has been documented (Driver & Shapiro, 1992).

The mechanisms of memory reprocessing during sleep are far from understood. It is though that during sleep, a central mechanism for memory consolidation is the covert reactivation of neuronal populations used for encoding the respective materials during prior learning (Maquet, 2001; McNaughton, et al., 2003; Stickgold, Hobson, Fosse, & Fosse, 2001). The hippocampal replay of previously encoded events drives a transfer of information to the neocortex in which the memory becomes consolidated and integrated into long-term representations (McClelland, McNaughton, & O'Reilly, 1995; McNaughton, et al., 2003; Wilson & McNaughton, 1994). Different sleep stages are thought to contribute to consolidation of memory in different ways. The dual-process hypothesis argues that SWS facilitates the consolidation of declarative memory, whereas REM sleep facilitates the consolidation of implicit memory (Plihal & Born, 1997). Alternatively, the double-step hypothesis contends that SWS and REM sleep each play complementary roles and act serially to consolidate the memory trace (Ficca, Lombardo, Rossi, & Salzarulo, 2000; Giuditta, et al., 1995).

There are many potential confounding factors in the relationship between sleep and memory consolidation during pregnancy. Firstly, changes in respiratory function during pregnancy can lead to alterations in maternal oxygenation during sleep (Connolly, et al., 2001; Prodromakis, Trakada, Tsapanos, & Spiropoulos, 2004). Hypoxic episodes during sleep can be associated with damage to the brain if they frequently recur (Gibson, Pulsinelli, Blass, & Duffy, 1981) and the hippocampus is particularly vulnerable to oxygen deprivation (Caine & Watson, 2000).

Another important consideration is the role of attention. The clearest effect of sleep loss is sleepiness (Bonnet, 2000), which has been related to response slowing and attentional lapses (Durmer & Dinges, 2005). Lapses in attention decrease the ability of the person to focus and give necessary effort to complete a task successfully (Johnson, 1982; Meddis, 1982).

Depressive symptomatology in the prenatal period is also common with rates between 14% and 37% (Andersson, et al., 2003; A. M. Lee, et al., 2007; Priest, Austin, Barnett, & Buist, 2008). Individuals with disordered mood have previously been shown to exhibit impaired memory function (Bearden, et al., 2006; Sweeney, Kmiec, & Kupfer, 2000). Pregnant women identified as being depressed report poorer sleep quality (Field, et al., 2007; Jomeen & Martin, 2007), and sleep deprivation is a reliable predictor of both prenatal (Field, et al., 2007; Skouteris, Germano, Wertheim, Paxton, & Milgrom, 2008) and postnatal mood changes (Wilkie & Shapiro, 1992; Wolfson, Crowley, Anwer, & Bassett, 2003).

The purpose of this study was to examine the relationship between sleep and memory during pregnancy, by establishing whether memory impairment in pregnancy can be attributed to sleep disturbances whilst accounting for the potential confounders of attention, mood, hormone level and hypoxaemia during sleep. It was hypothesised that pregnant women would perform more poorly on episodic and procedural memory tasks in comparison to nonpregnant women, and that this would be associated with measures of sleep disruption. This study also investigated the relationship between episodic and procedural memory and sleep stages, testing both the dual-process and the double-step hypotheses of memory consolidation during sleep.

Method

Participants

Twenty-six women in the third trimester of pregnancy (T3: 30-38 weeks gestation), 20 women in the first trimester of pregnancy (T1: 9-14 weeks gestation) and 24 nonpregnant women (control group) participated in the study. The Human Research Ethics Committees at each institution involved in this research approved this study and informed consent was obtained from all participants (see Appendix B). Four hundred and thirty pregnant women from the Outpatient Obstetrics Clinic of a major maternity hospital were consecutively approached to participate in the study, of these 56 agreed. Participant declination was mostly due to the time commitment involved, unwillingness to have a sleep study and inability to be away from home overnight. After volunteering to participate, ten pregnant women withdrew prior to data collection due to pregnancy-related complications or inability to schedule an appropriate night to attend the sleep laboratory. Nonpregnant women were recruited from advertisements in the hospital newsletter and from friends of the pregnant participants. Participants were excluded if they had a multiple or complicated pregnancy (including hypertension, gestational diabetes mellitus and preeclampsia), a significant medical, psychological or psychiatric co-morbidity, a previously diagnosed sleep disorder, or a history of head injury or memory problems. Those with uncorrected hearing or a visual impairment, poor English language skills and those taking anti-depressant medication were also excluded.

Materials

The demographic information collected included date of birth, handedness, relationship status, number of children, level of education, and employment status. Gestation in number of weeks was also collected for the pregnant participants. The instruments administered include:

- Depression Anxiety Stress Scale – Short version (DASS21; Lovibond & Lovibond, 1995).
- Wechsler Abbreviated Scale of Intelligence (WASI; The Psychological Corporation, 1999).
- Test of Memory Malingering (TOMM; Tombaugh, 1996). Participants in this study were deemed to be giving sufficient effort if they scored at least 45 out of 50 (90%) on the second trial.
- Wechsler Memory Scale – Third Edition (WMS-III; Wechsler, 1997). The scaled scores from the four primary subtests of Logical Memory, Faces, Verbal Paired Associates and Family Pictures were used to assess episodic memory. The Rarely Missed Index for Logical Memory Recognition (Killgore & DellaPietra, 2000) was also calculated as a measure of response validity.
- Rey Auditory-Verbal Learning Test (RAVLT; Rey, 1964). Memory retention on the RAVLT was defined as the number of words retained on delayed recall as a percentage of the number of words recalled on the fifth immediate recall trial; therefore a higher percentage indicates better memory retention.
- Austin (Milner) Maze (Milner, 1965; Walsh, 1985). Errors on each of 10 trials were calculated as the number of times the participant presses a button that is not on the correct path. Delayed recall was assessed by the number of errors made on one further trial. Memory retention was defined as the number of errors made on the delay trial minus the number of errors made on the tenth learning trial, resulting in a 'difference' score.
- Motor Sequence Learning. This procedural memory task is the same as the Finger-tapping Task used by Walker, Brakefield, Morgan, Hobson and Stickgold (2002), but for the purpose of this study will be termed Motor Sequence Learning so as not to confuse with the Finger Tapping Test (Reitan, 1979) used in

neuropsychological test batteries. Motor Sequence Learning requires participants to press four numeric keys on a standard computer keyboard with the fingers of their left (non-dominant) hand, repeating the five element sequence 4-1-3-2-4 as quickly and as accurately as possible for a period of 30 seconds. The numeric sequence was displayed at the top of the screen at all times to exclude any working memory component to the task. Training consisted of ten 30-second trials with 30-second rest periods between trials. The scores (number of sequences and number of errors) from the final two trials were averaged and taken as the "posttraining" performance. The averaged scores of two further 30-second trials assessed delayed performance. Memory retention was defined as the number of sequences and errors made on delay minus those made on "posttraining". A positive difference score therefore represents an increased number of sequences or errors after the retention interval.

- Mirror-Tracing Task (Model 31010; Lafayette Instrument Co., Lafayette, Indiana). For this procedural memory task, participants were instructed to quickly and accurately trace a flat, six-pointed star with a pencil while only a mirror-inverted image of the star was visible. Performance on each of ten trials was assessed by the number of errors (drawing outside the edges of the star) and the time taken to trace the star. The averaged scores from the final two trials were taken as the "posttraining" performance, and the averaged scores of two further trials assessed delayed performance. Memory retention was defined as the tracing time and errors made on delay minus those made on "posttraining"; again a positive difference score represents an increase in tracing time or errors after the retention interval.
- Test of Variables of Attention (TOVA; The TOVA Company, Los Alamitos, California). Variables measured include response time, variability of response

time (consistency), errors of commission (impulsivity) and errors of omission (inattention).

- Polysomnography. Overnight PSG was conducted in-laboratory with the Somté (Compumedics, Abbotsford, Australia) portable sleep-monitoring device to control for variations in external disruptions in the home environment and to provide greater comfort for the participants. Portable sleep-monitoring systems are commonly used in clinical settings and have been shown to have a high level of agreement with standard laboratory-based systems (Churchward, et al., 2006; Mykytyn, Sajkob, Neill, & McEvoy, 1999). PSG recordings were sleep staged by a single experienced sleep technologist who was blinded to pregnancy status, in accordance with standard criteria (Rechtschaffen & Kales, 1968). Sleep parameters included total sleep time (TST), number of minutes spent in Stage 1 sleep (NREM1), Stage 2 sleep (NREM2), SWS (Stage 3 and 4 combined) and REM sleep, number of awakenings during sleep and wake after sleep onset (WASO). Sleep cycle analysis was based on that used by Mazzoni et al. (1999). A sleep cycle was defined as a sequence of non-REM (NREM) and REM sleep not interrupted by a waking period longer than 2 minutes. To define a NREM/REM sequence, both NREM and REM periods had to be longer than 2 minutes. REM epochs of shorter than 2 minutes were included in the previous sleep state. A sequence of NREM stages interrupted by a period of wake longer than 2 minutes was not considered part of a NREM/REM cycle. Variables measured were the number of sleep cycles, average sleep cycle length in minutes, and total cycle time (TCT) as a proportion of total sleep time (TCT/TST). Arousals from sleep were measured in accordance with the rules set out by the ASDA Atlas Task Force (Bonnet, et al., 1992). Lowest arterial oxygen saturation

during sleep was recorded, as well as percentage of TST with arterial oxygen saturation less than 95%.

Procedure

Participants arrived at the sleep laboratory in the evening, having refrained from drinking alcohol and caffeinated beverages from midday. The testing battery was administered as presented in Table 1. All participants were tested at the same time of day by the same investigator. The evening testing session took approximately two hours and participants were given rest breaks as requested.

Table 1

Schedule of Neuropsychological Testing and Estimated Administration Time

Order of Testing	Administration Time (mins)
Demographics	< 5
DASS21	< 5
WASI	30
TOMM	10
Motor Sequence Learning	10
Mirror Tracing Task	10
Austin Maze	10
WMS-III	20
RAVLT	5
TOVA	22

Note. DASS21 = Depression Anxiety Stress Scale – Short version; WASI = Wechsler Abbreviated Scale of Intelligence; TOMM = Test of Memory Malingering; WMS-III = Wechsler Memory Scale – Third Edition; RAVLT = Rey Auditory-Verbal Learning Test; TOVA = Test of Variables of Attention.

On completion of testing, participants were set-up with the portable sleep-monitoring device and allowed to go to bed in a private room. Participants were left undisturbed until they were woken eight hours after lights out time. Approximately 30 minutes after waking, the delayed components of the memory tests were administered in the same order as in the evening, and blood samples were taken for serum progesterone levels due to its potentially soporific effect (Herrmann & Beach, 1978; Söderpalm, Lindsey, Purdy, Hauger, & de Wit, 2004).

Statistical Analysis

All statistical analyses were performed with the Statistical Package for Social Sciences 15.0 (SPSS Inc., Chicago, Illinois). Data were checked for linearity and normality and non-normally distributed variables were either square root or log transformed as appropriate. The few extreme univariate outliers found (z score > 3.29) were assigned a raw score one unit larger or smaller than the next most extreme score in the distribution, as recommended by Tabachnick and Fidell (2007). Data was screened for multivariate outliers using Mahalanobis distance (Tabachnick & Fidell, 2007) and none were found. Four third-trimester women, one first-trimester woman and one control woman were unable to complete the Mirror-Tracing Task due to its difficulty. TOVA data for one first-trimester woman was invalid due to an unanticipated disruption during the fourth quarter of the test. Up until this point performance was within normal limits and therefore this participant was included in all other analyses.

Chi-square tests and one-way between-groups analysis of variance (ANOVA) were used to compare the three groups on demographic variables and intellectual functioning. One-way between-groups multivariate analysis of variance (MANOVA) was used to compare groups on memory retention on the WMS-III subtests along with the RAVLT and Austin Maze, and to compare groups on procedural memory retention. One-way between-groups MANOVA was also used to compare groups on sleep parameters

and mood state. A mixed 3 (group) x 4 (quarter) ANOVA was used to analyse TOVA response time and response time variability. In order to determine which variables contributed to memory retention during pregnancy, one-way between-groups analysis of covariance (ANCOVA) were conducted. The correlation matrix was examined to check for multicollinearity. Potential covariates were those that correlated with memory retention and met the homogeneity of regression assumption. As progesterone is strongly linked to pregnancy status it could not be considered a covariate, so the effect of progesterone on memory was investigated using multiple regression. The relationship between memory retention and parameters of sleep was investigating using bivariate correlations.

Effect sizes were calculated using eta squared and partial eta squared with 95% confidence intervals according to Smithson's (2003) method. Effect sizes of .01, .06 and .14 are considered small, medium and large in magnitude respectively. On those items where a significant difference between groups was detected, further investigation was conducted with post hoc Tukey tests with the significance level set at $p < .05$. All values are given in mean ± standard deviation for normally distributed variables or median (Mdn) and interquartile (IQR) range for non-normally distributed variables.

Results

Participants

The average age in years of the third-trimester (M = 32.2, SD = 3.6), first-trimester (M = 29.4, SD = 3.3) and control groups (M = 29.3, SD = 5.9) did not differ (p = .09). Further demographic details for each of the groups are presented in Table 2. The three participant groups did not differ in terms of handedness, education level, employment status or whether they already had children. However, not too surprisingly, significantly more pregnant women were in a stable relationship as compared to the control group.

Table 2

Percentage of Participants in Each Demographic Category

	Control (n = 24)	T1 (n = 20)	T3 (n = 26)	χ^2	p
Right handed	87.5	95.0	96.2	1.60	.45
Relationship status				25.61**	<.001
Married/De facto	37.5	85	92.3		
Relationship	25	15	7.7		
Single	37.5	0	0		
Has children	25	55	46.2	4.43	.11
Tertiary educated	87.5	100	76.9	5.38	.07
Employment				8.20	.09
Full time	50	45	38.5		
Part time	50	50	38.5		
Unemployed	0	5	23		

Note. Values given in percentages. T1 = first trimester of pregnancy; T3 = third trimester of pregnancy.

** $p < .01$

Intellectual Functioning

The third-trimester, first-trimester and control groups were equivalent in terms of Verbal and Performance IQ, and the Full Scale IQ did not differ across groups (control: M = 114.8, SD = 8.2; T1: M = 111.1, SD = 8.6; T3: M = 114.1, SD = 10.7; $F(2,67) = 0.96$, p = .39).

Measures of Effort

All participants scored 45 or greater on the second trial of the TOMM, indicating that no participant was feigning memory difficulties. Two control participants scored

under the cutoff of 136 on the Rarely Missed Index for Logical Memory Recognition. However, both participants scored above average on overall General Memory on the WMS-III and were deemed to be giving sufficient effort during testing. All participants performed better on RAVLT recognition as compared to the first trial (Greiffenstein, Baker, & Gola, 1996) and delayed recall (Bernard, Houston, & Natoli, 1993; Flowers, Sheridan, & Shadbolt, 1996), further indicating sufficient effort towards testing.

Memory Retention

The means, standard deviations, significance levels and effect sizes with 95% confidence intervals (CI) for each between-group comparison on memory retention scores for each memory test are presented in Table 3.

Episodic memory. Measures of verbal episodic memory retention (Logical Memory, Verbal Paired Associates, RAVLT) differed significantly across the groups, *Wilks*= .65, $F(6,130) = 5.26$, $p < .001$, partial $n^2 = .20$, (CI .06 - .28). In particular, the first-trimester pregnant group retained significantly less information on the Logical Memory task as compared to the third-trimester pregnant and control groups, and the effect size was large. The third-trimester pregnant group retained a significantly lower percentage of words from the RAVLT over the retention interval as compared to the control group, with a large effect size. There were no differences across the groups on retention for the Verbal Paired Associates task.

Measures of visual episodic memory retention (Faces, Family Pictures and Austin Maze) did not differ across the groups, *Wilks*= .94, $F(6,130) = 0.73$, $p = .63$, partial $n^2 = .03$, (CI .00 - .06). All groups retained close to 100% on the Family Pictures task and on average, participants performed better on the Faces task after the retention interval. On the Austin Maze, all groups showed an increase in errors made on delay compared to the tenth trial of learning.

Table 3

Mean (± SD) of Memory Retention Scores for Each Group and Level of Significance and Effect Sizes for Between-Group Comparisons

Subtest	Control (n = 24)	T1 (n = 20)	T3 (n = 26)	F	p	partial $n^{2\dagger}$
			Episodic Tasks			
LM %	$82.4 \pm 11.4_a$	$66.2 \pm 18.1_b$	$79.1 \pm 15.1_a$	$7.02^{\ddagger}$**	.002	.17 (.03, .32)
VPA %	99.5 ± 4.9	93.4 ± 12.9	94.2 ± 13.5	$2.05^{\ddagger}$	.14	.06 (.00, .17)
Faces %	106.3 ± 8.4	103.4 ± 10.0	105.3 ± 8.1	$0.60^{\ddagger}$	.55	.02 (.00, .10)
FP %[¥]	100.0 (98.1–103.0)	100.0 (97.7–101.2)	98.4 (95.6–100.0)	$0.84^{\ddagger}$	.44	.02 (.00, .11)
RAVLT %	$87.7 \pm 13.0_a$	$78.4 \pm 18.9_{ab}$	$72.3 \pm 16.2_b$	$5.79^{\ddagger}$**	.005	.15 (.02, .29)
Maze	1.2 ± 1.4	1.8 ± 1.6	1.2 ± 2.1	$0.70^{\ddagger}$	.50	.02 (.00, .11)
			Procedural Tasks			
MS seq.	3.9 ± 3.6	3.5 ± 1.7	2.7 ± 2.0	$1.48^{\S}$	.24	.04 (.00, .15)
MS seq. %	17.7 ± 19.0	17.4 ± 10.3	13.2 ± 11.3	$0.73^{\S}$	.49	.02 (.00, .11)
MS errors	-1.2 ± 1.9	-0.9 ± 1.7	-0.5 ± 1.2	$1.28^{\S}$	.29	.04 (.00, .15)
MT time sec.	-2.2 ± 5.4	0.8 ± 5.0	-2.6 ± 6.3	$2.17^{\P}$	.12	.07 (.00, .20)
MT time %	-5.4 ± 16.1	2.7 ± 14.3	-4.9 ± 17.3	$1.63^{\P}$	.20	.05 (.00, .17)
MT errors	-5.0 ± 5.5	-3.2 ± 3.7	-3.5 ± 2.9	$1.08^{\P}$	.35	.03 (.00, .14)

Note. Means in the same row that do not share subscripts differ at $p < .05$ in the Tukey significant difference comparison. LM = Logical Memory; VPA = Verbal Paired Associates; FP = Family Pictures; RAVLT = Rey Auditory-Verbal Learning Test; Maze = Austin Maze Errors; MS seq. = Motor Sequence Learning number of sequences; MS seq. % = Motor Sequence Learning retention score as a percentage; MT time = Mirror-tracing; MT time % = Mirror-tracing time retention score as a percentage; T1 = first trimester of pregnancy; T3 = third trimester of pregnancy.

[†] 95% confidence intervals given in parentheses (upper, lower). [‡] $df = 2,67$. [§] $df = 2,66$. [¶] $df = 2,61$.

[¥] Values given as *Mdn* (*IQR)* as variable was transformed.

** $p < .01$, * $p < .05$

Procedural memory. On average, all groups similarly improved over the retention interval on the Motor Sequence Learning task by increasing the number of sequences and decreasing the number of errors, *Wilks*= .94, $F(4,130) = 1.06$, $p = .38$, partial $n^2 = .03$, (CI .00 - .08). On the Mirror-Tracing Task, the control and third-trimester pregnant group improved their tracing time on average over the retention interval, whereas the first-trimester pregnant group tended to have a slightly increased tracing time. All groups decreased their error rate over the retention interval, and overall there was no significant difference across groups on this task, *Wilks*= .91, $F(4,120) = 1.49$, $p = .21$, partial $n^2 = .05$, (CI .00 - .11).

Potential Factors Influencing Verbal Episodic Memory Retention

Sleep Parameters. The means, standard deviations, significance levels and effect sizes with 95% confidence intervals for each between-group comparison for sleep parameters are presented in Table 4. Measures of sleep fragmentation (TST, WASO, number of awakenings and arousals/hr) differed significantly across the groups, *Wilks*= .69, $F(8,128) = 3.34$, $p = .002$, partial $n^2 = .17$, (CI .03 - .24). In particular, women in the third trimester of pregnancy spent significantly less time asleep than the controls and had significantly more cortical arousals per hour than both the first-trimesters and controls. WASO was significantly less in the control group as compared to both pregnant groups. The effect sizes for these differences were all medium to large. The overall difference in time spent in each sleep stage across the groups demonstrated a strong trend, *Wilks* = .80, $F(8,128) = 1.94$, $p = .059$, partial $n^2 = .11$, (CI .00 - .16). However, one-way ANOVA revealed that third-trimester pregnant women spent significantly less time in REM sleep and SWS sleep when compared to the control group. The effect sizes of these differences were medium to large. Measures of sleep cycle architecture (number of sleep cycles, average sleep cycle length, TCT/TST (%)) differed significantly across the groups, *Wilks*= .80, $F(6,130) = 2.56$, $p = .02$, partial $n^2 = .11$, (CI .00 - .17). The control group spent

Table 4

Mean (± SD) of Sleep Parameters for Each Group and Level of Significance and Effect Sizes for Between-Group Comparisons

Sleep parameter	Control (n = 24)	T1 (n = 20)	T3 (n = 26)	$F^{\dagger}$	P	partial $n^{2\ \ddagger}$
TST (min)	$427.2 \pm 42.4_{a}$	$403.7 \pm 38.4_{ab}$	$388.6 \pm 55.9_{b}$	4.28*	.018	.11 (.00, .25)
WASO (min)	$28.0 \pm 19.5_{a}$	$51.0 \pm 35.6_{b}$	$59.1 \pm 33.8_{b}$	6.95**	.002	.17 (.03, .31)
Awakenings	15.3 ± 4.1	16.2 ± 4.7	18.6 ± 6.9	2.55	.09	.07 (.00, .19)
Arousals/hr[§]	8.8	10.6	14.5	10.46**	<.001	.24 (.00, .38)
	$(7.1 – 10.9)_{a}$	$(7.4 – 14.0)_{a}$	$(10.6 – 18.2)_{b}$			
NREM1 (min)	27.8 ± 12.2	29.4 ± 15.6	35.6 ± 15.6	2.00	.14	.06 (.00, .17)
NREM2 (min)	167.1 ± 39.3	163.5 ± 43.5	166.2 ± 34.4	0.05	.95	.001 (.00, .03)
SWS (min)	$157.5 \pm 39.5_{a}$	$147.4 \pm 61.4_{ab}$	$123.2 \pm 42.5_{b}$	3.40*	.04	.09 (.00, .22)
REM (min)	$75.0 \pm 18.1_{a}$	$63.4 \pm 15.2_{ab}$	$62.1 \pm 20.3_{b}$	3.65*	.03	.10 (.00, .23)
Cycles (n.)	4.5 ± 1.3	4.2 ± 1.5	3.8 ± 1.0	2.29	.11	.06 (.00, .18)
Cycles (min)	82.4 ± 22.1	74.6 ± 18.6	70.3 ± 21.0	2.16	.12	.06 (.00, .18)
TCT/TST (%)	$83.9 \pm 17.1_{a}$	$73.1 \pm 14.3_{b}$	$66.9 \pm 21.2_{b}$	5.64**	.005	.14 (.01, .28)
Min O2 (%)	92.0 ± 1.5	92.5 ± 1.9	92.3 ± 1.8	0.59	.56	.02 (.00, .10)
O2 < 95% %TST	8.2 ± 16.0	11.2 ± 16.5	18.3 ± 24.5	1.73	.19	.05 (.00, .16)

Note. Means in the same row that do not share subscripts differ at p < .05 in the Tukey significant difference comparison. TST = total sleep time; WASO = wake after sleep onset; O2 = oxygen saturation; T1 = first trimester of pregnancy; T3 = third trimester of pregnancy.

† df = 2,67. ‡ 95% confidence intervals given in parentheses (upper, lower). § values given as *Mdn* (*IQR)* as variable was transformed.

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

significantly more TST in sleep cycles than pregnant women. Measures of overnight arterial oxygen saturation did not differ across the groups.

Attention. The average number of omission and commission errors made by each group did not differ on any quarter of the attention test, as for the total omission errors (control: *M* = 0.8, *SD* = 2.5; T1: *M* = 0.4, *SD* = 0.8; T3: *M* = 0.5, *SD* = 0.7) and commission errors (control: *M* = 8.5, *SD* = 6.2; T1: *M* = 9.9, *SD* = 8.0; T3: *M* = 11.7, *SD* = 8.7), *Wilks*= .93, *F*(4,130) = 1.15, *p* = .34. As shown in Figure 1, there was no interaction effect between the three groups and test quarter on the TOVA for response time, *Wilks*= .98, *F*(6,128) = 0.21, *p* = .97, and response time variability, *Wilks*= .93, *F*(6,128) = 0.80, *p* = .57. A non-significant between-subjects effect indicates that the groups did not differ overall on response time, *F*(2,66)= 0.98, *p* = .31, or response time variability, *F*(2,66)= 1.36, *p* = .26.

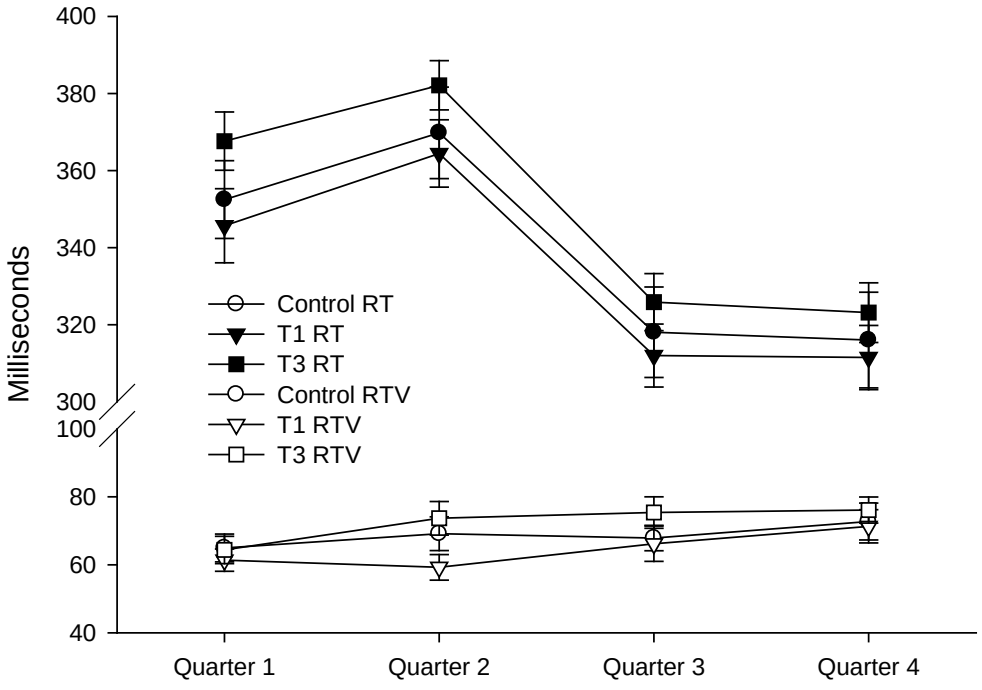

Figure 1. Mean response time (RT) and mean response time variability (RTV) for the control (*n* = 24), T1 (*n* = 19), and T3 (*n* = 26) groups for each quarter of the Test of Variables of Attention (TOVA). The groups performed equivalently on each quarter of the test. Vertical lines depict standard errors of the mean. T1 = first trimester of pregnancy, T3 = third trimester of pregnancy.

Progesterone. Progesterone level was significantly higher in the third-trimester pregnant group (*Mdn* = 413nmol/L, *IQR* = 311.5-509.3) when compared to the first-trimester pregnant group (68.5, 58.6-82.3), which was significantly higher than that in the control group (4.2, 2.6-7.9; $F(2,65) = 392.38$, $p < .001$, $n^2 = 0.92$).

Mood state. The average DASS21 scores are shown in Table 5. Mood did not differ across the groups, *Wilks* = .87, $F(6,128) = 1.52$, $p = .18$, $n^2 = .07$, (CI .00 to .12.).

Table 5

Median Scores on the DASS21 for Each Group and Level of Significance and Effect Sizes for Between-Group Comparisons

	Control	T1	T3	$F^{\dagger}$	p	n^2
Depression	2 (0-4)	2 (2-5.5)	2 (0-4)	.43	.65	.01
Anxiety	1 (0-4)	2 (0-4)	4 (0-6)	1.72	.19	.05
Stress [‡]	9.6 ± 5.9	8.4 ± 7.9	8.3 ± 6.3	.26	.77	.01

Note. Interquartile range (IQR) in parentheses. DASS21 = Depression Anxiety Stress Scale – short version; T1 = first trimester of pregnancy; T3 = third trimester of pregnancy. Normal range – Depression = 0-9, Anxiety = 0-7, Stress = 0-14.

[†] $df = 2,67$. [‡] values given as $M \pm SD$.

Why is Verbal Episodic Memory Retention Reduced during Pregnancy?

To investigate potential contributors to reduced Logical Memory retention in the first trimester of pregnancy and reduced RAVLT retention in the third trimester of pregnancy, the correlation matrix for memory retention, sleep parameters, attention, mood state and progesterone for all participants is shown in Table 6. As progesterone is strongly linked to the progression of pregnancy, it could not be used in further covariate analyses so its influence on memory retention needs to be investigated separately for each group.

Table 6

Intercorrelations between Logical Memory Retention, RAVLT Retention, Sleep Parameters, Attention, Mood State and Progesterone

	1	2	3	4	5	6	7	8	9	10	11	12†	13†	14
1. LM		.50**	.11	.14	-.15	.24*	.18	-.10	.09	.14	.11	-.08	-.10	-.06
2. RAVLT			.03	.09	-.10	.22^	.15	.04	.19	-.12	-.07	-.003	-.08	.15
3. S1 (min)				.16	-.53**	.07	.09	-.12	-.01	-.06	-.07	-.07	-.27*	-.12
4. S2 (min)					-.50**	.29*	.44**	-.08	.23^	.02	-.25*	-.07	-.27*	-.22
5. SWS (min)						.001	-.01	.27*	.13	-.13	.11	-.07	.10	.02
6. REM (min)							.48**	.16	.49**	-.13	-.08	-.12	-.20	-.15
7. Cycle (n.)								-.31**	.55**	.09	.02	-.10	-.32**	-.28*
8. Cycle (min)									.57**	-.16	.01	-.14	-.13	.16
9. TCT/TST										.05	.11	-.25*	-.35**	-.05
10. RT											.65**	-.10	-.05	-.05
11. RTV												-.09	-.06	.02
12. Dep†													.42**	.42**
13. Anx†														.48**
14. Stress														
M	76.5	79.3	31.1	165.7	141.9	66.9	4.2	75.7	74.5	328.8	76.7	2	2	8.8
SD	16.2	17.1	14.7	38.3	49.4	18.9	1.3	21.1	19.2	41.3	18.2	0 - 4	0 - 4	6.6

Note. $N = 70$. LM = Logical Memory; RAVLT = Rey Auditory-Verbal Learning Test; S1 = Stage 1; S2 = Stage 2; SWS = slow wave sleep; REM = rapid eye movement; TCT = total cycle time; TST = total sleep time; RT = response time; RTV = response time variability; Dep = depression; Anx = anxiety.

† Values given as *Mdn* (*IQR)* as variable was transformed.

** $p < .01$, *$p < .05$, ^$p < .1$.

Within the control group, progesterone was not associated with Logical Memory or RAVLT retention. After combining the first- and third-trimester pregnant groups, progesterone did not significantly explain any additional variance in Logical Memory retention, $F(1,42) = 0.52$, $p = .48$, or RAVLT retention, $F(1,42) = 2.09$, $p = .16$, over and above that explained by number of weeks gestation.

Logical memory retention. As shown in Table 6, Logical Memory retention was significantly but weakly associated with higher levels of REM sleep. Logical Memory retention was not related to any other measure of sleep, attention or mood. Correlation matrices for each individual group revealed no other significant correlations.

To determine whether REM sleep impacts on the relationship between pregnancy and Logical Memory retention, a one-way between-groups ANCOVA was performed. After adjustment by minutes in REM sleep, Logical Memory retention still differed significantly across pregnancy groups, as summarised in Table 7, with $F(2, 66) = 6.07$, $p = .004$, partial $n^2 = .16$, (CI .02 - .30). The adjusted marginal means displayed in Table 8 show that the first-trimester group scored significantly less on Logical Memory retention as compared to the control group. There was no relationship between the number of minutes spent in REM sleep and Logical Memory Retention score, $F(1, 66) = 2.51$, $p = .12$, $n^2 = .04$, (CI .00 - .16). The results of this ANCOVA indicate that time spent in REM sleep is not contributing to reduced Logical Memory retention in the first trimester of pregnancy.

Table 7

Analysis of Covariance of Logical Memory Retention and RAVLT Retention

Source of Variance	Adjusted SS	Df	MS	*F*
		Logical Memory Retention		
Pregnant Group	2648.44	2	1324.22	6.07**
Covariate				
REM (min)	547.58	1	547.58	2.51
Error	14394.66	66	218.10	
		RAVLT Retention		
Pregnant Group	2247.98	2	1123.99	4.36*
Covariate				
REM (min)	255.12	1	255.12	.99
Error	17025.70	66	257.97	

** $p < .01$, *$p < .05$

RAVLT retention. As presented in Table 6, the correlation between RAVLT retention and REM sleep demonstrated a strong trend ($p = .06$), with better retention on the RAVLT weakly related to higher levels of REM sleep. RAVLT retention is not correlated with any other sleep measures, attention variables or mood state, and correlation matrices for each pregnant group revealed no other significant correlations.

To determine whether REM sleep has an impact on the relationship between pregnancy and RAVLT retention, a one-way between-groups analysis of covariance was performed. After adjustment for minutes in REM sleep, RAVLT retention still differed significantly across pregnancy groups, as summarised in Table 7, with F (2, 66) = 4.36, p = .02, partial n^2 = .12, (CI .00 - .25). The adjusted marginal means displayed in Table 8 show that the third-trimester group scored significantly less on RAVLT retention as

compared to the control group. There was no relationship between the number of minutes spent in REM sleep and RAVLT retention score, F (1, 66) = 0.99, p = .32, partial n^2 = .02, (CI .00 - .11). These results only differ slightly to the one-way ANOVA result for RAVLT retention (see Table 3), indicating that controlling for REM sleep only marginally improved the mean scores for RAVLT retention.

Table 8

Adjusted and Unadjusted Mean Logical Memory Retention and RAVLT Retention Scores for Each Pregnancy Group

Pregnancy Group	Adjusted Mean	Unadjusted Mean
	Logical Memory Retention	
Control	81.1	82.4
T1	66.7	66.2
T3	79.9	79.1
	RAVLT Retention	
Control	86.8	87.7
T1	78.8	78.4
T3	72.8	72.3

Note. T1 = first trimester of pregnancy; T3 = third trimester of pregnancy.

Relationship between Memory and Sleep

In order to test the dual-process and double-step hypotheses of memory consolidation during sleep, a correlation matrix was produced and is presented in Table 9. As shown, Logical Memory retention and RAVLT retention were only correlated with minutes of REM sleep, and these relationships were weak. Verbal Paired Associates

Table 9

Intercorrelations between Memory Retention Scores and Sleep Parameters

	1	2	3	4†	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20
1. LM		.17	.33**	-.07	.50**	.04	.05	-.02	-.11	.03	.11	.14	-.15	.24*	.10	-.03	.19	.18	-.10	.09
2. VPA			-.05	-.06	.24	.08	.12	.11	.12	.04	.23^	.13	-.32**	.20^	-.07	.03	.05	.10	.15	.29*
3. Faces				.09	.07	-.07	-.18	.02	-.05	.13	-.09	.08	.02	.05	.07	.03	-.07	.04	-.17	-.13
4. Fam Pic†					-.08	.17	-.09	.18	-.003	-.06	-.14	-.07	.21^	-.09	.09	.02	-.05	-.20^	-.04	-.27*
5. RAVLT						.17	.07	-.16	.18	.04	.03	.09	-.10	.22^	.07	-.10	.08	.15	.04	.19
6. Maze							.07	-.01	.16	.01	-.02	-.25*	.09	-.20	-.19	.18	-.07	-.28*	-.07	.19
7. MSL seq								-.29*	-.08	-.17	-.01	-.16	.09	.06	-.02	.04	.02	.06	-.05	.05
8. MSL error									-.003	-.05	.02	.30*	-.08	-.08	.13	-.01	-.06	.05	-.16	-.13
9. MT time										.26^	.05	.10	-.10	-.06	-.03	.05	-.02	-.11	.04	-.08
10. MT error											.10	.01	-.06	.13	.04	-.09	.03	-.03	.07	.03
11. S1 (min)												.16	-.53**	.07	-.05	.03	.39**	.09	-.12	-.01
12. S2 (min)													-.50**	.29*	.43**	-.34**	-.08	.44**	-.08	.23^
13. SWS (min)														.001	.45**	-.34**	-.19	-.01	.27*	.13
14. REM (min)															.62**	-.49**	-.19	.48**	.16	.49**
15. TST (min)																-.77**	-.17	.55**	.23^	.50**
16. WASO																	.33**	-.42**	-.32**	-.50**
17. Awakening																		.03	-.22^	-11
18. Cycle (n.)																			-.31**	.55**
19. Cycle (min)																				.57**
20. TCT/TST																				
M	76.5	95.8	105.1	100	79.3	1.4	3.4	-0.8	-1.6	-3.9	31.2	165.7	141.9	66.9	406.1	46.1	16.8	4.2	75.7	74.5
SD	16.2	11.3	8.7	96.8-101.6	17.1	1.7	2.6	1.6	5.8	4.2	14.7	38.3	49.4	18.9	49.1	32.7	5.6	1.3	21.1	19.2

Note. $N = 70$. LM = Logical Memory; VPA = Verbal Paired Associates; Fam Pic = Family Pictures; RAVLT = Rey Auditory-Verbal Learning Test; MSL = Motor Sequence Learning; MT = Mirror-Tracing; S1 = Stage 1; S2 = Stage 2; SWS = slow wave sleep; REM = rapid eye movement; TST = total sleep time; WASO = wake after sleep onset; TCT = total cycle time.

† Values given as *Mdn* (*IQR)* as variable was transformed.

** $p < .01$, *$p < .05$, ^$p < .1$

retention was significantly negatively correlated with minutes in SWS, and had positive but weak relationships with REM and Stage 1 sleep (p = .09 and p = .06 respectively). Family Pictures retention showed a tendency towards a positive association with SWS (p = .08). However due to the limited variability in Verbal Paired Associates and Family Pictures retention scores, these correlations are misleading and do not accurately reflect any relationship. Increased Stage 2 sleep was significantly but weakly associated with improvement on errors made after the retention interval on the Austin Maze, but a higher number of errors on the Motor Sequence Learning task. Faces retention, Motor Sequence Learning number of sequences, and Mirror-Tracing time and number of errors was not correlated with any measure of sleep.

In terms of sleep cycles, spending a higher proportion of TST within sleep cycles was significantly related to higher scores on Verbal Paired Associates and Family Pictures retention; but again these associations are misleading. A greater number of sleep cycles was weakly associated with an improved error rate on the Austin Maze after the retention interval. Retention scores on Logical Memory, Faces, RAVLT, Motor Sequence Learning and Mirror-Tracing were unrelated to sleep cycle architecture.

In sum, the dual-process hypothesis was not supported, as REM sleep was not related to any measures of procedural memory retention and SWS was not reliably associated with any episodic memory retention measures. In terms of the double-step hypothesis, no strong associations between sleep cycle architecture and memory retention were found.

Discussion

The results support the initial hypothesis of memory difficulties during pregnancy, with the pregnant women performing more poorly on tasks of verbal episodic memory retention but not on tasks of visual episodic or procedural memory retention. In particular, the first-trimester pregnant women retained less information from the

paragraph recall task, whereas the third-trimester women retained less information from the word-list task, as compared to nonpregnant women. The magnitude of the effect sizes for these differences in performance was large.

In order to explain reduced verbal memory retention during pregnancy, a number of factors were measured. Attention, mood, and nocturnal arterial oxygen saturation did not differ across the three groups, and none of these were associated with verbal memory retention. Although progesterone level varied greatly across the groups, this hormone was also unable to explain any variance in memory retention.

Our key hypothesis was that sleep disruption during pregnancy would be a factor in reduced memory retention. Pregnant women, particularly those in the third trimester, had more disrupted sleep compared to nonpregnant women. Specifically, they spent less time asleep and had more cortical arousals during sleep. They also spent less time in SWS and REM sleep. Women in the first trimester of pregnancy spent more time awake during the night compared to nonpregnant women, and both pregnant groups spent less of their TST within sleep cycles, indicating more fragmented sleep. The amount of information retained on the paragraph recall task and the word-list task was significantly but weakly related to time spent in REM sleep only. However, further analyses indicated that contrary to expectation, the reduced amount of REM sleep in both pregnant groups did not account for differences in verbal episodic memory retention.

In contrast to the dual-process hypothesis, the amount of REM sleep overnight was not related to any measure of procedural memory retention and the amount of SWS overnight was not reliably associated with any episodic memory retention measure. Similarly, no strong associations between sleep cycle architecture and memory retention were found on any task, giving no support to the double-step hypothesis of memory consolidation during sleep.

Our results contrast the previous experimental studies which have noted that explicit memory is enhanced after early sleep periods dominated by SWS (Barrett & Ekstrand, 1972; Drosopoulos, Wagner, & Born, 2005; Fowler, Sullivan, & Ekstrand, 1973; Plihal & Born, 1997, 1999; Plihal, Pietrowsky, & Born, 1999; Yaroush, Sullivan, & Ekstrand, 1971), or those showing that implicit memory benefits from sleep with high amounts of REM sleep in the later part of the night (Plihal & Born, 1997, 1999; Plihal, et al., 1999). Additionally, our results do not support studies showing that both episodic and implicit memory are related to sleep architecture, or the structure of sleep cycles during the night (Ficca, et al., 2000; Gais, Plihal, Wagner, & Born, 2000; Mazzoni, et al., 1999; Stickgold, Whidbee, Schirmer, Patel, & Hobson, 2000).

For the motor sequence learning task, the degree of improvement over the sleep interval for the first-trimester pregnant and nonpregnant groups was comparable to previous studies showing overnight improvements in speed of between 17-20% (Kuriyama, Stickgold, & Walker, 2004; Walker, et al., 2002; Walker, et al., 2003). The third-trimester pregnant group showed a lesser improvement of 13.2%. Unlike other studies (Fischer, Hallschmid, Elsner, & Born, 2002; Walker, et al., 2002) however, we were unable to attribute overnight improvement in speed to either Stage 2 sleep or REM sleep. Our inability to attribute any parameter of sleep to improvements in motor-skill speed may lend support to Rickard and colleagues (Rickard, Cai, Rieth, Jones, & Ard, 2008) who concluded that sleep does not uniquely enhance procedural memory performance, and improvements may be due to other factors such as a build-up of fatigue over the course of training which dissipates between sessions.

One possible reason for the discrepancy between our results and the majority finding a relationship between sleep and memory consolidation could be a key difference in experimental design. Most methodologies include manipulation of sleeping conditions in order to test hypotheses, whereas our study compared a group of “normal” sleepers

against those who were expected to have disrupted sleep. For example, by dividing the retention interval into either early night sleep or late night sleep, Plihal and Born (1997) found that time spent in SWS was five times longer during the early than late sleep retention interval, and time in REM sleep was twice as long during late than early sleep. In comparison, the third-trimester pregnant women in our study had 34 minutes less SWS and 13 minutes less REM sleep on average than the nonpregnant women. It may be that sleep stage architecture needs to be significantly altered before memory consolidation is affected. In a similar vein are the findings that even short sleep periods may be sufficient to promote memory consolidation. For example, declarative and procedural memory performance has been shown to benefit from half a night of sleep (Tucker & Fishbein, 2009), and declarative memory retention has been shown to improve after hour-long napping (Tucker, et al., 2006) and even with short six minute naps, suggesting that the mere onset of sleep may initiate the active processes of memory consolidation (Lahl, Wispel, Willigens, & Pietrowsky, 2008).

Side effects of sleep deprivation can include emotional and attentional disorders, reduced motivation and disturbances in biological rhythms; these disturbances may affect behavioural performance (Rauchs, Desgranges, Foret, & Eustache, 2005). Our study attempted to control for as many contributing factors as possible. Measures of mood, attention and progesterone were all taken, and none of these were related to memory retention. It has also been argued that women may subconsciously perform more poorly on testing due to cultural expectations of cognitive decline during pregnancy (Crawley, Grant, & Hinshaw, 2008). Incorporating well-validated tests of effort into our methodology revealed that all pregnant participants were giving sufficient effort towards testing, and therefore reduced motivation was unlikely to be a factor.

Progesterone is one of the most active hormones during pregnancy, but oestradiol, testosterone, oxytocins and cortisol also change dramatically (Buckwalter, et al., 1999).

Kinsley et al. (2006) showed that progesterone and oestradiol are capable of altering the concentration of dendritic spines in the CA1 region of the female rat hippocampus; a key area involved in memory consolidation. In nonpregnant studies, fluctuations in circulating endogenous or exogenous oestrogens have been associated with cognitive changes (Kampen & Sherwin, 1994; Lokken & Ferraro, 2006; Sherwin, 1994). Although our single measure of progesterone did not relate to reduced memory performance, it may be that a more complex interplay of a combination of pregnancy hormones is involved.

One of the key arguments of opponents to the theory of memory consolidation during sleep is that sleep deprivation techniques (particularly in animal studies) produce several secondary effects that are very stressful, and that this stress largely accounts for learning impairments (Vertes, 2004; Vertes & Eastman, 2000). The problem however, is how exactly do we measure stress in humans? Stress is multi-factorial, and may manifest itself in a physical, emotional or mental change that alters the body's normal state of functioning. Whilst this study aimed to control for as many influences as possible, there is the possibility that some other unmeasured stress-related factors are involved in the reduced memory retention scores of the pregnant women.

A major problem facing this area of research is that the terms sleep, memory and consolidation all refer to complex phenomena, none of which can be treated as a singular event (Stickgold, 2005). For example, this study focused on the classification of sleep into stages and cycles. However, others have investigated more fine-grained parameters of sleep in an attempt to relate sleep to memory consolidation. The intensity of REM sleep in terms of number and density of rapid eye movements has been shown to increase during the night rather than actual time spent in REM sleep, following procedural task acquisition (C. T. Smith, Nixon, & Nader, 2004). Verbal memory retention and procedural learning have each been related to the number of sleep spindles overnight, but not the amount of time spent in any sleep stage (Clemens, Fabo, & Halasz, 2005; Fogel &

Smith, 2006; Gais, Molle, Helms, & Born, 2002; Morin, et al., 2008; Schabus, et al., 2008). Investigation of EEG spectral power has suggested that REM sleep theta activity is involved in declarative memory consolidation (Fogel, Smith, & Cote, 2007). This vast range of findings suggests that brain plasticity during sleep may not involve a unitary process.

Limitations

While our study did not support the memory consolidation during sleep hypothesis, we used only one of many experimental approaches commonly used to test this hypotheses (Peigneux, Laureys, Delbeuck, & Maquet, 2001; C. Smith, 2001). Our methodology of measuring only one night of sleep did not allow us to record changes in sleep parameters compared to baseline following memory training, similarly we were unable to tell how the night of sleep prior to testing impacted on the initial encoding process in the memory testing session.

The pregnant women in this study slept less and had poorer sleep quality than the nonpregnant women, but they would not be classified as 'sleep deprived' in the usual experimental sense. Given the relatively small differences in sleep parameters across pregnancy groups compared to traditional sleep deprivation studies, we would only expect to find small effects on measures of memory consolidation. It may be that a much larger sample size with more power was required to identify any relationship between sleep and memory consolidation, however the sample size of our study was large enough to have an 80% chance of finding correlations as small as $r = .35$ at a significance level of .05. Unfortunately recruitment difficulties due to the requirement of having an overnight sleep study during pregnancy prevented us from increasing the study's power any further.

Alternatively, although many studies have found positive results using partial or full deprivation of REM or NREM sleep, this type of sleep manipulation may not be so

applicable to the real world. Investigation of a phenomenon such as sleep and memory problems during pregnancy may be more practical and relevant to the general population.

An unanticipated limitation of this study relates to the memory tasks used. The main neuropsychological test used to measure episodic memory retention was the WMS-III, which is widely known and commonly used for both research and clinical populations. On average the participants in this study were of 'above average' intelligence, however on three out of four of the WMS-III core subtests they averaged close to or above 100% retention, even after a delay period of approximately nine hours (well exceeding the recommended 30 minute delay for clinical purposes). Since this study was conducted, the 4th edition of the WMS had been released (Wechsler, 2009), which has eliminated both the Faces and Family Pictures subtests in favour of more visually oriented tasks, with an increased focus on visual working memory. These tasks may represent visual memory ability more purely as they allow less opportunity to apply verbal descriptions to the visual stimuli in order to aid recall.

Conclusions

The current study has demonstrated that pregnancy is associated with reduced verbal episodic memory retention as compared to nonpregnant women, with visual and procedural memory remaining unaffected. Pregnant women also demonstrated significant disruption of sleep patterns, with less total sleep time, more awakenings, less deep sleep and less REM sleep. In contrast to popular theories of memory consolidation during sleep, reduced memory retention and sleep disruption were not related in our sample. Furthermore, overnight memory retention was unrelated to attention, mood, hormone level, or nocturnal arterial oxygen saturation.

Although our results do not support the hypotheses of memory consolidation during sleep, it is possible that pregnant women in this study had a sufficient amount of sleep to support interactions between the hippocampus and neocortex to strengthen

representations during sleep, and that some other unmeasured factor resulted in reduced memory performance. Memory function during pregnancy still remains a controversial topic, as do the reasons behind any observed changes. As discussed, any involvement sleep has on memory consolidation is likely to be complex and multi-factorial and future research in this area is still required.

Acknowledgments

The authors would like to thank the staff at the Austin Health Sleep Laboratory and the Mercy Hospital for Women Outpatients Department for their support of this project and we appreciate the valuable contribution made by each of the research participants.

This research was funded by La Trobe University and the Austin Health Medical Research Foundation.

References

Andersson, L., Sundström-Poromaa, I., Bixo, M., Wulff, M., Bondestam, K., & åStröm, M. (2003). Point prevalence of psychiatric disorders during the second trimester of pregnancy: a population-based study. *American Journal of Obstetrics and Gynecology, 189*(1), 148-154.

Barrett, T. R., & Ekstrand, B. R. (1972). Effect of sleep on memory: III. Controlling for time-of-day effects. *Journal of Experimental Psychology, 96*(2), 321-327.

Bearden, C. E., Glahn, D. C., Monkul, E. S., Barrett, J., Najt, P., Villarreal, V., et al. (2006). Patterns of memory impairment in bipolar disorder and unipolar major depression. *Psychiatry Research, 142*((2-3)), 139-150.

Bernard, L. C., Houston, W., & Natoli, L. (1993). Malingering on neuropsychological memory tests: potential objective indicators. *Journal of Clinical Psychology, 49*, 45-53.

Bonnet, M. H. (2000). Sleep deprivation. In M. Kryger, T. Roth & W. C. Dement (Eds.), *Principles and practice of sleep medicine 3rd edition*. Philadelphia, Pennsylvania: W. B. Saunders Company.

Bonnet, M. H., Carley, D., Carskadon, M. A., Easton, P., Guilleminault, C., Harper, R. M., et al. (1992). EEG arousals: scoring rules and examples: a preliminary report from the Sleep Disorders Atlas Task Force of the American Sleep Disorders Association. *Sleep, 15*, 173-184.

Brindle, P. M., Brown, M. W., Brown, J., Griffith, H. B., & Turner, G. M. (1991). Objective and subjective memory impairment in pregnancy. *Psychological Medicine, 21*, 647-653.

Brunner, D. P., Münch, M., Biedermann, K., Huch, R., Huch, A., & Borbély, A. A. (1994). Changes in sleep and sleep electroencephalogram during pregnancy. *Sleep, 17*(7), 576-582.

Buckwalter, J. G., Stanczyk, F. Z., McCleary, C. A., Bluestein, B. W., Buckwalter, D. K., Rankin, K. P., et al. (1999). Pregnancy, the postpartum, and steroid hormones: effects on cognition and mood. *Psychoneuroendocrinology, 24*, 69-84.

Caine, D., & Watson, J. D. (2000). Neuropsychological and neuropathological sequelae of cerebral anoxia: A critical review. *Journal of the International Neuropsychological Society, 6*, 86-99.

Casey, P. (2000). A longitudinal study of cognitive performance during pregnancy and new motherhood. *Archives of Women's Mental Health, 3*, 65-76.

Casey, P., Huntsdale, C., Angus, G., & Janes, C. (1999). Memory in pregnancy. II: Implicit, incidental, explicit, semantic, short-term, working and prospective memory in primigravid, multigravid and postpartum women. *Journal of Psychosomatic Obstetrics and Gynaecology, 20*, 158-164.

Christensen, H., Leach, L. S., & Mackinnon, A. (2010). Cognition in pregnancy and motherhood: Prospective cohort study. *The British Journal of Psychiatry, 196*, 126-132.

Christensen, H., Poyser, C., Pollitt, P., & Cubis, J. (1999). Pregnancy may confer a selective cognitive advantage. *Journal of Reproductive and Infant Psychology, 17*(1), 7-25.

Churchward, T., O'Donoghue, F., Rochford, P., Pierce, R. J., Barnes, M., & Higgins, S. (2006). Diagnostic accuracy and cost effectiveness of home based PSG in OSA. (Abstract). *Sleep and Biological Rhythms, 4*(s1), A11.

Clemens, Z., Fabo, D., & Halasz, P. (2005). Overnight verbal memory retention correlates with the number of sleep spindles. *Neuroscience, 132*(2), 529-535.

Connolly, G., Razak, A. R. A., Hayanga, A., Russell, A., McKenna, P., & McNicholas, W. T. (2001). Inspiratory flow limitation during sleep in pre-eclampsia: Comparison with normal pregnant and nonpregnant women. *The European Respiratory Journal, 18*, 672-676.

Crawley, R. A., Grant, S., & Hinshaw, K. (2008). Cognitive changes in pregnancy: Mild decline or societal stereotype? *Applied Cognitive Psychology, 22*, 1142-1162.

de Groot, R. H. M., Hornstra, G., Roozendaal, N., & Jolles, J. (2003). Memory performance, but not information processing speed, may be reduced during early pregnancy. *Journal of Clinical and Experimental Neuropsychology, 25*(4), 482-488.

de Groot, R. H. M., Vuurman, E. F. P. M., Hornstra, G., & Jolles, J. (2006). Differences in cognitive performance during pregnancy and early motherhood. *Psychological Medicine, 36*, 1023-1032.

Driver, H. S., & Shapiro, C. M. (1992). A longitudinal study of sleep stages in young women during pregnancy and postpartum. *Sleep, 15*(5), 449-453.

Drosopoulos, S., Wagner, U., & Born, J. (2005). Sleep enhances explicit recollection in recognition memory. *Learning & Memory, 12*, 44-51.

Durmer, J. S., & Dinges, D. F. (2005). Neurocognitive consequences of sleep deprivation. *Seminars in Neurology, 25*(1), 117-129.

Ficca, G., Lombardo, P., Rossi, L., & Salzarulo, P. (2000). Morning recall of verbal material depends on prior sleep organization. *Behavioural Brain Research, 112*, 159-163.

Field, T., Diego, M., Hernandez-Reif, M., Figueiredo, B., Schanberg, S., & Kuhn, C. (2007). Sleep disturbances in depressed pregnant women and their newborns. *Infant Behavior and Development, 30*(127-133).

Fischer, S., Hallschmid, M., Elsner, A. L., & Born, J. (2002). Sleep forms memory for finger skills. *Proceedings of the National Academy of Sciences of the United States of America, 99*(18), 11987-11991.

Flowers, K. A., Sheridan, M. R., & Shadbolt, H. (1996). Simulation of amnesia by normals on the Rey Auditory Verbal Learning Test. *Journal of Neurolinguistics, 9*, 147-156.

Fogel, S. M., Smith, C., & Cote, K. A. (2007). Dissociable learning-dependent changes in REM and non-REM sleep in declarative and proce¬dural memory systems. *Behavioural Brain Research, 180*, 48-61.

Fogel, S. M., & Smith, C. T. (2006). Learning-dependent changes in sleep spindles and stage 2 sleep. *Journal of Sleep Research, 15*, 250-255.

Fowler, M. J., Sullivan, M. J., & Ekstrand, B. R. (1973). Sleep and Memory. *Science, 179*, 302-304.

Gais, S., Molle, M., Helms, K., & Born, J. (2002). Learning-dependent increases in sleep spindle density. *The Journal of Neuroscience, 22*(15), 6830-6834.

Gais, S., Plihal, W., Wagner, U., & Born, J. (2000). Early sleep triggers memory for early visual discrimination skills. *Nature Neuroscience, 3*(12), 1335-1339.

Gibson, G. E., Pulsinelli, W., Blass, J. P., & Duffy, T. E. (1981). Brain dysfunction in mild to moderate hypoxia. *American Journal of Medicine, 70*, 1247-1254.

Giuditta, A., Ambrosini, M. V., Montagnese, P., Mandile, P., Cotugno, M., Grassi Zucconi, G., et al. (1995). The sequential hypothesis of the function of sleep. *Behavioral Brain Research, 69*(1-2), 157-166.

Greiffenstein, M. F., Baker, J., & Gola, T. (1996). Comparison of multiple scoring methods for Rey's malingered amnesia measures. *Archives of Clinical Neuropsychology, 11*(4), 283-293.

Herrmann, W. M., & Beach, R. C. (1978). Experimental and clinical data indicating the psychotropic properties of progestogens. *Postgraduate Medical Journal, 54*(Suppl. 2), 82-87.

Hertz, G., Fast, A., Feinsilver, S. H., Albertario, C. L., Schulman, H., & Fein, A. M. (1992). Sleep in normal late pregnancy. *Sleep, 15*(3), 246-251.

Janes, C., Casey, P., Huntsdale, C., & Angus, G. (1999). Memory in pregnancy. I: Subjective experiences and objective assessment of implicit, explicit and working memory in primigravid and primiparous women. *Journal of Psychosomatic Obstetrics and Gynaecology, 20*, 80-87.

Johnson, L. C. (1982). Sleep deprivation and performance. In W. B. Webb (Ed.), *Biological rhythms, sleep and performance*. New York: John Wiley & Sons Ltd.

Jomeen, J., & Martin, C. R. (2007). Assessment and relationship of sleep quality to depression in early pregnancy. *Journal of Reproductive and Infant Psychology, 25*(1), 87-89.

Kampen, D. L., & Sherwin, B. B. (1994). Estrogen use and verbal memory in healthy postmenopausal women. *Obstetrics and Gynecology, 83*(6), 979-983.

Keenan, P. A., Yaldoo, D. T., Stress, M. E., Fuerst, D. R., & Ginsburg, K. A. (1998). Explicit memory in pregnant women. *American Journal of Obstetrics and Gynecology, 179*, 731-737.

Killgore, W. I. S., & DellaPietra, L. (2000). Using the WMS-III to detect malingering: Empirical validation of the Rarely Missed Index (RMI). *Journal of Clinical and Experimental Neuropsychology, 22*(6), 761-771.

Kinsley, C. H., Trainer, R., Stafisso-Sandoz, G., Quadros, P., Marcus, L. K., Hearon, C., et al. (2006). Motherhood and the hormones of pregnancy modify concentrations of hippocampal neuronal dendritic spines. *Hormones and Behavior, 49*, 131-142.

Kuriyama, K., Stickgold, R., & Walker, M. P. (2004). Sleep-dependent learning and motor-skill complexity. *Learning & Memory, 11*(6), 705-713.

Lahl, O., Wispel, C., Willigens, B., & Pietrowsky, R. (2008). An ultra short episode of sleep is sufficient to promote declarative memory performance. *Journal of Sleep Research, 17*(1), 3-10.

Lee, A. M., Lam, S. K., Sze Mun Lau, S. M., Chong, C. S., Chui, H. W., & Fong, D. Y. (2007). Prevalence, course and risk factors for antenatal anxiety and depression. *Obstetrics and Gynecology, 110*(5), 1102-1112.

Lee, K. A., Zaffke, M. E., & McEnany, G. (2000). Parity and sleep patterns during and after pregnancy. *Obstetrics and Gynecology, 95*(1), 14-18.

Lokken, K. L., & Ferraro, F. R. (2006). The relationship between menopausal status, phase of menstrual cycle, and replacement estrogen on cognition in healthy women without dementia. *The Journal of Psychology, 140*(6), 533-547.

Lovibond, S. H., & Lovibond, P. F. (1995). *Manual for the Depression Anxiety Stress Scales* (2nd ed.). Sydney: Psychology Foundation.

Maquet, P. (2001). The role of sleep in learning and memory. *Science, 294*, 1048-1052.

Mazzoni, G., Gori, S., Formicola, G., Gneri, C., Massetani, R., Murri, L., et al. (1999). Word recall correlates with sleep cycles in elderly subjects. *Journal of Sleep Research, 8*(3), 185-188.

McClelland, J. L., McNaughton, B. L., & O'Reilly, R. C. (1995). Why there are complementary learning systems in the hippocampus and neocortex: Insights from the successes and failures of connectionist models of learning and memory. *Psychological Review, 102*(3), 419-457.

McNaughton, B. L., Barnes, C. A., Battaglia, F. P., Bower, M. R., Cowen, S. L., Ekstrom, A. D., et al. (2003). Off-line reprocessing of recent memory and its role in memory consolidation: A progress report. In P. Maquet (Ed.), *Sleep and brain plasticity* (pp. 225-246). New York: Oxford University Press.

Meddis, R. (1982). Cognitive dysfunction following loss of sleep. In A. Burton (Ed.), *The pathology and psychology of cognition* (pp. 225-252). London: Methuen.

Milner, B. (1965). Visually-guided maze learning in man: Effects of bilateral hippocampal bilateral frontal, and bilateral cerebral lesions. *Neuropsychologia, 3*, 317-338.

Morin, A., Doyon, J., Dostie, V., Barakat, M., Hadj Tahar, A., Korman, M., et al. (2008). Motor sequence learning increases sleep spindles and fast frequencies in post-training sleep. *Sleep, 31*(8), 1149-1156.

Mykytyn, I., Sajkob, D., Neill, A., & McEvoy, R. (1999). Portable computerized polysomnography in attended and unattended settings. *Chest, 115*, 114-122.

Parsons, C., & Redman, S. (1991). Self-reported cognitive change during pregnancy. *The Australian Journal of Advanced Nursing, 9*(1), 20-29.

Peigneux, P., Laureys, S., Delbeuck, X., & Maquet, P. (2001). Sleeping brain, learning brain. The role of sleep for memory systems. *Neuroreport, 12*(18), A111-A124.

Plihal, W., & Born, J. (1997). Effects of early and late nocturnal sleep on declarative and procedural memory. *Journal of Cognitive Neuroscience, 9*(4), 534-547.

Plihal, W., & Born, J. (1999). Effects of early and late nocturnal sleep on priming and spatial memory. *Psychophysiology, 36,* 571-582.

Plihal, W., Pietrowsky, R., & Born, J. (1999). Dexamethasone blocks sleep induced improvement of declarative memory. *Psychoneuroendocrinology, 24,* 313-331.

Priest, S. R., Austin, M. P., Barnett, B. B., & Buist, A. (2008). A psychosocial risk assessment model (PRAM) for use with pregnant and postpartum women in primary care settings. *Archives of Women's Mental Health, 11*(5-6), 307-317.

Prodromakis, E., Trakada, G., Tsapanos, V., & Spiropoulos, K. (2004). Arterial oxygen tension during sleep in the third trimester of pregnancy. *Acta Obstetricia et Gynecologia Scandinavica, 83,* 159-164.

Rauchs, G., Desgranges, B., Foret, J., & Eustache, F. (2005). The relationships between memory systems and sleep stages. *Journal of Sleep Research, 14,* 123-140.

Rechtschaffen, A., & Kales, A. (1968). *A manual of standardized terminology, techniques, and scoring system for sleep stages of human subjects*. Los Angeles: Brain Information Service.

Reitan, R. (1979). *Manual for Administration of Neuropsychological Test Batteries for Adults and Children*. Tucson: Reitan Neuropsychological Laboratory.

Rey, A. (1964). *L'examen clinique on psychologie*. Paris: Presses Universitaires de France.

Rickard, T. C., Cai, D. J., Rieth, C. A., Jones, J., & Ard, M. C. (2008). Sleep does not enhance motor sequence learning. *Journal of Experimental Psychology. Learning, Memory, and Cognition, 34*(4), 834-842.

Schabus, M., Kerstin, H., Thomas, P., Anderer, P., Gruber, G., Parapatics, S., et al. (2008). Interindividual sleep spindle differences and their relationship to learning-related enhancements. *Brain Research, 1191,* 127-135.

Schorr, S. J., Chawla, A., Devidas, M., Sullivan, C. A., Naef III, R. W., & Morrison, J. C. (1998). Sleep patterns in pregnancy: A longitudinal study of polysomnography recordings during pregnancy. *Journal of Perinatology, 18*(6), 427-430.

Sharp, K., Brindle, P. M., Brown, M. W., & Turner, G. M. (1993). Memory loss during pregnancy. *British Journal of Obstetrics and Gynaecology, 100,* 209-215.

Sherwin, B. B. (1994). Estrogenic effects on memory in women. *Annals of the New York Academy of Sciences, 743,* 213-230.

Silber, M., Almkvist, O., Larsson, B., & Uvnas-Moberg, K. (1990). Temporary peripartal impairment in memory and attention and its possible relation to oxytocin concentration. *Life Sciences, 47*, 57-65.

Skouteris, H., Germano, C., Wertheim, E. H., Paxton, S. J., & Milgrom, J. (2008). Sleep quality and depression during pregnancy: a prospective study. *Journal of Sleep Research, 17*, 217-220.

Smith, C. (2001). Sleep states and memory processes in humans: procedural versus declarative memory systems. *Sleep Medicine Reviews, 5*(6), 491-506.

Smith, C. T., Nixon, M. R., & Nader, R. S. (2004). Posttraining increases in REM sleep intensity implicate REM sleep in memory processing and provide a biological marker of learning potential. *Learning & Memory, 11*, 714-719.

Smithson, M. (2003). *Confidence Intervals*. Belmont, CA: Sage.

Söderpalm, A. H., Lindsey, S., Purdy, R. H., Hauger, R., & de Wit, H. (2004). Administration of progesterone produces mild sedative-like effects in men and women. *Psychoneuroendocrinology, 29*(3), 339-354.

Stickgold, R. (2005). Sleep-dependent memory consolidation. *Nature, 437*, 1272-1278.

Stickgold, R., Hobson, J. A., Fosse, R., & Fosse, M. (2001). Sleep, learning, and dreams: Off-line memory reprocessing. *Science, 294*, 1052-1057.

Stickgold, R., Whidbee, D., Schirmer, B., Patel, V., & Hobson, J. A. (2000). Visual discrimination task improvement: A multi-step process occurring during sleep. *Journal of Cognitive Neuroscience, 12*(2), 246-254.

Sweeney, J. A., Kmiec, J. A., & Kupfer, D. J. (2000). Neuropsychologic impairments in bipolar and unipolar mood disorders on the CANTAB neurocognitive battery. *Biological Psychiatry, 48*, 674-685.

Tabachnick, B. G., & Fidell, L. S. (2007). *Using multivariate statistics* (5th ed.). Boston: Pearson Education, Inc.

The Psychological Corporation. (1999). *Wechsler Abbreviated Scale of Intelligence (WASI)*. San Antonio, TX: The Psychological Corporation.

Tombaugh, T. N. (1996). *Test of memory malingering (TOMM)*. New York: Multi Health Systems.

Tucker, M. A., & Fishbein, W. (2009). The impact of sleep duration and subject intelligence on declarative and motor memory performance: how much is enough? *Journal of Sleep Research, 18*(3), 304-312.

Tucker, M. A., Hirota, Y., Wamsley, E. J., Lau, H., Chaklader, A., & Fishbein, W. (2006). A daytime nap containing solely non-REM sleep enhances declarative but not procedural memory. *Neurobiology of Learning and Memory, 86*, 241-247.

Vertes, R. P. (2004). Memory consolidation in sleep: Dream or reality. *Neuron, 44*, 135-148.

Vertes, R. P., & Eastman, K. E. (2000). The case against memory consolidation in REM sleep. *Behavioral and Brain Sciences, 23*(6), 867-876.

Walker, M. P., Brakefield, T., Morgan, A., Hobson, J. A., & Stickgold, R. (2002). Practice with sleep makes perfect: sleep-dependent motor skill learning. *Neuron, 35*, 205-211.

Walker, M. P., Brakefield, T., Seidman, J., Morgan, A., Hobson, J. A., & Stickgold, R. (2003). Sleep and the time course of motor skill learning. *Learning & Memory, 10*, 275-284.

Walsh, K. (1985). *Understanding brain damage. A primer of neuropsychological evaluation*. London: Churchill Livingstone.

Wechsler, D. (1997). *Wechsler Memory Scale. Third edition manual*. San Antonio, TX: The Psychological Corporation.

Wechsler, D. (2009). *Wechsler Memory Scale - Fourth Edition*. San Antonio, TX: Pearson.

Wilkie, G., & Shapiro, C. M. (1992). Sleep deprivation and the postnatal blues. *Journal of Psychosomatic Research, 36*(4), 309-316.

Wilson, M. A., & McNaughton, B. L. (1994). Reactivation of hippocampal ensemble memories during sleep. *Science, 265*(5172), 676-679.

Wolfson, A. R., Crowley, S. J., Anwer, U., & Bassett, J. L. (2003). Changes in sleep patterns and depressive symptoms in first-time mothers: Last trimester to 1-year postpartum. *Behavioral Sleep Medicine, 1*(1), 54-67.

Yaroush, R., Sullivan, M. J., & Ekstrand, B. R. (1971). Effect of sleep on memory II: Differential effect of the first and second half of the night. *Journal of Experimental Psychology, 88*(3), 361-366.

Chapter 6

General Discussion

The aim of this thesis was to relate the theory of memory consolidation during sleep to the pregnant population, in order to establish whether memory problems during pregnancy could be at all attributable to the commonly reported symptom of sleep disturbance. This thesis was submitted following an approved alternative format as a series of published or submitted manuscripts, and therefore each empirical chapter contains its own detailed discussion. The following section provides a summary of the major findings of this thesis and the implications of these, followed by limitations of the current study and directions for future research.

Summary of Research Findings

Given the frequency of reported memory problems observed during pregnancy but the discrepant literature regarding objective testing, the purpose of Chapter 2 was to attempt to confirm previous research findings regarding deficits in memory function during pregnancy, by investigating both episodic and procedural memory performance during early and late pregnancy.

The key finding of Chapter 2 was that women in the first and third trimester of pregnancy performed significantly worse on verbal episodic memory tasks comprising of paragraph recall, word list recall and verbal recognition when compared to a nonpregnant control group. The magnitude of the effect sizes was all moderate to large. Performance on the verbal memory tasks did not differ as a function of pregnancy trimester, and overall memory performance was not affected by whether the pregnancy was the woman's first or subsequent pregnancy. Another key finding was that pregnant women did not show any deficits on any of the visual episodic or procedural memory tasks. In terms of subjective reports, pregnant women were more likely than nonpregnant women to notice a change in their memory quality. This difference however appeared due to pregnant women over-rating their memory abilities prior to pregnancy rather than underrating their current memory.

In an attempt to explain any observable memory differences across pregnancy, objective measures of progesterone, attention, and mood were taken. Pregnant women in this study did not show attention deficits or disturbed mood state, and neither of these variables was related to memory performance. Higher progesterone level in the pregnant women was related to poorer performance on immediate paragraph and word list recall, however less than 20% of the variance in these tasks was explained by this hormone.

In line with theories of memory consolidation during sleep (Maquet, 2001; McNaughton, et al., 2003; Stickgold, Hobson, Fosse, & Fosse, 2001), a key hypothesis of this thesis was that disturbed sleep may impact on the pregnant woman's ability to store new memories. The main purpose of Chapter 3 was to investigate both objective and subjective changes in sleep patterns associated with pregnancy.

The main findings of Chapter 3 were that sleep in the third trimester of pregnancy was characterised by decreased sleep efficiency, increased wake after sleep onset and increased cortical arousals. There was a trade off between lesser amounts of deep sleep for higher amounts of the lighter Stage 1 sleep, and less time was spent in rapid eye movement (REM) sleep as compared to nonpregnant women. Women in the first trimester of pregnancy also had disrupted sleep but to a lesser degree, with more time spent awake after sleep onset and a lesser proportion of Stage 4 sleep when compared to nonpregnant women. Sleep efficiency and time in REM sleep showed a trend towards the pattern seen in the third trimester of pregnancy.

Cortical arousals from sleep during pregnancy have not previously been reported. In this study, it was found that women in the third trimester of pregnancy experienced more cortical arousals than first-trimester and nonpregnant women, regardless of whether they were spontaneous or a consequence of limb movements or respiratory events.

Subjective changes in sleep such as night awakenings and difficulty returning to sleep after waking were frequently reported by the pregnant women, mostly due to

discomfort, bodily aches and increased frequency of urination. A further indicator of compromised sleeping comfort was that third-trimester pregnant women spent significantly less of their sleep time lying on their back.

As with changes in memory performance, this study attempted to measure potential pregnancy-related factors that could explain changes in sleep patterns. Contrary to suggestions that progesterone has sedating properties (Herrmann & Beach, 1978; Söderpalm, Lindsey, Purdy, Hauger, & de Wit, 2004), higher progesterone in the third trimester of pregnancy was actually associated with increased awakenings and more time awake during the night. Current level of depression, anxiety and stress symptoms did not differ across the pregnancy groups, and therefore changes in sleep patterns were not the result of mood state.

In the course of investigating sleep patterns during pregnancy, another unanticipated phenomenon became apparent. Changes in respiratory physiology occur during pregnancy (Edwards, Middleton, Blyton, & Sullivan, 2002), and examination of the raw sleep study data suggested that respiration changes may extend into sleep. Also, restless legs syndrome (RLS) is a common movement disorder experienced during pregnancy (Manconi, Govoni, De Vito, Economou, Cesnik, Casetta, et al., 2004; Tunç, Karadag, Dogulu, & Inan, 2007), which can often be related to periodic limb movements of sleep (PLMS). However, very few studies have reported on PLMS during pregnancy. Further investigation of sleep-disordered breathing (SDB) and PLMS during normal pregnancy was the aim of Chapter 4.

Analysis of SDB showed that 31% of the third-trimester pregnant sample scored an overall Apnoea/Hypopnoea Index (AHI/hr) of greater than 5, compared with 24% of the first-trimester pregnant women and only 4% of the nonpregnant women. Although median AHI/hr values did not differ significantly between the pregnant and nonpregnant groups, there was a much wider variation in scores amongst the pregnant women.

Snoring was also significantly more prevalent amongst the third-trimester pregnant women when compared to the nonpregnant women, with women in the first trimester also snoring more frequently than the controls. Although snoring, snorting and gasping was more commonly reported by the pregnant women, comparison to objective snoring measures revealed that some pregnant women still under-report their snoring habits.

In terms of leg movements, women in the third trimester of pregnancy featured higher rates of PLMS, with almost a third of these women obtaining a PLMS index of greater than 5 per hour, which is considered pathological (Montplaisir, Nicolas, Godbout, & Walters, 2000). In comparison, only 4% of the nonpregnant women had a similar PLMS frequency.

Chapters 2 and 3 revealed that verbal memory is reduced during pregnancy, and that sleep during pregnancy is compromised. The purpose of Chapter 5 was to see whether any interpretation of the memory consolidation during sleep hypothesis could be applied to explain the occurrence of memory problems during pregnancy.

Firstly, pregnant women were shown to have poorer memory retention overnight for tasks of verbal episodic memory, but not visual episodic or procedural memory. Interestingly, the first-trimester pregnant women retained less information from the paragraph recall task, whereas the third-trimester pregnant women retained less information from the word list task, as compared to nonpregnant women. Similarly to Chapter 2, reduced verbal memory retention during pregnancy was not related to measures of attention, mood, progesterone level or nocturnal arterial oxygen saturation.

Although pregnant women, particularly those in the third trimester, had more disrupted sleep as compared to nonpregnant women, correlational analyses revealed that reduced verbal episodic memory retention was weakly but significantly related to time spent in REM sleep only. However, covariate analyses found that the reduced amount of

time spent in REM sleep for both pregnant groups could not account for the differences in verbal memory retention.

Within the sample as a whole, no significant relationships were found between any type of memory retention and parameter of sleep. Contrary to the dual-process hypothesis, the amount of REM sleep overnight was not related to any procedural memory measure, and the amount of SWS overnight was not reliably associated with any measure of episodic memory retention. No strong associations between sleep cycle architecture and memory retention were found, providing no support for the double-step hypothesis of memory consolidation during sleep.

Implications of the Studies

Firstly, the findings from Chapter 2 indicate that reduced verbal episodic memory retention is a feature of pregnancy. A closer examination of the patterns of recall and recognition on the memory tasks suggested that reduced verbal memory performance in pregnancy appeared to be due to reduced immediate memory span, retrieval problems and a disorganised encoding style. However, pregnant women displayed normal rates of learning over trials. Importantly, there were areas of memory consolidation that remained unaffected in pregnancy, namely visual episodic memory and procedural memory. Also, considering the length of the testing session and the number of different tasks completed, the pregnant women performed especially well and did not display signs of attentional fatigue compared to the nonpregnant women as measured by the sustained attention task.

Although only one area of memory weakness was found, subjective reports indicated that 72% of our sample had noticed a change in their ability to recall or remember things since becoming pregnant. It was considered that pregnant women may be more inclined to notice or even over-interpret everyday cognitive slips and attribute them to pregnancy, but it is possible that these women are reporting actual phenomenon. Even minor memory difficulties or the perception of these may have implications for

tasks of everyday living for pregnant women. Pregnant women lacking confidence in their memory abilities may benefit from compensatory techniques such as making lists, using a diary or devising a reminder system. Given that differences in verbal memory were mostly due to a reduced immediate memory span, pregnant women may want to avoid overwhelming themselves with too much information at one time, and may benefit from repetition. Findings of unimpaired visual episodic and procedural memory should be encouraging for pregnant women. As she approaches motherhood, the pregnant woman has many new skills to learn, so the ability to improve learning with repetition and to master 'how to' tasks is important.

Apart from ruling out associations with mood and attention, the study design did not allow for attribution of causality for reduced verbal memory. However, the discrepant findings between verbal and visual/procedural performance suggests that as different kinds of memory are thought to have different functional and neuroanatomical systems (Smith, 2001), some neurotransmitter or hormone is acting differently on those areas involved in verbal memory, such as the left hippocampus and nearby cortical areas, as compared to the brain regions thought to be involved in visual and procedural memory, such as the right hippocampus and temporal lobe, and the neostriatum respectively (Knowlton, Mangels, & Squire, 1996).

In this study, progesterone was found to account for approximately 20% of the variance in two measures of verbal memory. Hormones markedly affect neuronal structure and function in a variety of ways (Kinsley, et al., 2006), and pregnancy is characterised by a significantly longer duration of substantially elevated hormones. Kinsley et al. (2006) demonstrated that the pregnancy hormones oestradiol and progesterone stimulate the proliferation of dendritic spines in the CA1 region of the female rat hippocampus. Dendritic spines are believed to be important sites for enhancement of synaptic efficacy and networks involved in learning and neural plasticity

(Leuner & Shors, 2004). Given the role of the hippocampus in learning and memory, Kinsley et al.'s data suggest a mechanism for enhancements in the necessary behaviours characteristic of the maternal female. Although an association between progesterone and verbal memory was found, the results actually contradict Kinsley et al. in that increased progesterone level was related to a decrease in memory performance in our human sample.

The findings from Chapter 3 showed that pregnancy is associated with disruption of sleep. The high frequency of cortical arousals found in the pregnant group has not been previously reported. Firstly, these cortical arousals may give some insight into why pregnant women are waking more often during sleep. Women in the third trimester of pregnancy experienced more cortical arousals, including those as a consequence of limb movements or respiratory events, as compared to first-trimester and nonpregnant women. The occurrence of limb movements and respiratory events in sleep during pregnancy then became the focus of Chapter 4. Secondly, frequent cortical arousal often results in disrupted or fragmented sleep with reduced restorative power (Bonnet, 2000); this was evidenced by the increased amount of Stage 1 sleep in the third-trimester pregnant group. Sleep fragmentation has often been associated with negative consequences, such as increased objective and subjective sleepiness, decreased psychomotor performance and negative mood changes (Bonnet & Arand, 2003). Arousal from sleep has also been significantly correlated with objective measures of daytime alertness (Carskadon, Brown, & Dement, 1982; Martin, Engleman, Kingshott, & Douglas, 1997) and increases in blood pressure (Davies, Belt, Roberts, Ali, & Stradling, 1993; Morrell, et al., 2000).

Although the consequences of sleep deprivation are widely recognised, the sleep characteristics of the pregnant women in our sample more resembled what could be termed sleep restriction, in that many women in the study slept for less than six hours in total. Sleep restriction has the potential to become chronic over the many months of

pregnancy, and can result in a range of neurobehavioural deficits including lapses of attention, slowed working memory, reduced cognitive throughput, depressed mood, and perseveration of thought (Banks & Dinges, 2007). Short-term sleep restriction has also been shown to result in a number of abnormal physiologic changes, including reduced glucose tolerance (Spiegel, Leproult, & Van Cauter, 1999), increased blood pressure (Tochikubo, Ikeda, Miyajima, & Ishii, 1996) and increased inflammatory markers (Meier-Ewert, et al., 2004). People frequently underestimate the cognitive impact of sleep restriction and overestimate their performance readiness when sleep restricted (Van Dongen, Maislin, Mullington, & Dinges, 2003), which may have potentially dangerous implications for activities of daily living, such as driving. Furthermore, an epidemiological study found an increased incidence of sleep-related crashes in drivers reporting less than seven hours of sleep per night on average (Stutts, Wilkins, Scott Osberg, & Vaughn, 2003).

The effects of sleep restriction specific to the pregnant population have been considered. Women who slept less than 6 hours a night during the last month of pregnancy had longer labours and were 4.5 times more likely to have a caesarean delivery (Lee & Gay, 2004). In a study of sleep obtained in the five days preceding childbirth, Beebe and Lee (2007) found a significant relationship between the amount of sleep on the night before hospitalisation and pain perception in women with spontaneous labour. Self-report findings suggest that sleep quality earlier in pregnancy may contribute to the development of higher levels of depressive symptoms later in pregnancy (Skouteris, Germano, Wertheim, Paxton, & Milgrom, 2008). Wilkie and Shapiro (1992) showed a significant correlation between self-reported sleep disruption in the third trimester of pregnancy and emotional distress in the week after giving birth. A history of sleep disruption in the latter stages of pregnancy may also have aetiological importance in the development of postnatal blues. This relationship appears to have a cyclical effect, with

further research showing that newborns of depressed mothers also have more sleep disturbances and spend more time fussing and crying (Field, et al., 2007).

Many pregnant women voice concerns about sleeping position. This study found that although time spent sleeping supinely was reduced, women in the third trimester of pregnancy still spent close to 20 percent of the night in the supine position. The underlying rationale on any advice for sleep position is that the uterus may compress the inferior vena cava and, to a lesser extent, the aorta and cause a decrease in the blood return to the heart, with a decrease in cardiac output (Farine & Seaward, 2007). Pregnant women who lie in the supine position may develop syncopal symptoms, however only 4% of patients in five studies of maternal sleep position had pre-syncopal symptoms related to aortocaval occlusion secondary to a supine position (Bamber & Dresner, 2003; Chen, Kuo, Yang, Lo, & Tsai, 1999; Clark, et al., 1991; Ellington, Katz, Watson, & Spielman, 1991; Kauppila, Koskinen, Puolakka, Tuimala, & Kuikka, 1980). Even in this small minority of symptomatic women, there was no evidence of foetal compromise and therefore advice often given to pregnant women about sleeping position is said to be irrelevant. Instead, women should be told that a small minority of pregnant women feel faint when lying flat; the pregnant women will easily be able to determine this for herself (Farine & Seaward, 2007).

Following on from Chapter 3, Chapter 4 showed that snoring and PLMS more commonly occurred in pregnant women when compared to nonpregnant women. The pregnant women in this study generally did not display discrete obstructive respiratory events like those more often seen in males with obstructive sleep apnoea (OSA), rather their pattern of flow limitation and snoring more closely resembled upper airway resistance syndrome (UARS). Even this lesser degree of SDB has been related to marked impairment in daytime function (Guilleminault, Stoohs, Clerk, Cetel, & Maistros, 1993), symptoms of insomnia, fatigue and depressive mood (Guilleminault, et al., 2006), and

development of hypertension (Guilleminault, Stoohs, Shiomi, Kushida, & Schnittger, 1996) in women. The implications of these studies are that a relatively low AHI/hr value in the pregnant population should not automatically exclude diagnosis of a significant sleep-related breathing disorder, and appropriate treatment may need to be considered.

Another key finding from this study was that self-reported snoring and apnoea symptoms were not always congruent with objective measures, giving support to Olivarez et al.'s (2010) recent study demonstrating the poor predictive ability of SDB questionnaires. The implications of these findings are enormous given that the majority of pregnancy studies rely on self-reported snoring symptoms due to the difficulty in collecting objective data via polysomnography (PSG). This casts doubt on the validity of the conclusions made by studies linking self-reported snoring during pregnancy to negative outcomes such as pregnancy-induced hypertension and pre-eclampsia (Bourjeily, Raker, Chalhoub, & Miller, 2010; Franklin, et al., 2000; Perez-Chada, et al., 2007).

Significantly more pregnant women in this study had a PLMS index of greater than 5 per hour, as compared to the nonpregnant women. Intense limb movements during sleep may cause arousal, thereby producing insomnia or excessive daytime sleepiness. Mild PLMS can also occur without concomitant nocturnal sleep disruption (Montplaisir, et al., 2000). Within this study, there were no correlations between PLMS index and parameters of sleep. In the case that PLMS do impact on either sleep continuity or daytime functioning (in the way of sleepiness), individuals with PLMS may be diagnosed with periodic limb movement disorder (Stiasny, Oertel, & Trenkwalder, 2002). Treatment of periodic leg movements should be considered when they significantly disrupt sleep, and secondary causes such as other sleep or movement disorders must be excluded. Effective medications for PLMS in the nonpregnant state include a benzodiazepine (clonazepam) and a dopaminergic agent such as L-Dopa or carbidopa (Santiago, Nolledo, Kinzler, & Santiago, 2001). However, there are no evidence-based

treatment recommendations for pregnant women with PLMS. Conservative measures to consider during pregnancy include avoidance of caffeine, correction of electrolyte abnormalities, and administration of folate supplements if folate deficiency is present (Golbe, 1994). Pharmacological treatment should be avoided and the woman informed that RLS and PLMS symptoms usually disappear or become much better after delivery (Stiasny, et al., 2002).

The purpose of Chapter 5 was to incorporate the results found from the earlier chapters, to investigate whether sleep disruption during pregnancy could be a factor for memory difficulties experience as hypothesised by the memory consolidation during sleep hypothesis. The current study found that reduced episodic memory retention was weakly related to REM sleep, however differences in REM sleep were not at all responsible for the memory difficulties observed. In the sample as a whole, episodic and procedural memory retention was not related to any measure of sleep staging or sleep disruption. These findings can be interpreted in a number of ways. Firstly, these results may give support to those contesting a relationship between sleep and memory consolidation in humans (Siegel, 2001; Vertes, 2004; Vertes & Eastman, 2000). Research demonstrating offline reactivation of hippocampal memory representations during sleep has primarily been undertaken on rats using single and multiple unit recordings (Kudrimoti, Barnes, & McNaughton, 1999; Pavlides & Winson, 1989; Qin, McNaughton, Skaggs, & Barnes, 1997; Stickgold, et al., 2001; Wilson & McNaughton, 1994). As it is difficult to reveal signs of a replay of newly acquired memories during sleep in humans (Gais & Born, 2004), theories of memory consolidation during sleep in humans have been based upon animal models. Signs of memory consolidation during sleep in humans can only be investigated with non-invasive techniques such as electroencephalography or positron emission tomography, to reveal electrophysiological and functional changes. The outcomes of these research designs, such as the current study design, can only be

used to infer what may be happening at a neuronal level. In the context of this study, we would infer that a lack of association between sleep disturbance and memory retention indicates that during sleep, there is no covert reactivation of neuronal populations in the hippocampus used for encoding during prior learning, and that memory consolidation occurs independently of sleep processes.

Alternatively, the memory consolidation during sleep hypothesis may be a valid one, but we were unable to lend support to this theory due to study design. Traditionally, studies testing memory consolidation during sleep will have one or more experimental groups that are either deprived of or restricted to substantially reduced amounts of either REM sleep or SWS. In contrast, our experimental groups were the first and third trimester of pregnancy, and although these groups displayed less REM sleep and SWS when compared to nonpregnant women, the differences were relatively minor in comparison to deprivation studies. It may be that the amount of sleep the pregnant women achieved was still sufficient for sleep-dependent memory consolidation to occur, and that sleep stage architecture needs to be significantly altered before this process is interrupted. This interpretation of the findings is also supported by research demonstrating that even short periods of sleep such as half a night (Tucker & Fishbein, 2009), hour-long napping (Tucker, et al., 2006) and even short six minute naps (Lahl, Wispel, Willigens, & Pietrowsky, 2008) are adequate to initiate the active processes of memory consolidation.

Another interpretation of the results is that memory consolidation does occur during sleep, but as only one aspect of sleep was studied, any relationship was missed. Sleep is a complex process, and there are several mechanisms that could account for changes in memory observed across sleep. This study looked at electrophysiological mechanisms in terms of sleep stages, but neurotransmitter- and neuroendocrine-related mechanisms are also known to play a part in memory function and exhibit different

activity between SWS and REM sleep as well as wakefulness (Gais & Born, 2004). It is possible that multiple different neurophysiological sleep processes are at work during memory consolidation, and that these processes differ depending on the type of memory to be consolidated.

Unfortunately, this study was not able to identify sleep disturbance as a cause of reduced verbal memory retention during pregnancy. However, a number of potential factors including the effects of progesterone, attention and mood were able to be ruled out. Only speculation can be made as to what other pregnancy-related changes may be responsible for this phenomenon, leaving the door open for future research studies in this area.

Limitations of the Current Thesis

The main limitation of this study was the cross-sectional rather than longitudinal design, which was ultimately chosen for a number of reasons. Firstly, longitudinal memory research is very difficult due to the paucity of rigorous memory tests with multiple equivalent forms (Lezak, Howieson, & Loring, 2004), especially tests that are suitable for a non-clinical population. Secondly, multiple consecutive nights of PSG or one night in each pregnancy trimester for each participant to characterise sleep patterns would have been ideal. However, undertaking multiple sleep studies at appropriate time points can be a major problem with the study of pregnant women and they are often unwilling to undergo additional measurements and procedures. The requirement for them to be away from home and family responsibilities is also undesirable. Thirdly, recruitment of pregnant women still in their first trimester proved very difficult, as many do not attend their first antenatal appointment at the hospital until they are already 12 weeks gestation or more. The difficulty in recruiting pregnant women to this research was reflected in the low response rate and the high dropout rate due to complications of pregnancy; had this study been longitudinal in design recruitment would have been yet

more challenging. Although limited by the sample size, the series of studies was at least comparable to or larger than many existing PSG studies (Brunner, et al., 1994; Driver & Shapiro, 1992; Hertz, et al., 1992; Schorr, et al., 1998).

The fact that the study measured sleep in an unfamiliar laboratory setting may be a criticism of this research, however the sleeping environment was controlled so that the women were not differentially affected by external stimuli, and this allowed all women to experience the same minor discomforts that may be associated with the monitoring equipment. Although the pregnant women had more disrupted sleep, it was actually found that more pregnant women reported sleeping similarly to normal whilst in the laboratory, whereas the nonpregnant group tended to report poorer sleep quality than usual.

Another limitation of the current study relates to potential biases in recruitment. The nature of this study may have attracted pregnant women who believed that they had a sleep or memory problem, and they may have been more likely to volunteer. However, in the course of recruiting, some pregnant women actually declined participation citing poor sleep as a reason not to spend a night in the sleep laboratory. Another possible recruitment bias in this study that may feature in many research studies was the tendency for willing participants to have higher intellectual functioning and more education that the general population, as shown by our demographic details. It is conceivable that women who are highly educated and from a higher socio-economic background may be more inclined to understand the value of research and thus be interested in being involved.

The design of this study may in itself be a limitation. The pregnant women slept less and had poorer sleep quality than the nonpregnant women, but they would not be classified as ‘sleep deprived’ in the usual experimental sense. Given the relatively small differences in sleep parameters across pregnancy groups compared to traditional sleep deprivation studies, it may have been difficult to find any large effect on measures of

memory consolidation in any case. On the other hand, a strength of this study was the application of the memory and sleep hypothesis to a real population rather than to an artificial situation, and therefore fully depriving participants of certain sleep stages may not be all that practicable. The sample size in this study was large enough to have an 80% chance of finding correlations as small as r = .35 at a significance level of .05, however it may be that a large sample size with more power was still required.

An unforeseen limitation of this study relates to the memory tasks used. To test verbal and visual episodic memory this study used the Wechsler Memory Scale – Third Edition (WMS-III; Wechsler, 1997), which is a widely known and commonly used neuropsychological test for both research and clinical population, which has extensive normative data stratified by age. The Wechsler Abbreviated Scale of Intelligence (WASI; The Psychological Corporation, 1999) allowed us to determine that our participant group overall was within the 'above average' intelligence range. However, testing revealed that on three out of the four WMS-III core subtests, participants averaged close to or equal to 100% on memory retention, even after an extended delay period (which well exceeded the recommended delay time of 30 minutes for clinical purposes). Even considering the sample demographics, this level of performance on these memory retention tasks was unexpected. Since this study was conducted, the 4th edition of the WMS had been released (Wechsler, 2009), which has eliminated both the problematic Faces and Family Pictures subtests in favour of more visually oriented tasks, and has an increased focus on visual working memory. These tasks may represent visual memory ability more purely than the tasks used in our study, as they allow less opportunity to apply verbal descriptions to the visual stimuli in order to aid recall.

Directions for Future Research

Although memory problems are commonly reported during pregnancy and are even depicted as comical at times, whether actual measurable changes occur is still an

area of debate both in scientific circles and in the general media. As memory is not a unitary process, it has proven difficult for researchers to obtain consistent results. More research is required to establish a pattern of memory function (or dysfunction) that is associated with pregnancy, in order to develop ways to overcome their impact on everyday functioning. This study investigated a wide variety of possible reasons for memory changes during pregnancy, including sleep, mood, attention, and progesterone, but was unable to find the answer. Identifying the causes of reduced memory abilities during pregnancy may help to find ways of preventing memory problems occurring, or to alleviate their impact.

The presence of sleep disruption during pregnancy has been a fairly consistent finding. However, the prevalence of sleep-related breathing disorders during pregnancy remains unknown, as does whether pregnancy only exacerbates existing SDB or whether it can develop in previously unaffected women. In recent years SDB during pregnancy has become a new focus area in research (Bourjeily, Ankner, & Mohsenin, 2011; Edwards & Sullivan, 2008), especially due to the maternal and foetal implications this condition may have. Studies have begun to associate self-reported snoring to negative outcomes such as hypertension, pre-eclampsia and gestational diabetes (Bourjeily, et al., 2010; Franklin, et al., 2000; Perez-Chada, et al., 2007; Qiu, Enquobahrie, Frederick, Abetew, & Williams, 2010), but these associations need to be confirmed with objective measures of SDB. A large prospective study is also needed to reveal how the many proposed mechanisms such as narrowed upper airway size (Izci, et al., 2006), nasopharyngeal oedema (Pilkington, et al., 1995), hormonal influences on upper airway and diaphragmatic drive (Edwards & Sullivan, 2008), and gestational weight gain contribute to SDB in pregnancy. More information about the factors contributing to SDB during pregnancy will hopefully assist in the development of a simple predictive tool to determine which women are more at risk.

Given that SDB in pregnant women appears to be characterised by increased amounts of flow limitation and snoring as opposed to repetitive episodes of complete obstruction, only using the AHI/hr calculated on PSG may not truly reflect disease severity. Future research should focus on developing other methods of measuring SDB or even devising a different diagnostic criterion for pregnant women, taking into account how these measures relate to maternal and foetal outcomes.

A number of studies have focused on RLS during pregnancy (Manconi, Govoni, De Vito, Economou, Cesnik, Casetta, et al., 2004; Manconi, Govoni, De Vito, Economou, Cesnik, Mollica, et al., 2004; Tunç, et al., 2007), and although related to PLMS, the latter is a distinct condition that requires confirmation via PSG. Dzaja, Wehrle, Lancel and Pollmacher (2009) have recently shown that RLS during pregnancy is associated with increased amounts of PLMS, and considering RLS affects about a quarter of women during pregnancy (Manconi, Govoni, De Vito, Economou, Cesnik, Casetta, et al., 2004; Tunç, et al., 2007) it is surprising that no studies have specifically investigated PLMS during pregnancy and their implications.

There is already a large body of empirical research focusing on whether memory is consolidated during sleep, and how this occurs. This study was unable to shed any additional light on this, and considering the conflicting findings and the complexities of the constructs of both memory and sleep, there is still a need for future research to address this in order to clarify which mechanisms of sleep, if any, do in fact promote consolidation of all areas of memory.

Conclusion

The purpose of this series of studies was to establish whether memory impairments in pregnancy could be attributed to sleep disturbances, while controlling for confounding variables such as attention, mood, hormone level and nocturnal oxygen saturation. The first and third trimester of pregnancy is associated with reduced verbal

memory performance compared to nonpregnant women, mostly as a consequence of reduced immediate memory span. However, visual and procedural memory remains unaffected. Pregnant women should be reassured that any memory problems experienced during pregnancy should be minor, and that teaching of compensatory techniques can improve confidence in their abilities.

Sleep during pregnancy is characterised by decreased sleep efficiency and increased awakenings, less time in REM sleep, and less deep sleep in favour of more light, non-restorative sleep. Sleep-related conditions such as snoring and leg movements were also more commonly seen in the pregnant women. Sleep is vital for physical and mental well-being, so assessing sleep quality throughout pregnancy is important. Health professionals should understand the characteristics of sleep during pregnancy, in order to recognise when referral to a sleep specialist may be required.

In contrast to the dual-process and double-step hypotheses of memory consolidation during sleep, reduced verbal memory retention in pregnancy was not the result of sleep disturbances. Although pregnant women in this study experienced disrupted sleep, they may still have had a sufficient amount to support the interplay between the hippocampus and neocortex to strengthen memory representations during sleep. The question of why memory difficulties exist during pregnancy remains unanswered. Although this study discounted sleep architecture as a contributing factor, a combination of other electrophysiological-, neurotransmitter- and neuroendocrine-related mechanisms of sleep known to play a part in memory function may be involved and hence there remains plenty of scope for further research in this area.

References

Bamber, J. H., & Dresner, M. (2003). Aortocaval compression in pregnancy: The effect of changing the degree and direction of lateral tile on maternal cardiac output. *Anesthesia and Analgesia, 97*(1), 256-258.

Banks, S., & Dinges, D. F. (2007). Behavioral and physiological consequences of sleep restriction. *J Clin Sleep Med, 3*(5), 519-528.

Beebe, K. R., & Lee, K. A. (2007). Sleep disturbance in late pregnancy and early labor. *Journal of Perinatal and Neonatal Nursing, 23*(2), 103-108.

Bonnet, M. H. (2000). Sleep deprivation. In M. Kryger, T. Roth & W. C. Dement (Eds.), *Principles and practice of sleep medicine 3rd edition*. Philadelphia, Pennsylvania: W. B. Saunders Company.

Bonnet, M. H., & Arand, D. L. (2003). Clinical effects of sleep fragmentation versus sleep deprivation. *Sleep Medicine Reviews, 7*, 297-310.

Bourjeily, G., Ankner, G., & Mohsenin. (2011). Sleep-disordered breathing in pregnancy. *Clinical Chest Medicine, 32*, 175-189.

Bourjeily, G., Raker, C. A., Chalhoub, M., & Miller, M. A. (2010). Pregnancy and fetal outcomes of symptoms of sleep-disordered breathing. *European Respiratory Journal, 36*, 849-855.

Brunner, D. P., Münch, M., Biedermann, K., Huch, R., Huch, A., & Borbély, A. A. (1994). Changes in sleep and sleep electroencephalogram during pregnancy. *Sleep, 17*(7), 576-582.

Carskadon, M. A., Brown, E. D., & Dement, W. C. (1982). Sleep fragmentation in the elderly: Relationship to daytime sleep tendency. *Neurobiology of Aging, 3*, 321-327.

Chen, G. Y., Kuo, C. D., Yang, M. J., Lo, H. M., & Tsai, Y. S. (1999). Comparison of supine and upright positions on autonomic nervous activity in late pregnancy: The role of aortocaval compression. *Anaesthesia, 54*(3), 215-219.

Clark, S. L., Cotton, D. B., Pivarnik, J. M., Lee, W., Hankins, G. D., Benedetti, T. J., et al. (1991). Position change and central hemodynamic profile during normal third-trimester pregnancy and post partum. *American Journal of Obstetrics and Gynecology, 164*(3), 883-887.

Davies, R. J., Belt, P. J., Roberts, S. J., Ali, N. J., & Stradling, J. R. (1993). Arterial blood pressure responses to graded transient arousal from sleep in normal humans. *Journal of Applied Physiology, 74*, 1123-1130.

Driver, H. S., & Shapiro, C. M. (1992). A longitudinal study of sleep stages in young women during pregnancy and postpartum. *Sleep, 15*(5), 449-453.

Dzaja, A., Wehrle, R., Lancel, M., & Pollmacher, T. (2009). Elevated estradiol plasma levels in women with restless legs during pregnancy. *Sleep, 32*(2), 169-174.

Edwards, N., Middleton, P. G., Blyton, D. M., & Sullivan, C. E. (2002). Sleep disordered breathing and pregnancy. *Thorax, 57*, 555-558.

Edwards, N., & Sullivan, C. A. (2008). Sleep-disordered breathing in pregnancy. *Sleep Med Clin, 3*, 81-95.

Ellington, C., Katz, V. L., Watson, W. J., & Spielman, F. J. (1991). The effect of lateral tilt on maternal and fetal hemodynamic variables. *Obstetrics and Gynecology, 77*(2), 201-203.

Farine, D., & Seaward, P. G. (2007). When it comes to pregnant women sleeping, is left right? *Journal of Obstetrics and Gynaecology Canada, 29*(10), 841-842.

Field, T., Diego, M., Hernandez-Reif, M., Figueiredo, B., Schanberg, S., & Kuhn, C. (2007). Sleep disturbances in depressed pregnant women and their newborns. *Infant Behavior and Development, 30*(127-133).

Franklin, K. A., Holmgren, P., Jonsson, F., Poromaa, N., Stenlund, H., & Svanborg, E. (2000). Snoring, pregnancy-induced hypertension, and growth retardation of the fetus. *Chest, 117*, 137-141.

Gais, S., & Born, J. (2004). Declarative memory consolidaton: Mechanisms acting during human sleep. *Learning & Memory, 11*, 679-685.

Golbe, L. I. (1994). Pregnancy and movement disorders. *Neurologic Clinics, 12*(3), 497-508.

Guilleminault, C., Kirisoglu, C., Poyares, D., Palombini, L., Leger, D., Farid-Moayer, M., et al. (2006). Upper airway resistance syndrome: a long-term outcome study. *J Psychiatr Res, 40*(3), 273-279.

Guilleminault, C., Stoohs, R. A., Clerk, A., Cetel, M., & Maistros, P. (1993). A cause of excessive daytime sleepiness. The upper airway resistance syndrome. *Chest, 104*(3), 781-787.

Guilleminault, C., Stoohs, R. A., Shiomi, T., Kushida, C., & Schnittger, I. (1996). Upper airway resistance syndrome, nocturnal blood pressure monitoring, and borderline hypertension. *Chest, 109*(4), 901-908.

Herrmann, W. M., & Beach, R. C. (1978). Experimental and clinical data indicating the psychotropic properties of progestogens. *Postgraduate Medical Journal, 54*(Suppl. 2), 82-87.

Hertz, G., Fast, A., Feinsilver, S. H., Albertario, C. L., Schulman, H., & Fein, A. M. (1992). Sleep in normal late pregnancy. *Sleep, 15*(3), 246-251.

Izci, B., Vennelle, M., Liston, W. A., Dundas, K. C., Calder, A. A., & Douglas, N. J. (2006). Sleep-disordered breathing and upper airway size in pregnancy and post-partum. *The European Respiratory Journal, 27*, 321-327.

Kauppila, A., Koskinen, M., Puolakka, J., Tuimala, R., & Kuikka, J. (1980). Decreased intervillous and unchanged myometrial blood flow in supine recumbency. *Obstetrics and Gynecology, 55*(2), 203-205.

Kinsley, C. H., Trainer, R., Stafisso-Sandoz, G., Quadros, P., Marcus, L. K., Hearon, C., et al. (2006). Motherhood and the hormones of pregnancy modify concentrations of hippocampal neuronal dendritic spines. *Hormones and Behavior, 49*, 131-142.

Knowlton, B. J., Mangels, J. A., & Squire, L. R. (1996). A neostriatal habit learning system in humans. *Science, 273*(5280), 1399-1402.

Kudrimoti, H. S., Barnes, C. A., & McNaughton, B. L. (1999). Reactivation of hippocampal cell assemblies: Effects of behavioral state, experience, and EEG dynamics. *The Journal of Neuroscience, 19*(10), 4090-4101.

Lahl, O., Wispel, C., Willigens, B., & Pietrowsky, R. (2008). An ultra short episode of sleep is sufficient to promote declarative memory performance. *Journal of Sleep Research, 17*(1), 3-10.

Lee, K. A., & Gay, C. L. (2004). Sleep in late pregnancy predicts length of labor and type of delivery. *American Journal of Obstetrics and Gynecology, 191*, 2041-2046.

Leuner, B., & Shors, T. J. (2004). New spines, new memories. *Molecular Neurobiology, 29*, 117-130.

Lezak, M. D., Howieson, D. B., & Loring, D. W. (2004). *Neuropsychological Assessment* (4th ed.). New York: Oxford University Press, Inc.

Manconi, M., Govoni, V., De Vito, A., Economou, N. T., Cesnik, E., Casetta, I., et al. (2004). Restless legs syndrome and pregnancy. *Neurology, 63*, 1065-1069.

Manconi, M., Govoni, V., De Vito, A., Economou, N. T., Cesnik, E., Mollica, G., et al. (2004). Pregnancy as a risk factor for restless legs syndrome. *Sleep Medicine, 5*, 305-308.

Maquet, P. (2001). The role of sleep in learning and memory. *Science, 294*, 1048-1052.

Martin, S. E., Engleman, H. M., Kingshott, R. N., & Douglas, N. J. (1997). Microarousals in patients with sleep apnoea/hypopnoea syndrome. *Journal of Sleep Research, 6*, 276-280.

McNaughton, B. L., Barnes, C. A., Battaglia, F. P., Bower, M. R., Cowen, S. L., Ekstrom, A. D., et al. (2003). Off-line reprocessing of recent memory and its role in memory consolidation: A progress report. In P. Maquet (Ed.), *Sleep and brain plasticity* (pp. 225-246). New York: Oxford University Press.

Meier-Ewert, H. K., Ridker, P. M., Rifai, N., Regan, M. M., Price, N. J., Dinges, D. F., et al. (2004). Effect of sleep loss on C-reactive protein, an inflammatory marker of cardiovascular risk. *Journal of the American College of Cardiology, 43*, 678-683.

Montplaisir, J., Nicolas, A., Godbout, R., & Walters, A. S. (2000). Restless legs syndrome and periodic limb movement disorder. In M. Kryger, T. Roth & W. C. Dement (Eds.), *Principles and practice of sleep medicine 3rd edition*. Philadelphia, Pennsylvania: W. B. Saunders Company.

Morrell, M. J., Finn, L., Kim, H., Peppard, P. E., Badr, M. S., & Young, T. (2000). Sleep fragmentation, awake blood pressure, and sleep-disordered breathing in a population-based study. *American Journal of Respiratory and Critical Care Medicine, 162*, 2091-2096.

Olivarez, S. A., Maheshwari, B., McCarthy, M., Zacharias, N., van den Veyver, I., Casturi, L., et al. (2010). Prospective trial on obstructive sleep apnea in pregnancy and fetal heart rate monitoring. *Obstetrics and Gynecology, 202*, 552.e551-557.

Pavlides, C., & Winson, J. (1989). Influences of hippocampal place cell firing in the awake state on the activity of these cells during subsequent sleep episodes. *The Journal of Neuroscience, 9*(8), 2907-2918.

Perez-Chada, D., Videla, A. J., O'Flaherty, M. E., Majul, C., Catalini, A. M., Caballer, C. A., et al. (2007). Snoring, witnessed sleep apnoeas and pregnancy-induced hypertension. *Acta Obstetricia et Gynecologica Scandinavica, 86*, 788-792.

Pilkington, S., Carli, F., Dakin, M., Romney, M., De Witt, K., Doré, C., et al. (1995). Increase in Mallampati score during pregnancy. *Br J Anaesth, 74*(6), 638-642.

Qin, Y., McNaughton, B. L., Skaggs, W. E., & Barnes, C. A. (1997). Memory reprocessing in corticocortical and hippocampocortical neuronal ensembles. *Philosophical Transactions of the Royal Society of London. Series B, Biological Sciences, 352*, 1525-1533.

Qiu, C., Enquobahrie, D., Frederick, I. O., Abetew, D., & Williams, M. A. (2010). Glucose intolerance and gestational diabetes risk in relation to sleep duration and snoring during pregnancy: a pilot study. *BMC Women's Health, 10*, 17.

Santiago, J. R., Nolledo, M. S., Kinzler, W., & Santiago, T. V. (2001). Sleep and sleep disorders in pregnancy. *Ann Intern Med, 134*, 396-408.

Schorr, S. J., Chawla, A., Devidas, M., Sullivan, C. A., Naef III, R. W., & Morrison, J. C. (1998). Sleep patterns in pregnancy: A longitudinal study of polysomnography recordings during pregnancy. *Journal of Perinatology, 18*(6), 427-430.

Siegel, J. M. (2001). The REM sleep-memory consolidation hypothesis. *Science, 294*, 1058-1063.

Skouteris, H., Germano, C., Wertheim, E. H., Paxton, S. J., & Milgrom, J. (2008). Sleep quality and depression during pregnancy: a prospective study. *Journal of Sleep Research, 17*, 217-220.

Smith, C. (2001). Sleep states and memory processes in humans: procedural versus declarative memory systems. *Sleep Medicine Reviews, 5*(6), 491-506.

Söderpalm, A. H., Lindsey, S., Purdy, R. H., Hauger, R., & de Wit, H. (2004). Administration of progesterone produces mild sedative-like effects in men and women. *Psychoneuroendocrinology, 29*(3), 339-354.

Spiegel, K., Leproult, R., & Van Cauter, E. (1999). Impact of sleep debt on metabolic and endocrine function. *Lancet, 354*, 1435-1439.

Stiasny, K., Oertel, W. H., & Trenkwalder, C. (2002). Clinical symptomatology and treatment of restless legs syndrome and periodic limb movement disorder. *Sleep Medicine Reviews, 6*(4), 253-265.

Stickgold, R., Hobson, J. A., Fosse, R., & Fosse, M. (2001). Sleep, learning, and dreams: Off-line memory reprocessing. *Science, 294*, 1052-1057.

Stutts, J. C., Wilkins, J. W., Scott Osberg, J., & Vaughn, B. V. (2003). Driver risk factors for sleep-related crashes. *Accid Anal Prev, 35*(3), 321-331.

The Psychological Corporation. (1999). *Wechsler Abbreviated Scale of Intelligence (WASI).* San Antonio, TX: The Psychological Corporation.

Tochikubo, O., Ikeda, A., Miyajima, E., & Ishii, M. (1996). Effects of insufficient sleep on blood pressure monitored by a new multibiomedical recorder. *Hypertension, 27*, 1318-1324.

Tucker, M. A., & Fishbein, W. (2009). The impact of sleep duration and subject intelligence on declarative and motor memory performance: how much is enough? *Journal of Sleep Research, 18*(3), 304-312.

Tucker, M. A., Hirota, Y., Wamsley, E. J., Lau, H., Chaklader, A., & Fishbein, W. (2006). A daytime nap containing solely non-REM sleep enhances declarative but not procedural memory. *Neurobiology of Learning and Memory, 86*, 241-247.

Tunç, T., Karadag, Y. S., Dogulu, F., & Inan, L. E. (2007). Predisposing factors of restless legs syndrome in pregnancy. *Movement Disorders, 22*(5), 627-631.

Van Dongen, H. P., Maislin, G., Mullington, J. M., & Dinges, D. F. (2003). The cumulative cost of additional wakefulness: dose-response effects on neurobehavioral functions and sleep physiology from chronic sleep restriction and total sleep deprivation. *Sleep, 26*(2), 117-126.

Vertes, R. P. (2004). Memory consolidation in sleep: Dream or reality. *Neuron, 44*, 135-148.

Vertes, R. P., & Eastman, K. E. (2000). The case against memory consolidation in REM sleep. *Behavioral and Brain Sciences, 23*(6), 867-876.

Wechsler, D. (1997). *Wechsler Memory Scale. Third edition manual*. San Antonio, TX: The Psychological Corporation.

Wechsler, D. (2009). *Wechsler Memory Scale - Fourth Edition*. San Antonio, TX: Pearson.

Wilkie, G., & Shapiro, C. M. (1992). Sleep deprivation and the postnatal blues. *Journal of Psychosomatic Research, 36*(4), 309-316.

Wilson, M. A., & McNaughton, B. L. (1994). Reactivation of hippocampal ensemble memories during sleep. *Science, 265*(5172), 676-679.

Higher Degrees Committee (Research)
Thesis by Published and Unpublished Papers

1 As an alternative to the traditional format for a higher degree thesis, it is permissible for candidates to submit a thesis in the form of a series of articles arising from the candidate's higher degree research. These must be along a central theme and may or may not be already published. The presentation of the articles should take into account current regulations for PhDs (see R21.2.9), for Professional Doctorates (see R21.3.9) and for Masters by Research (see R21.5.9). Where the thesis includes work of joint authorship the candidate shall include in the thesis a signed declaration for each article, stating the extent and nature of his or her contribution and justifying the inclusion of the material. A signed declaration from at least one of the co-authors should also be included, verifying the extent and nature of the candidate's contribution.

2 The presentation of a thesis as a collection of articles must include at least one substantial integrating article, or preferably a separate introduction, general discussion and conclusion that in combination provide an integration of the material presented. In addition, a clear statement must be included in the thesis indicating which chapters are based on published articles and providing full publication details of these articles.

3 The number of articles to be included will depend on the content and length of each and should take full account of the University's requirements for the degree as well as the amount of research expected for the degree in that discipline. Each disciple area may have specific requirements, in addition to those described in these guidelines and in the university regulations.

4 With respect to the regulation governing the completion of work undertaken during candidature, (see point 1), it is expected that unless written approval is given to include work undertaken prior to candidature at La Trobe University, e.g., a small proportion of data collected during the Honours degree to be re-analysed, all work will have been completed during the period of candidature. Work published prior to commencement of candidature must **not** be included in the thesis, although reference to such material is permitted.

5 With respect to the regulation governing joint authorship (see point 1) the candidate is expected to have made a significant and leading contribution to the work reported, equivalent to that expected for a traditional thesis.

6 A published book can also be submitted as a thesis for a Masters, PhD or professional doctorate, provided that it fulfills the requirements set out in the above five clauses of these guidelines.

7 The thesis will be examined in the normal way and according to the normal requirements set out for the degree (see Appendix A and Appendix D of the Handbook for Candidates and Supervisors for Masters Degrees by Research and Doctoral Degrees). Examiners of a thesis by published and unpublished papers will be given a copy of these guidelines.

8 The decision to submit a thesis in the form of a series of published and unpublished articles should be given careful consideration. Candidates should note that this is not an accepted practice in all disciplines. Moreover, it is likely, especially with a series of articles along one theme, that there will be considerable repetition across the articles which may detract from the presentation of the thesis. For these reasons, it may be more appropriate to prepare the thesis in the traditional format, including reprints of any published articles arising from the thesis as an appendix.

AB Amended 26.11.07
Thesis by Publication.doc (modified from GuidAltThesisFormatREV2.doc)

PARTICIPANT INFORMATION AND CONSENT FORM

EPISODIC AND PROCEDURAL MEMORY CONSOLIDATION DURING SLEEP: CAN MEMORY IMPAIRMENT DURING PREGNANCY BE ATTRIBUTED TO SLEEP DISTURBANCE?

Project Number: 02971

Principal Researcher: Prof. Rob J. Pierce
Associate Researchers: Dr. Maree Barnes, Prof. Michael Permezel, Prof. Simon Crowe, Mr. Martin Jackson, Ms. Danielle Wilson, Dr. Lenore Ellett.

---

1. YOUR CONSENT

You are invited to take part in a research project looking at commonly reported memory problems during pregnancy, and whether sleep disturbance could be a contributing factor. This Participant Information and Consent Form is 8 pages long. Please make sure you have all the pages.

This Participant Information Form contains detailed information about the research project. Its purpose is to explain to you as openly and clearly as possible all the procedures involved in this project before you decide whether or not to take part in it. Please read this Participant Information Form carefully. Feel free to ask questions about any information in the document. You may also wish to discuss the project with a relative or friend or your local health worker. Feel free to do this.

Once you understand what the project is about and if you agree to take part in it, you will be asked to sign the Consent Form. By signing the Consent Form, you indicate that you understand the information and that you give your consent to participate in the research project.

You will be given a copy of the Participant Information and Consent Form to keep as a record.

2. PURPOSE AND BACKGROUND

The purpose of this project is to investigate commonly reported memory problems experienced during pregnancy. Many studies have explored the memory changes that women often report during pregnancy, but studies employing actual memory tests have had mixed results. Some of these have shown that memory does get worse during pregnancy, but others have disagreed with this finding. Therefore, the first purpose of this study is to clarify the findings surrounding pregnancy and different types of memory.
Secondly, this project will investigate a possible explanation for memory problems during pregnancy. Some studies have suggested that the effect on memory may be

due to the hormonal changes during pregnancy, while others have suggested that lack of sleep may be the problem. Studies that have asked pregnant women about their sleep found that up to 9 in 10 women reported some form of sleep disturbance. The use of overnight sleep monitoring revealed that pregnant women tend to spend less time asleep and wake more often during the night, and some studies showed that they have less deep sleep.

One common belief is that during sleep, memories of things that happened during the day may be put into different parts of the brain for long-term storage. It is thought that lack of sleep during pregnancy may be interfering with this memory storage. If so, then memory should become progressively worse as the pregnancy progresses. This will be the second purpose of our study.

A total of approximately 90 people will participate in this project.

You are invited to participate in this research project because memory problems during pregnancy are commonly reported, but few studies have actually documented this. The experience of forgetting in day-to-day life can be frustrating and upsetting.

Danielle Wilson will submit this research to La Trobe University as the basis for the degree of Master of Science. This research project has received funding from the Austin Hospital Medical Research Foundation and La Trobe University.

3. PROCEDURES

You have been invited to participate in this study that is looking at the relationship between sleep and memory in pregnancy. This project will involve three groups of women:

1. Pregnant women in the first trimester (experimental group)
2. Pregnant women in the third trimester (experimental group)
3. Non-pregnant women (control group)

You will be part of the group of pregnant women in the third trimester.

By comparing memory tests and sleep patterns in these three groups, we will be able to determine whether pregnant women experience difficulties with their memory and sleep, and whether these problems are related.

At the beginning of your involvement in this research project, we will invite you to attend the hospital for an interview so we can fully explain to you what is involved. After signing the informed consent form on page 8 of this document, you will be asked to fill out a questionnaire to determine whether you are eligible to continue in this study. This appointment should take approximately 1 hour.

If you are eligible to continue, you will then be invited to undertake an overnight sleep study in the sleep laboratory. On the evening of the sleep study, you will be invited to complete several neuropsychological tests (details are below) to measure your attention and memory abilities. The sleep study may be done on the same day as the interview appointment, or you may choose to come back on another day to complete this. The testing session will take approximately 2 hours, and breaks may

be taken as required. Testing will be conducted at the sleep laboratory, in a quiet and distraction free environment. At the completion of testing, you will be allowed to go to bed and sleep.

When you wake in the morning, you will again complete several neuropsychological tests to measure you attention and memory abilities. After completion of these tasks, a blood sample will be taken to measure your hormonal levels, and you will be then allowed to go home.

4. WHAT ARE THE TESTS?

A. Personal Information

You will be asked to fill in a form with details of your age, marital status, education level, current employment, height and weight. You will also be asked details about your current pregnancy (e.g. number of weeks, any previous pregnancies, single or multiple).

B. Questionnaires

i) Depression Anxiety and Stress Scale
This is a brief self-report questionnaire designed to measure depression, anxiety and stress.
ii) Sleep Questionnaire
This will ask you about how well you have been sleeping during the past 2 weeks, and about your general sleepiness level.
iii) Memory Questionnaire
This will ask you about your memory functioning during the last two weeks.

C. Neuropsychological Tests – approximately 2 hours

i) Estimate of Intellectual Functioning
This is a 30-minute test to obtain a reliable measure of your general intelligence. This involves doing a pen and paper test as well as some block building tasks.
ii) Memory tests
Your memory abilities will be measured with a short series of tests involving recall of written, spoken and spatial information.
iii) Vigilance test
You will be asked to press a button on a computer keyboard in response to figures appearing on the screen. We will measure how long it takes you to respond each time the figures appear. This task will take approximately 20 minutes.

D. Overnight Sleep Study

The overnight sleep study takes place in the sleep laboratory. You will be asked to arrive at approximately 7pm in the evening to undertake the neuropsychological tests before going to bed, and the sleep study will finish at 6.30am the next morning. Following this, you will complete the neuropsychological tests and have a blood sample taken, and you will be able to leave by approximately 7.30am.

When you come in, you will be met by the researcher and shown to your private room. Bathroom facilities are shared. There is a small lounge/television room for your use, and microwave / fridge facilities are available. You should have your dinner before coming to the hospital, bring night attire, toiletries, and are welcome to bring your own pillow. You should bring all your own medication and take any medication as you would normally. Since caffeine is a stimulant, you are asked to refrain from drinking coffee, tea or coke from 4pm on the afternoon of the overnight study. If you wish, you may bring non-caffeinated drinks with you to the hospital. Alcohol should be avoided from 12 midday on the day of this study.

The researcher is a trained scientist or nurse who is experienced in this area. He/she will explain the equipment and procedures to you, then will attach several electrodes to your head, face, chest and legs to monitor your heart and the activity of your brain, your eyes, and the muscles of your face and legs. You will also have 2 bands strapped around your chest and abdomen to monitor your breathing, an airflow detector attached to your nose and an oxygen sensor attached to a finger. This may sound very uncomfortable and restrictive, but you are able to walk around, read, watch television, eat and drink. After the memory and attention testing you will be asked to go to bed, and the electrodes will be plugged in to a board at the head of your bed.

E. Measure of Hormones

A blood sample will be taken in the morning at the Pathology Department, which will be used to measure the effects of progesterone levels on your memory and sleep.

5. COLLECTION OF BLOOD SAMPLES FOR RESEARCH PURPOSES

By consenting to take part in this study, you also consent to the collection, storage and use of blood samples. A small amount of blood (5ml or ¼ tablespoon) will be sampled from the inside of your elbow by a trained pathology nurse. All samples will be handled by the Department of Laboratory Medicine according to their normal procedures. Data from the blood samples will be entered in a coded manner into our research study database. Thus all information regarding the sample will be recorded using a subject ID number only. The sample will be destroyed at the conclusion of the study.

6. POSSIBLE BENEFITS

There will be no direct to you for participating in this study. You will not be paid for your participation in this trial.

7. POSSIBLE RISKS

Possible risks, side effects and discomforts include

1) The main discomfort will be the time commitment we are asking of you (one overnight study), and the fatigue that the tests may cause.
2) Blood Test – there may be some discomfort or bruising from the needle.
3) During the sleep study, the cream used to attach the wires may cause some skin irritation.
4) If our testing does reveal any significant abnormalities, you will be referred to a

specialist for further investigation.

There may be additional unforeseen or unknown risks.

8. OTHER TREATMENTS WHILST ON STUDY

It is important to tell your doctor and the research staff about any treatments or medications you may be taking, including non-prescription medications, vitamins or herbal remedies and any changes to these during your participation in the study.

9. PRIVACY, CONFIDENTIALITY AND DISCLOSURE OF INFORMATION

At the end of the study you will receive a copy of your results and these will be explained to you by one of the researchers. We will happily send a copy to any doctor at your request. The results of the study will be published, but your identity will not be revealed, nor will your results be shared with anyone else for any other purpose. Members of the Hospital Ethics Committee may ask to look at your results, but no other people will be authorised to access them. The records dealing with this study will be kept in safe storage for 7 years, and then shredded.

Your confidentiality will be respected at all times. You are free to decline or withdraw from participation in this study at any time and this will not affect your present or future relationship with this hospital or doctor. If at any time you or your doctor feels it is in your best interest to discontinue, you will be withdrawn from the study. At all stages of the study, you will be encouraged to ask questions.

Any information obtained in connection with this research project that can identify you will remain confidential and will only be used for the purpose of this research project. It will only be disclosed with your permission, except as required by law. If you give us your permission by signing the Consent Form, we plan to publish the results in a scientific journal. In any publication, information will be provided in such a way that you cannot be identified.

In accordance with the National Medical Health and Research Council guidelines, the Human Research Ethics Committee is required to conduct audits of research projects from time to time. It may therefore be possible that the Human Research Ethics Committee which has approved this research, will seek to view a copy of your signed consent form, or to contact you, to ensure that the research is being conducted according to the ethical standards required by these guidelines.

In accordance with the *Freedom of Information Act* 1982 (Vic), you have the right to access and to request correction of information held about you by Austin Health or Mercy Hospital for Women.

10. NEW INFORMATION ARISING DURING THE PROJECT

During the research project, new information about the risks and benefits of the project may become known to the researchers. If this occurs, you will be told about this new information. This new information may mean that you can no longer participate in this research. If this occurs, the person(s) supervising the research will stop your participation. In all cases, you will be offered all available care to suit your needs and medical condition.

11. FURTHER INFORMATION OR ANY PROBLEMS

Ms. Danielle Wilson, Dr. Maree Barnes, Professor Michael Permezel, Dr. Lenore Ellett, Professor Rob Pierce, Professor Simon Crowe, and Mr. Martin Jackson will be coordinating this study. If you have any questions or concerns, they can be contacted on:

Danielle Wilson	ph 9496-5756 during hours, or leave a message after hours.
Maree Barnes:	ph 9496-5756 during hours.
	After hours: through the hospital switchboard, ph 9496-5000.
Rob Pierce:	ph 9496-3688 during hours.
	After hours: through the hospital switchboard, ph 9496-5000.
Lenore Ellett:	through the Mercy hospital switch board, ph 8458 4444
Simon Crowe	ph 9479-1380 during hours, or leave a message after hours.
Martin Jackson	ph 9479-2472 during hours, or leave a message after hours.

If you have any complaints about any aspect of the project, the way it is being conducted or any questions about your rights as a research participant, then you may contact:

- Andrew Crowden, Chairman of the Austin Health Human Research Ethics Committee. Telephone: 9496 2901.
- Vicky Karitinos, Secretary, Research Ethics Committee at Mercy Health and Aged Care. Telephone: 8458 4808.

12. PARTICIPATION IS VOLUNTARY

Participation in any research project is voluntary. If you do not wish to take part you are not obliged to. If you decide to take part and later change your mind, you are free to withdraw from the project at any stage. You will be able to have your tissue sample and data withdrawn from the research project if you wish.
Your decision whether to take part or not to take part, or to take part and then withdraw, will not affect your routine treatment, your relationship with those treating you or your relationship with Austin Health or Mercy Hospital for Women.
Before you make your decision, a member of the research team will be available so that you can ask any questions you have about the research project. You can ask for any information you want. Sign the Consent Form only after you have had a chance to ask your questions and have received satisfactory answers.
If you decide to withdraw from this project, please notify a member of the research team before you withdraw. This notice will allow that person or the research supervisor to inform you if there are any health risks or special requirements linked to withdrawing.

13. ETHICAL GUIDELINES

This project will be carried out according to the *National Statement on Ethical Conduct in Research Involving Humans* (March 2007) produced by the National Health and Medical Research Council of Australia. This statement has been developed to protect the interests of people who agree to participate in human research studies.
The ethical aspects of this research project have been approved by the Human Research Ethics Committee of Austin Health. Approval for this research has also been given by the Mercy Hospital for Women and La Trobe University.

CONSENT FORM TO PARTICIPATE IN RESEARCH

Project Title: Episodic And Procedural Memory Consolidation During Sleep: Can Memory Impairment During Pregnancy Be Attributed To Sleep Disturbance?

Project Number: 02971

- I have read and I understand the Participant Information and Consent Form, Version 2 dated 06/08/2007.
- I have had an opportunity to ask questions and I am satisfied with the answers I have received.
- I understand that this involves risks and inconveniences as listed on page 4 of this document.
- I freely agree to participate in this project according to the conditions in the Participant Information Form.
- I will be given a copy of the Participant Information and Consent Form to keep.
- I understand that the researcher has agreed not to reveal my identity and personal details if information about this project is published or presented in any public form.
- I understand that I can leave the research project at any time and that this will not change my relationship with my doctor.

Participant's Name (printed) .....

Signature..... Date.....

Name of Witness to Participant's Signature (printed) .....

Signature..... Date.....

Declaration by researcher: I have given a verbal explanation of the research project, its procedures and risks and I believe that the participant has understood that explanation.
Researcher's Name (printed) .....

Signature..... Date.....

* A senior member of the research team must provide the explanation and provision of information concerning the research project.

Note: All parties signing the Consent Form must date their own signature.

Memory Questionnaire

1. On a scale of 1-10, with 1= extremely poor to 10= extremely good, how would you rate the quality of your memory over the past two weeks?

---

2. On a scale of 1-10, with 1= extremely poor to 10= extremely good, how would you rate the quality of your memory generally? (when not pregnant)

---

3. Have you noticed any changes in your ability to recall or remember things since being pregnant?

Yes No

4. Have you noticed any changes in your concentration or attention span since being pregnant?

Yes No

5. How frequent would lapses in your memory occur?

Never Rarely Often Always

Background Information

The following information is needed so that we can gain a general description of who participates in the study. Please indicate your current situation by ticking the boxes, filling in the blanks, or circling the number which best suits you.

1. What is your age? _____ years	2. How many weeks pregnant are you? _____ weeks
3. What is your current relationship status? 1. Single 2. Currently in a relationship 3. Married/De Facto 4. Divorced/Separated 5. Widowed	4. Do you have any children at home? ☐ Yes ☐ No If Yes, how many? _____ Age of children _____
5. What level of education have you completed? 1. Incomplete high school 2. High school 3. Diploma/TAFE course 4. Undergraduate degree 5. Postgraduate degree 6. Other (please specify) _____	6. Are you currently studying? ☐ Yes ☐ No If Yes, what is your current enrolment status? 1. Full-time 2. Part-time 3. Other (please specify) _____
7. What is your employment status? 1. Unemployed 2. Casual employment 3. Part-time employment 4. Full-time employment 5. Other (please specify) _____	

Sleep Questionnaire

1. On a scale of 1-10, with 1= extremely poor to 10= extremely good, how would you rate the quality of your sleep over the past two weeks?

---

2. On a scale of 1-10, with 1= extremely poor to 10= extremely good, how would you rate the quality of your sleep generally? (when not pregnant)

---

3. On average, how many hours per night would you sleep? (please circle)

Less than 4 4-6 6-8 8-10 10 plus

4. Do you have difficulty falling asleep? (please circle)

Yes No

5. On average, how many minutes would it take you to fall asleep once in bed? (please circle)

0-10 10-20 20-30 30-60 60+

6. On average, how many times would you wake up during the night? (please circle)

None 1-2 3-4 5 times or more

7. On a scale of 1-4, indicate how often you would wake during the night for the following reasons –

1= never 2 = rarely 3 = often 4 = always

Uncomfortable position	1	2	3	4
Fetal movement	1	2	3	4
Need to urinate	1	2	3	4
Contractions	1	2	3	4
Back pain/leg cramps	1	2	3	4
Temperature	1	2	3	4
Shortness of breath	1	2	3	4
Children/partner	1	2	3	4
Other _____	1	2	3	4

8. After waking, do you have difficulty falling back asleep?

Yes No

9. On a scale of 1-10, with 1= not at all refreshed to 10= extremely refreshed, how refreshed do you feel when you wake in the morning?

---

10. Do you experience tiredness during the day?

Yes No

11. Do you take naps during the day?

Yes No

Participant No. _____ Date _____

***During the last fortnight*, have you had, or have you been told about the following symptoms:**

(show the frequency by putting a cross in one box)

	never	rarely, less than once a week	1-2 times a week	3-4 times a week	5-7 times a week	don't know
1. snorting or gasping	☐	☐	☐	☐	☐	☐
2. loud snoring	☐	☐	☐	☐	☐	☐
3. breathing stops, choke or struggle for breath	☐	☐	☐	☐	☐	☐

Thank you!

Appendix G

Copy of Published Manuscript – Chapter 2

Wilson, D. L., Barnes, M., Ellett, L., Permezel, M., Jackson, M., & Crowe, S. F. Compromised verbal episodic memory with intact visual and procedural memory during pregnancy. *Journal of Clinical and Experimental Neuropsychology.* First published online 14 March 2011. DOI: 10.1080/13803395.2010.550604

Journal of Clinical and Experimental Neuropsychology

Publication details, including instructions for authors and subscription information:
http://www.tandfonline.com/loi/ncen20

Compromised verbal episodic memory with intact visual and procedural memory during pregnancy

Danielle L. Wilson [a b], Maree Barnes [b], Lenore Ellett [c], Michael Permezel [c], Martin Jackson [a] & Simon F. Crowe [a]

[a] School of Psychological Science, La Trobe University, Bundoora, VIC, Australia

[b] Institute for Breathing and Sleep, Austin Health, Heidelberg, VIC, Australia

[c] Mercy Hospital for Women, Heidelberg, VIC, Australia

Available online: 04 Jul 2011

To cite this article: Danielle L. Wilson, Maree Barnes, Lenore Ellett, Michael Permezel, Martin Jackson & Simon F. Crowe (2011): Compromised verbal episodic memory with intact visual and procedural memory during pregnancy, Journal of Clinical and Experimental Neuropsychology, 33:6, 680-691

To link to this article: http://dx.doi.org/10.1080/13803395.2010.550604

JOURNAL OF CLINICAL AND EXPERIMENTAL NEUROPSYCHOLOGY
2011, 33 (6), 680–691

Psychology Press
Taylor & Francis Group

Compromised verbal episodic memory with intact visual and procedural memory during pregnancy

Danielle L. Wilson[1,2], Maree Barnes[2], Lenore Ellett[3], Michael Permezel[3], Martin Jackson[1], and Simon F. Crowe[1]

[1]School of Psychological Science, La Trobe University, Bundoora, VIC, Australia
[2]Institute for Breathing and Sleep, Austin Health, Heidelberg VIC, Australia
[3]Mercy Hospital for Women, Heidelberg VIC, Australia

This study investigated episodic and procedural memory performance in early and late pregnancy. Twenty-six women in the third trimester of pregnancy, 20 women in the first trimester of pregnancy, and 24 nonpregnant controls were administered a battery of verbal and visual episodic memory tasks and two procedural memory tasks. Results indicated that compared to controls, both pregnant groups had reduced scores on immediate and delayed verbal episodic memory tasks, but were unimpaired on visual and procedural memory tasks. Verbal memory differences could not be accounted for by mood state or attention; however, progesterone level accounted for a small amount of the variation. Although memory differences were minor, the perception of memory problems may have implications for everyday living for pregnant women.

Keywords: Pregnant; Explicit; Implicit; Recall; Recognition; Attention.

Anecdotal reports of memory problems during pregnancy are abundant. In particular, pregnant women frequently rate their memory as worse than normal (Crawley, Dennison, & Carter, 2003; McDowall & Moriarty, 2000; Parsons & Redman, 1991) and are more likely than nonpregnant women to have memory complaints (Brindle, Brown, Brown, Griffith, & Turner, 1991; Casey, Huntsdale, Angus, & Janes, 1999; Janes, Casey, Huntsdale, & Angus, 1999; Sharp, Brindle, Brown, & Turner, 1993). However, subjective reports may not reliably indicate actual performance, and pregnant women may be more aware of their cognitive slips due to cultural expectations of cognitive decline during pregnancy (Crawley, Grant, & Hinshaw, 2008). Objective techniques have consequently been employed to investigate memory performance during pregnancy.

Explicit memory refers to the conscious recall or recognition of facts (semantic memory) or events (episodic memory) and is commonly tested in experimental settings. Compared to controls, pregnant women have shown significant deficits on explicit memory tasks such as word-list learning (Buckwalter et al., 1999; de Groot, Vuurman, Hornstra, & Jolles, 2006; Sharp et al., 1993), paragraph recall (Keenan, Yaldoo, Stress, Fuerst, & Ginsburg, 1998), and semantic fluency (de Groot, Hornstra, Roozendaal, & Jolles, 2003). Difficulty in discriminating relevant from irrelevant responses led Buckwalter et al. (1999) to conclude that pregnancy is associated with less effective, more haphazard learning styles. A recent meta-analysis indicated that pregnant women are specifically impaired on memory measures that place high demands on executive cognitive control (Henry & Rendell, 2007). In contrast to explicit memory, implicit memory can be acquired and reexpressed without conscious awareness, but behavioral performance is affected. Priming has been a focus, with pregnant women using significantly fewer words from a priming list to complete word stems than do controls (Brindle et al., 1991; Sharp et al., 1993).

This research was funded by La Trobe University and the Austin Health Medical Research Foundation. The authors have indicated no financial conflicts of interest. The authors would like to thank the staff at the Austin Health Sleep Laboratory for their support of this project, and we appreciate the valuable contribution made by each of the research participants.

Address correspondence to Simon F. Crowe, School of Psychological Science, La Trobe University, Bundoora, VIC, 3086, Australia (E-mail: s.crowe@latrobe.edu.au).

http://www.psypress.com/jcen DOI: 10.1080/13803395.2010.550604

Physiological and psychological factors differ as a function of stage of pregnancy and parity. Some investigators describe memory impairments appearing as early as the first trimester (de Groot et al., 2003; de Groot et al., 2006; Sharp et al., 1993), whereas others describe a maximal decline in memory in the second trimester (Shetty & Pathak, 2002) or the third trimester (Keenan et al., 1998). Memory performance is often unrelated to prior pregnancy history (Casey et al., 1999; McDowall & Moriarty, 2000; Parsons et al., 2004; Sharp et al., 1993); however, Brindle et al. (1991) found that only primigravid women were impaired on implicit memory measures.

Impaired memory function during pregnancy is not always observed (Casey, 2000; Casey et al., 1999; Christensen, Poyser, Pollitt, & Cubis, 1999). Specifically, pregnant women have been unimpaired on measures of verbal and visual recognition (Sharp et al., 1993), recall of visually presented objects (Brindle et al., 1991; Sharp et al., 1993), word-list recall (Brindle et al., 1991), story recall (Crawley et al., 2003; Crawley et al., 2008), prospective memory (Casey et al., 1999; Crawley et al., 2008), and priming (Casey et al., 1999; Janes et al., 1999; McDowall & Moriarty, 2000). A large experimental study conducted recently concluded that pregnancy and motherhood are not associated with persistent cognitive deterioration (Christensen, Leach, & Mackinnon, 2010).

Pregnancy is associated with dramatic hormonal changes; both estrogen and progesterone influence brain regions that subserve learning and memory (Dohanich, 2003). Estrogen administration appears to help enhance verbal memory and capacity for new learning (Kampen & Sherwin, 1994; Sherwin, 1997); however, there is little evidence to suggest that very high estrogen levels like those in pregnancy have a beneficial effect on memory (Brett & Baxendale, 2001). The actions of progesterone on memory structures has been rarely studied, though progesterone concentrations equivalent to term pregnancy levels in healthy premenopausal women have been associated with decreased verbal memory function (Freeman, Weinstock, Rickels, Sondheimer, & Coutifaris, 1992). Despite this, no consistent associations between hormones and cognition during pregnancy have been found (Buckwalter et al., 1999; Silber, Almkvist, Larsson, & Uvnas-Moberg, 1990).

Depressive symptomatology in the prenatal period is a significant problem, with reported prevalence rates between 14% and 37% (Andersson et al., 2003; Lee et al., 2007; Priest, Austin, Barnett, & Buist, 2008). Individuals with depressive mood disorders have been shown to exhibit significant impairments in explicit memory function (Bearden et al., 2006), particularly episodic memory (Sweeney, Kmiec, & Kupfer, 2000). Mood symptoms experienced by some women during pregnancy may plausibly impact on memory function. Pregnancy also triggers a major lifestyle adjustment, and the mother-to-be is likely to focus on their current state of pregnancy rather than on the world around them (Crawley, 2002). This high degree of introspection may result in attentional fluctuations and make encoding new information and learning new skills more difficult.

The experience of cognitive difficulties can be frustrating and upsetting for an individual. During a time such as pregnancy, women need to learn new information and skills pertaining to the care of their newborn infant and are required to comply with specific medical instructions. Memory problems at such a time would disadvantage the mother-to-be.

A discrepancy currently exists between the consistently reported memory problems during pregnancy and the conflicting findings on objective testing. Only a limited number of studies using well-established neuropsychological techniques exist, but variations in their methodologies and choice of memory tasks may have led to their contradictory conclusions. Furthermore, procedural memory, a type of implicit memory that includes motor and cognitive skill learning and perceptual "how to" learning (Lezak, Howieson, & Loring, 2004), has not been investigated in pregnancy.

This article aims to report the initial findings from a study looking at the impact of sleep on memory consolidation during pregnancy. Specifically, the purpose of this study is to investigate episodic and procedural memory performance during early and late pregnancy, whilst accounting for possible contributors to memory impairment including attentional deficits, hormonal change, and mood disturbance. Based on consistent reports of memory problems during pregnancy and objectively measured memory deficits in much of the literature, it is hypothesized that pregnant women will show impairments on memory tasks in comparison to the nonpregnant controls.

METHOD

Participants

The Human Research Ethics Committees at Austin Health, Mercy Hospital for Women, and La Trobe University approved this study, and informed consent was obtained from all participants. Four hundred and thirty pregnant women from the Outpatient Obstetrics Clinic at the Mercy Hospital for Women were consecutively approached to participate in the study; of these, 56 agreed. Participant declination was mostly due to the requirements of the broader study. After volunteering to participate, 10 pregnant women withdrew prior to data collection due to pregnancy-related complications or inability to attend the testing session. Nonpregnant women were recruited from advertisements in the hospital newsletter and from friends of the pregnant participants. Participants were excluded if they had a multiple pregnancy or pregnancy complicated by hypertension, diabetes, or preeclampsia, a significant medical, psychological, or psychiatric comorbidity, a history of head injury or memory problems, or poor English language skills, or if they were taking antidepressant medication. In total, 26 women in the third trimester of pregnancy (T3: 30–38 weeks gestation), 20 women in the first trimester of pregnancy (T1: 9–14 weeks gestation), and 24 nonpregnant women (control group) participated in the study.

Materials

Memory tasks were chosen for their widespread use in standardized neuropsychological testing and the availability of age- and sex-specific norms. As procedural memory has not yet been tested in pregnant women, task selection was based on previous research looking at procedural memory consolidation and sleep in nonpregnant samples.

Memory questionnaire

Participants rated their current and general (or when not pregnant) memory quality on a scale of 1 (*extremely poor*) to 10 (*extremely good*) and indicated whether they had noticed changes in memory and in attention and concentration since becoming pregnant (or over the past six months for control participants). Frequency of memory lapses over the past fortnight was rated on a scale of "always," "often," "rarely," or "never."

Depression anxiety stress scale–short version (DASS-21; Lovibond & Lovibond, 1995)

Current state of depression, anxiety, and stress was measured using 21 items scored on a 4-point severity/frequency scale to rate the extent to which they have experienced each state over the past week. The score range for each scale is 0–42.

Wechsler abbreviated scale of intelligence (WASI; Psychological Corporation, 1999)

The WASI is a short and reliable measure of intelligence, consisting of four subtests, which combine to yield the Full Scale IQ score. The WASI IQ scores are scaled on a metric of a mean of 100 and a standard deviation of 15.

Test of memory malingering (TOMM; Tombaugh, 1996)

This test assesses effort and feigning of memory complaints in adults. Each of two learning trials contains the same 50 line drawings of common objects shown for three seconds each. Following each trial, recognition is tested with the presentation of 50 paired pictures with one target item plus a new line-drawn object. Participants in this study were deemed to be giving sufficient effort if they scored at least 45 out of 50 (90%) on the second trial.

Wechsler memory Scale–third edition (WMS–III; Wechsler, 1997)

The scaled scores from the four primary subtests of Logical Memory, Faces, Verbal-Paired Associates, and Family Pictures were used to assess episodic memory. The Rarely Missed Index for Logical Memory Recognition (Killgore & DellaPietra, 2000) was also calculated as a measure of response validity.

Austin maze (Milner, 1965; Walsh, 1985)

The maze consists of a grid of 10 × 10 buttons that must be pressed in a certain order to get from one corner to the opposite corner. When the participant presses a button that is in the correct order they receive a green light, and when they venture off track the light turns red and they must try another path. Errors per trial are calculated as the number of times the participant presses a button that is not on the correct path. A maximum of 10 trials were allowed to complete 2 errorless trials; with the total score as the overall number of errors for the 10 trials. Delayed recall was assessed by the number of errors made on 1 further trial.

Rey auditory verbal learning test (RAVLT; Rey, 1964)

A list of 15 unrelated nouns is read aloud for five consecutive trials; each trial is then followed by a free-recall test. Only List A was used for this study. After the delay period, the participant is required to recall words without further presentation of the word list. Delayed recognition was tested whereby the participant must identify the 15 words from a list of 50 words read aloud containing all items from List A and 15 words phonemically and/or semantically similar to those in the list. Identified words that were not on List A were scored as "false-positive" responses.

Motor sequence learning

This procedural memory task is the same as the finger-tapping task used by Walker, Brakefield, Morgan, Hobson, and Stickgold (2002), but for the purpose of this study is termed Motor Sequence Learning so as not to be confused with the Finger Tapping Test (Reitan, 1979) used in neuropsychological test batteries. Motor Sequence Learning requires participants to press four numeric keys on a standard computer keyboard with the fingers of their left (nondominant) hand, repeating the five-element sequence 4–1–3–2–4 as quickly and as accurately as possible for a period of 30 s. The numeric sequence was displayed at the top of the screen at all times to exclude any working memory component to the task. Training consisted of ten 30-s trials with 30-s rest periods between trials. The scores (number of sequences and number of errors) from the first trial of training were taken as the "baseline" measure, and the averaged scores from the final two trials were taken as the "posttraining" performance. The averaged scores of two further 30-s trials assessed delayed performance.

Mirror-Tracing task (Model 31010; Lafayette Instrument Co., Lafayette, Indiana)

For this procedural memory task, participants were instructed to trace a flat, six-pointed star with a pencil while only a mirror-inverted image of the star was visible. Participants were instructed to be as quick and accurate as possible. Performance on each of 10 trials was assessed

by the number of errors (drawing outside the edges of the star) and the time taken to trace the star. The scores from the first trial were taken as the "baseline" measure, and the averaged scores from the final 2 trials were taken as the "posttraining" performance. The averaged scores of 2 further trials assessed delayed performance.

Test of variables of attention (TOVA; The TOVA Company, Los Alamitos, California)

The TOVA is a computerized attention task that measures responses to visual stimuli for 21.6 minutes. The TOVA contains two test conditions: target infrequent and target frequent. In the first half of the test (target infrequent), the target:nontarget ratio is 1:3.5; a target is presented (randomly) only once every 3.5 nontarget presentations. In the second half of the test (target frequent), the target:nontarget ratio is reversed (3.5:1). Variables measured include response time, variability of response time (consistency), errors of commission (impulsivity), and errors of omission (inattention).

Procedure

As the current study reports on part of a broader study investigating the impact of sleep on memory consolidation, immediate memory was tested in the evening prior to sleep, and delayed memory was tested the following morning.

Participants arrived at the research laboratory in the evening, having refrained from alcohol and caffeine from midday. The memory questionnaire and the DASS-21 were completed before the neuropsychological tests were administered as ordered in Table 1. All participants were tested at the same time of day by the same investigator, who was trained in neuropsychological test administration. The testing session took approximately two hours, and participants were given rest breaks as requested. The following morning (approximately nine hours later), the delayed component of the memory tests was administered, and blood samples were taken for serum progesterone levels.

TABLE 1
Schedule of neuropsychological testing and estimated administration time

Order of testing	*Administration time (min)*
Demographics and DASS-21	5
WASI	30
TOMM	10
Motor Sequence Learning	10
Mirror-Tracing Task	10
Austin Maze	10
WMS–III	20
RAVLT	5
TOVA	20

Note. DASS-21 = Depression Anxiety Stress Scale 21, WASI = Wechsler Abbreviated Scale of Intelligence, TOMM = Test of Memory Malingering, WMS–III = Wechsler Memory Scale–Third Edition, RAVLT = Rey Auditory Verbal Learning Test, TOVA = Test of Variables of Attention.

Statistical analysis

All statistical analyses were performed with the Statistical Package for Social Sciences 15.0 (SPSS Inc., Chicago, Illinois). Data were checked for linearity and normality, and non-normally distributed variables were transformed as appropriate. The few extreme univariate outliers found (z score > 3.29) were assigned a raw score one unit larger or smaller than the next most extreme score in the distribution, as recommended by Tabachnick and Fidell (2007). There were no extreme outliers on any of the WMS–III or RAVLT variables. A total of 4 third-trimester women, 1 first-trimester woman, and 1 control woman were unable to complete the Mirror-Tracing Task due to its difficulty. TOVA data for 1 first-trimester woman were invalid due to an unanticipated disruption during the fourth quarter of the test. Up until this point, performance was within normal limits, and therefore this participant was included in all other analyses. Chi-square tests were used to compare the pregnancy groups on demographic variables and subjective memory ability. One-way between-groups analysis of variance (ANOVA) was used to compare groups on the WMS–III subtests and the DASS-21. One-way between-groups multivariate analysis of variance was used to compare groups on overall RAVLT and Austin Maze performance, with between-subjects effects indicating on which task elements the groups differed. Procedural memory was analyzed with one-way analysis of covariance in order to control for existing differences in performance across the groups. A mixed 3 (group) $\times$ 4 (quarter) analysis of variance was used to analyze TOVA response time and response time variability. As progesterone is strongly linked to pregnancy status, it could not be a covariate for ANOVA; therefore the effect of progesterone on memory was investigated using multiple regression. Effect sizes were calculated using eta-squared and partial eta-squared with 95% confidence intervals according to Smithson's (2003) method. Effect sizes of .01, .06, and .14 are considered small, medium, and large in magnitude. In order to determine which groups differed on ANOVAs, post hoc Newman–Keuls tests were set at a significance level of $p < .05$. All values are given in mean $\pm$ standard deviation or median and interquartile range (IQR) for transformed variables.

RESULTS

Participants

The average age in years of the third-trimester ($M = 32.2$, $SD = 3.6$), first-trimester ($M = 29.4$, $SD = 3.3$), and control groups ($M = 29.3$, $SD = 5.9$) did not differ ($p = .09$). Further demographic details for each of the groups are presented in Table 2. The three groups did not differ in

TABLE 2
Percentage of participants in each demographic category

	Control	*T1*	*T3*	χ^2	*p*
Right-handed	87.5	95.0	96.2	1.60	.45
Relationship status				25.61**	<.001
Married/de facto	37.5	85	92.3		
In a relationship	25	15	7.7		
Single	37.5	0	0		
Has children	25	55	46.2	4.43	.11
Tertiary educated	87.5	100	76.9	5.38	.07
Employment				8.20	.09
Full time	50	45	38.5		
Part time	50	50	38.5		
Unemployed	0	5	23		

Note. T1 = first trimester of pregnancy. T3 = third trimester of pregnancy.
**$p < .01$.

terms of handedness, education level, employment status, or whether they already had children. However, significantly more pregnant women were in a stable relationship than in the control group.

Intellectual functioning

The third-trimester (T3), first-trimester (T1), and control groups were equivalent in terms of Verbal and Performance IQ, and subsequently Full Scale IQ did not differ across the groups (control: $M = 114.8$, $SD = 8.2$; T1: $M = 111.1$, $SD = 8.6$; T3: $M = 114.1$, $SD = 10.7$), $F(2, 67) = 0.96$, $p = .39$.

Measures of effort

All participants scored 45 or greater on the second trial of the TOMM, indicating that no participant was feigning memory difficulties.

Two control participants scored under the cutoff of 136 on the Rarely Missed Index for Logical Memory Recognition. However, both of these participants scored above average on overall General Memory on the WMS–III and were deemed to be giving sufficient effort during testing. Several aspects of the RAVLT performance were analyzed for signs of malingering or reduced effort. All participants recognized at least 11 words on the recognition component of the task (Berry & Schipper, 2008) and performed better on recognition than they had in the first trial (Greiffenstein, Baker, & Gola, 1996) and delayed recall (Bernard, Houston, & Natoli, 1993; Flowers, Sheridan, & Shadbolt, 1996), further indicating that sufficient effort was given towards testing. Also, no participant demonstrated "exceedingly poor learning" or "lack of primacy effect" as defined by Barrash, Suhr, and Manzel (2004) as part of their Exaggeration Index for auditory–verbal learning tests.

Episodic memory

The means, standard deviations, significance levels, and effect sizes with 95% confidence intervals for each between-group comparison on the WMS–III subtests are presented in Table 3. In terms of immediate memory, both the third- and first-trimester pregnant groups performed significantly worse on the Logical Memory task than did the control group; the effect size for this difference was large. Although the difference in scores across groups on the Verbal Paired Associates task was nearing significance, simple contrast tests showed that the third-trimester pregnant group scored significantly worse than the control group ($p = .018$). The groups did not differ on the Faces or Family Pictures subtests.

On delay, the third- and first-trimester pregnant groups performed significantly worse on the Logical Memory task but not on the Verbal Paired Associates task than did controls. Again, the effect size for the difference on Logical Memory was large. There was a ceiling effect on the Verbal Paired Associates task, with 92% of controls, 55% of first-trimester women, and 62% of third-trimester women recalling all word pairs on delay (see Table 3). The third- and first-trimester pregnant groups also performed significantly worse on the recognition components of the auditory subtests than did the controls; the effect size for this difference was moderate to large. Again, the groups did not differ on the Faces or Family Pictures subtests.

The average number of words recalled on each trial of the RAVLT by each group is shown in Table 4. Measures of immediate memory on the RAVLT (Trial 1, Trial 5, total) differed significantly across the groups, Wilks = .82, $F(6, 130) = 2.32$, $p = .04$, $\eta^2 = .10$, with confidence intervals from .00 to .16. Specifically, the control group recalled significantly more words on each trial and in total for the five trials than did both pregnant groups (apart from Trial 3 on which the controls recalled significantly more words than the third-trimester group only). Measures of delayed memory on the RAVLT also differed significantly across groups, Wilks = .77, $F(6, 130) = 2.96$, $p = .01$, $\eta^2 = .12$, with confidence intervals from .01 to .19. On delay, the control group recalled significantly more words, recognized significantly more words, and made fewer false-positive responses on recognition than did both pregnant groups.

TABLE 3
Mean (± SD) of immediate and delayed recall on the WMS–III subtests for each group and level of significance and effect sizes for between-group comparisons

	Subtest	*Control*	*T1*	*T3*	F^a	*p*	*Partial* $\eta^{2,b}$
Immediate recall	LM	$13.4 \pm 2.6_a$	$11.6 \pm 2.0_b$	$11.4 \pm 2.0_b$	5.95**	.004	.15 (.02, .27)
	VPA	13.1 ± 1.9	12.4 ± 2.3	11.4 ± 3.0	2.94	.06	.08 (.00, .21)
	Faces	11.0 ± 2.7	10.4 ± 1.6	11.7 ± 3.0	1.39	.26	.04 (.00, .14)
	Fam Pic	11.3 ± 2.2	10.7 ± 2.8	9.9 ± 3.1	1.57	.22	.05 (.00, .15)
Delayed recall	LM	$12.6 \pm 2.7_a$	$9.8 \pm 2.7_b$	$11.0 \pm 2.6_b$	6.44**	.003	.16 (.02, .30)
	VPA[c]	13 (12.3–13)	13 (10–13)	13 (10.8–13)	1.93	.15	.05 (.00, .17)
	Faces	12.4 ± 2.9	11.3 ± 2.7	12.6 ± 2.1	1.69	.19	.05 (.00, .16)
	Fam Pic	11.3 ± 2.3	10.7 ± 3.2	9.8 ± 3.1	1.49	.23	.04 (.00, .15)
	Aud Rec	$12.2 \pm 2.7_a$	$10.6 \pm 2.5_b$	$10.4 \pm 2.2_b$	3.71*	.03	.10 (.00, .23)

Note. WMS–III = Wechsler Memory Scale–Third Edition. T1 = first trimester of pregnancy. T3 = third trimester of pregnancy. Means in the same row that do not share subscripts differ at $p < .05$ in the Newman–Keuls significant difference comparison. LM = Logical Memory, VPA = Verbal Paired Associates, Fam Pic = Family Pictures, Aud Rec = Auditory Recognition.
[a] $df = 2, 67$.
[b] 95% Confidence intervals given in parentheses (upper, lower).
[c] Values given as *Mdn* (IQR) as variable was transformed, where *Mdn* = median, IQR = interquartile range.
*$p < .05$.
**$p < .01$.

TABLE 4
Mean (± SD) for RAVLT recall and recognition for each group and level of significance and effect sizes for between-group comparisons

Subtest	*Control*	*T1*	*T3*	F^a	*p*	*Partial* $\eta^{2,b}$
Trial 1	$8.3 \pm 2.1_a$	$7.1 \pm 1.6_b$	$7.0 \pm 2.0_b$	3.28*	.04	.09 (.00, .22)
Trial 2	$13.0 \pm 1.6_a$	$11.0 \pm 2.2_b$	$11.3 \pm 2.1_b$	6.90**	.002	.17 (.03, .31)
Trial 3	$14.2 \pm 1.3_a$	$13.3 \pm 1.7_{ab}$	$13.0 \pm 2.0_b$	3.61*	.03	.10 (.00, .23)
Trial 4	$14.7 \pm 0.6_a$	$14.0 \pm 1.0_b$	$13.8 \pm 1.5_b$	4.53*	.01	.12 (.00, .26)
Trial 5	$15.0 \pm 0.2_a$	$14.2 \pm 1.1_b$	$13.9 \pm 1.7_b$	5.01**	.009	.13 (.01, .27)
Total	$65.1 \pm 4.3_a$	$59.5 \pm 6.0_b$	$58.9 \pm 7.8_b$	6.80**	.002	.17 (.03, .31)
Delay	$13.1 \pm 2.0_a$	$11.3 \pm 3.1_b$	$10.4 \pm 2.7_b$	7.18**	.002	.18 (.03, .32)
Recognition	$15\ (15–15)_a$	$15\ (14–15)_b$	$15\ (14–15)_b$	3.68*	.03	.10 (.00, .23)
Recog FP	$0\ (0–0.8)_a$	$1\ (0–3.5)_b$	$2\ (0–3)_b$	6.19**	.003	.16 (.02, .30)

Note. RAVLT = Rey Auditory Verbal Learning Test. Recog FP = recognition false-positive responses. T1 = first trimester of pregnancy. T3 = third trimester of pregnancy. Means in the same row that do not share subscripts differ at $p < .05$ in the Newman–Keuls significant difference comparison.
[a] $df = 2, 67$.
[b] 95% Confidence intervals given in parentheses (upper, lower).
*$p < .05$.
**$p < .01$.

The average number of errors made on each trial of the Austin Maze by each group is shown in Figure 1. Measures of spatial episodic memory on the Austin Maze task (Trial 10 errors, learning over trials, total errors) did not differ across the groups, Wilks = .95, $F(6, 130) = 0.59$, $p = .74$, $\eta^2 = .03$, with confidence intervals from .00 to .05, and there was no difference in the number of errors made on delay, $F(2, 67) = 1.34$, $p = .27$, $\eta^2 = .04$, with confidence intervals from .00 to .14.

Procedural memory

Motor Sequence Learning performance for each group is shown in Figure 2. There were no differences across groups on the posttraining number of sequences, $F(2, 65) = 2.29$, $p = .11$, partial $\eta^2 = .07$, with confidence intervals from .00 to .19, or on posttraining number of errors, $F(2, 65) = 2.00$, $p = .14$, partial $\eta^2 = .06$, with confidence intervals from .00 to .18, after controlling for baseline scores. The difference in number of sequences on delay after controlling for posttraining scores was nearing significance, $F(2, 65) = 2.95$, $p = .06$, partial $\eta^2 = .08$, with confidence intervals from .00 to .21, with simple contrast tests revealing that the control group performed significantly better than the third-trimester group ($p = .02$). There were no differences across the groups on errors made on delay after controlling for posttraining scores, $F(2, 65) = 2.37$, $p = .10$, partial $\eta^2 = .07$, with confidence intervals from .00 to .19.

Mirror-Tracing Task performance for each group is shown in Figure 3. No differences across groups were

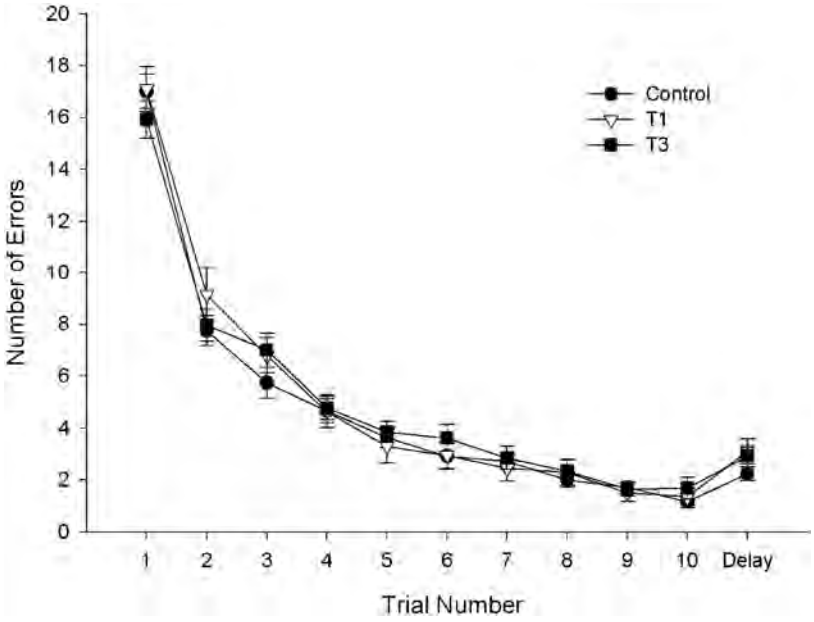

Figure 1. Mean number of errors (±*SE*) for the control ($n = 24$), T1 ($n = 20$), and T3 ($n = 26$) groups for each trial of the Austin Maze. There were no significant differences between groups on any trial of the task. T1 = first trimester of pregnancy. T3 = third trimester of pregnancy.

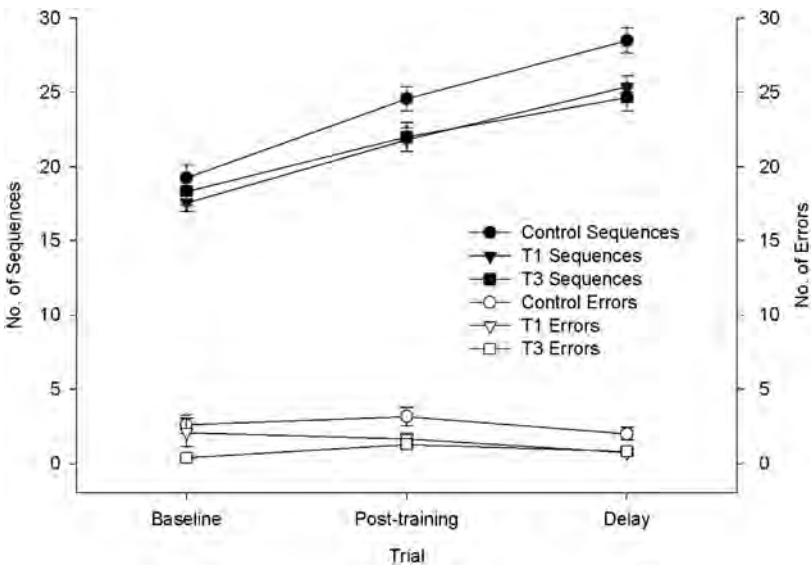

Figure 2. Mean number of sequences (±*SE*) and mean number of errors (±*SE*) for the control ($n = 24$), T1 ($n = 20$), and T3 ($n = 26$) groups for baseline, for posttraining, and on delay for the Motor Sequence Learning task. After controlling for posttraining performance, the control group completed significantly more sequences than the T3 group on delay ($p = .02$). T1 = first trimester of pregnancy. T3 = third trimester of pregnancy.

found on time taken to trace the star at posttraining, after controlling for baseline time, $F(2, 60) = 1.16$, $p = .32$, partial $\eta^2 = .04$, with confidence intervals from .00 to .14, or on delay after controlling for posttraining time, $F(2, 60) = 1.54$, $p = .22$, partial $\eta^2 = .05$, with confidence intervals from .00 to .17. There were no differences across groups on posttraining number of errors after controlling for baseline errors, $F(2, 60) = 0.80$, $p = .45$, partial $\eta^2 = .03$, with confidence intervals from .00 to .12, or on delay after controlling for posttraining errors, $F(2, 60) = 1.46$, $p = .24$, partial $\eta^2 = .05$, with confidence intervals from .00 to .16.

Attention

The average number of omission and commission errors made by each group did not differ on any quarter of the

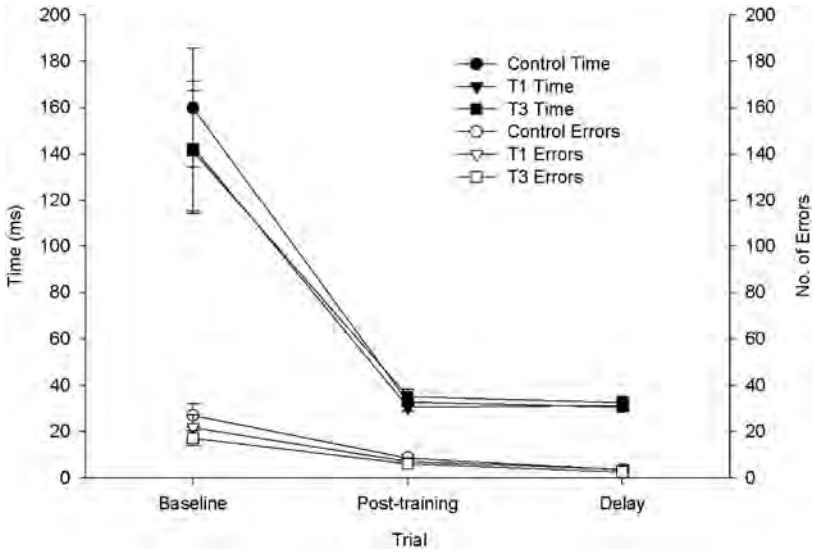

Figure 3. Mean tracing time (±*SE*) and mean number of errors (±*SE*) for the control ($n = 24$), T1 ($n = 20$), and T3 ($n = 26$) groups for baseline, for posttraining, and on delay for the Mirror-Tracing Task. The groups did not differ on any trial of the task. T1 = first trimester of pregnancy. T3 = third trimester of pregnancy.

test, and subsequently the total omission errors (control: $M = 0.8$, $SD = 2.5$; T1: $M = 0.4$, $SD = 0.8$; T3: $M = 0.5$, $SD = 0.7$) and commission errors (control: $M = 8.5$, $SD = 6.2$; T1: $M = 9.9$, $SD = 8.0$; T3: $M = 11.7$, $SD = 8.7$) did not differ, Wilks = .93, $F(4, 130) = 1.15$, $p = .34$.

As shown in Figure 4, there was no interaction effect between the three groups and test quarter on the TOVA for response time, Wilks = .98, $F(6, 128) = 0.21$, $p = .97$, and response time variability, Wilks = .93, $F(6, 128) = 0.80$, $p = .57$, indicating that the pattern of performance over time was similar across groups. A nonsignificant between-subjects effect indicated that the groups did not differ overall on response time, $F(2, 66) = 0.98$, $p = .31$, or response time variability, $F(2, 66) = 1.36$, $p = .26$.

Progesterone

Progesterone level was significantly higher in the third-trimester pregnant group ($Mdn = 413$ nmol/L, IQR = 311.5–509.3) than in the first-trimester pregnant group (68.5, 58.6–82.3), which was significantly higher than that in the control group (4.2, 2.6–7.9); $F(2, 65) = 392.38$, $p <$

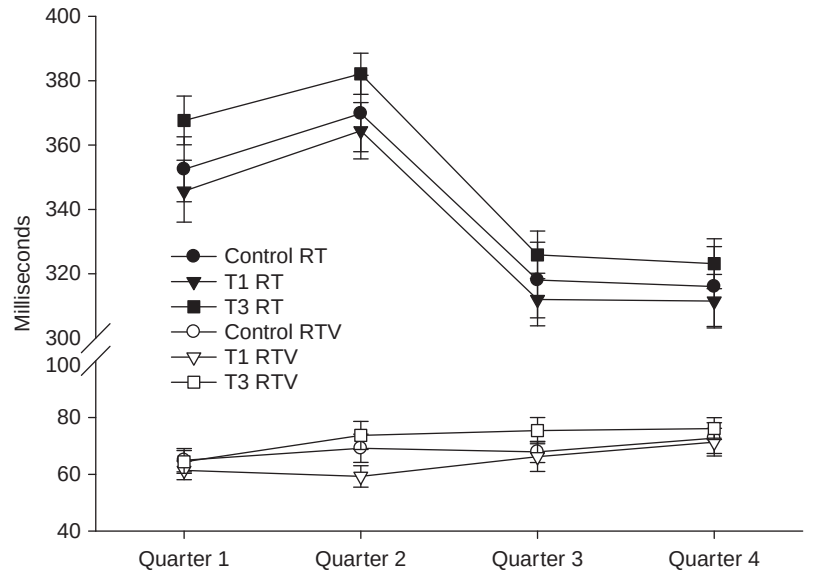

Figure 4. Mean response time (RT) and mean response time variability (RTV) for the control ($n = 24$), T1 ($n = 19$), and T3 ($n = 26$) groups for each quarter of the Test of Variables of Attention (TOVA). The groups performed equivalently on each quarter of the test. Vertical lines depict standard errors of the mean. T1 = first trimester of pregnancy. T3 = third trimester of pregnancy.

.001, $\eta^2 = 0.92$. Within the control group, progesterone level was not associated with verbal, visual, or procedural memory. After combining the third- and first-trimester pregnant groups, progesterone significantly explains an additional 19.5% of the variance in Logical Memory immediate recall, $F(1, 42) = 10.26$, $p = .003$, and 13% in the Trial 1 score on the RAVLT, $F(1, 42) = 6.26$, $p = .016$, over and above that explained by number of weeks gestation. In both instances, increased progesterone level was related to decreased memory performance ($pr = -.44$ and $-.36$, respectively).

Mood state

The average DASS-21 scores for each group are shown in Table 5. Mood did not differ across the groups, Wilks = .88, $F(6, 128) = 1.46$, $p = .20$, $\eta^2 = .06$, and depression, anxiety, and stress did not show any significant associations with memory variables.

Primiparous versus multiparous

Within the pregnant sample, there were 23 primiparous women (T3: $n = 14$; T1: $n = 9$) and 23 multiparous women (T3: $n = 12$; T1: $n = 11$). Comparison of the primiparous and multiparous participants on measures of IQ, episodic memory, and procedural memory revealed no significant differences.

Subjective memory abilities

Both pregnant groups reported a significantly greater fall in memory quality on average than did the control group. However, as shown in Table 6, this was because the third-trimester group rated their general memory as significantly better than controls, but their current memory as equivalent.

A total of 60% of women in the first trimester and 80.8% of women in the third trimester of pregnancy reported a change in their ability to recall or remember things since becoming pregnant, as compared to only 25% of controls ($\chi^2 = 15.94$, $p < .001$). A total of 75% of women in the first trimester of pregnancy reported a change in attention and concentration, which was significantly more than the third-trimester group (61.5%) and controls (33.3%; $\chi^2 = 8.25$, $p = .02$). Memory lapses were reported by 65% of the first-trimester group, significantly more than the third-trimester (46.2%) and control groups (25%; $\chi^2 = 7.13$, $p = .03$).

DISCUSSION

The results of the current study indicate that women in the first and third trimesters of pregnancy demonstrate reduced performance on episodic memory tasks compared to the control group. In particular, pregnant women performed significantly worse on verbal memory tasks comprising paragraph recall, word-list recall, and verbal recognition than did nonpregnant women, supporting previous work (de Groot et al., 2006; Keenan et al., 1998; Sharp et al., 1993). In addition, these group differences persisted after a long delay of time. The degree of reduction in scores demonstrated by the pregnant women on these tasks appears to be small, although the magnitudes of the effect sizes of these differences were all moderate to large. Apart from the word-pairs task (on which only third-trimester women had difficulty), the first- and third-trimester pregnant women performed similarly on verbal memory tasks, supporting earlier studies showing consistent performance spanning across pregnancy trimesters (de Groot et al., 2003; de Groot et al., 2006; Sharp et al., 1993). Primiparous and multiparous women did not perform differently on any memory task, supporting the contention that memory performance is unrelated to prior pregnancy history (Casey et al., 1999; McDowall & Moriarty, 2000; Parsons et al., 2004; Sharp et al., 1993).

Our findings contrast those that found no differences on verbal memory tasks between pregnant women and controls (Brindle et al., 1991; Casey et al., 1999; Crawley et al., 2003; Janes et al., 1999). However, closer inspection of these methodologies revealed that most measured only recognition memory, whilst another used word lists comprising semantic categories presented in both verbal and visual modalities. These cued memory tasks are less difficult than free recall and may explain why no differences in performance between pregnant women and controls could be found.

TABLE 5
Median scores on the DASS-21 for each group and level of significance and effect sizes for between-group comparisons

	Control	*T1*	*T3*	F^a	*p*	η^2
Depression	2 (0–4)	2 (2–5.5)	2 (0–4)	0.43	.65	.01
Anxiety	1 (0–4)	2 (0–4)	4 (0–6)	1.72	.19	.05
Stress[b]	9.6 ± 5.9	8.4 ± 7.9	8.3 ± 6.3	0.26	.77	.01

Note. Values are medians, with interquartile range (IQR) in parentheses. DASS-21 = Depression Anxiety Stress Scale–short version. T1 = first trimester of pregnancy. T3 = third trimester of pregnancy. Normal range: Depression = 0–9, Anxiety = 0–7, Stress = 0–14.
[a] $df = 2, 67$.
[b] Values given as mean ± standard deviation.

TABLE 6
Mean (± SD) for reported memory quality for each group and level of significance and effect sizes for between-group comparisons

	Control	*T1*	*T3*	F^a	*p*	η^2
Past 2 weeks	6.6 ± 1.2	6.0 ± 1.6	6.5 ± 2.0	0.96	.39	.03
Generally	$7.1 \pm 1.1_a$	$7.5 \pm 1.6_{ab}$	$8.3 \pm 1.2_b$	5.19**	.008	.13
Difference	$0.4 \pm 0.8_a$	$1.5 \pm 1.2_b$	$1.7 \pm 1.5_b$	7.70**	.001	.19

Note. Memory quality was rated on a scale of 1 (*extremely poor*) to 10 (*extremely good*). Means in the same row that do not share subscripts differ at $p < .05$ in the Newman–Keuls significant difference comparison. T1 = first trimester of pregnancy. T3 = third trimester of pregnancy.
[a] $df = 2, 67$.
** $p < .01$.

Pregnant women did not show deficits on any of the visual memory tasks, performing similarly to the nonpregnant women. This study is the first to investigate procedural memory performance during pregnancy. Overall, both pregnant groups were unimpaired on measures of procedural memory, apart from a slightly slower performance by the third-trimester pregnant group on the delayed component of Motor Sequence Learning.

Pregnant women were more likely than controls to notice a recent change in their memory quality. However, as found by Christensen et al. (1999), this difference in the women's ratings appear due to pregnant women overrating their memory level before pregnancy rather than to underrating their current memory.

Successful completion of memory tasks involves effective encoding, storage, and retrieval of information. Reduced immediate recall on all verbal memory tasks by the pregnant groups relative to the controls suggests deficiencies in the encoding process, resulting in a relatively decreased immediate memory span. Despite a reduced immediate memory span, pregnant women displayed normal rates of learning over trials. Comparing the delayed scores to the immediate scores, the first-trimester group showed a higher degree of forgetting on the paragraph recall task, whereas the third-trimester group had a higher degree of forgetting on the word-list task than did the nonpregnant women. Reduced recognition memory on story recall further implicates encoding problems, but satisfactory recognition memory on the word list suggests that retrieval problems may also contribute to memory difficulties. A high number of false-positive responses on recognition suggests a disorganized encoding style, making retrieval less reliable.

The potential cause of memory-related difficulties during pregnancy is up for debate. The possibility that pregnant women are more susceptible to attentional fluctuations was not supported by our findings. First, pregnant women did not show deficits in sustained attention on testing, and verbal recall differences persisted despite this. However, it is acknowledged that testing in the laboratory setting differs from the real world, in which pregnant women may be more introspective and readily distractible. Mood state was also unrelated to memory performance, with relatively substandard verbal recall in the absence of mood disturbance demonstrating that even pregnant women with sound mental health may experience memory-related difficulties. In regard to the potential influence of hormonal change, higher progesterone levels were weakly to moderately related to poorer performance on immediate paragraph and word-list recall. However, progesterone level explained less than 20% of the variance in these tasks, implying that several other factors are involved.

There is also the discordant finding that only verbal episodic memory was affected within the pregnant groups, and not visual episodic or procedural memory. Although our study design does not allow for attribution of causality to this discrepancy, we could speculate that as different kinds of memory are thought to have different functional and neuroanatomical systems (Smith, 2001), some neurotransmitter or hormone is acting differently on those areas involved in verbal memory (such as the left hippocampus and nearby cortical areas), as compared to the brain regions thought to be involved in visual and procedural memory (such as the right hippocampus and temporal lobe, and the neostriatum; Knowlton, Mangels, & Squire, 1996). Conversely, the differences between verbal and visual memory performance may be the result of differences in task difficulty, in that pregnant women may only be underperforming on tasks perceived as more challenging and overwhelming. As mentioned, this study represents the initial findings of an investigation into the impact of sleep on memory consolidation, and it is possible that sleep difficulties during pregnancy explain group differences on delayed memory performance. This hypothesis is currently under investigation by the authors.

It has been argued that women may subconsciously perform more poorly due to cultural expectations of cognitive decline during pregnancy (Crawley et al., 2008). Incorporating well-validated tests of malingering into our methodology revealed that all pregnant participants in this study were giving sufficient conscious effort towards testing. Unfortunately, sensitivity issues with symptom validity tests such as the TOMM have been raised (Greve, Ord, Curtis, Bianchini, & Brennan, 2008), although the TOMM has been shown to have similar predictive rates to those of other tests of malingering (Greiffenstein, Greve, Bianchini, & Baker, 2008). Furthermore, a slightly diminished performance resulting from negative cognitive expectations may go undetected by symptom validity testing, and therefore this cannot be ruled out as a contributing factor.

The results from the current study should be interpreted with caution. The participant groups in this study averaged a Full Scale IQ within the above-average range and were well educated. While above-average intellectual functioning generally translated to above-average verbal memory scores for the control group, observed weaknesses on verbal recall and recognition in the pregnant groups generally reduced their performances to within the average range. Although these group differences are statistically significant, the question is whether they are clinically important. Despite the long test battery administered, the pregnant women in this study were still able to perform within normal limits. However, 72% of the pregnant women reported a change in their ability to recall or remember things since becoming pregnant. It is possible that even these small differences may be noticeable, with the pregnant woman finding that her abilities are not up to their usual standard.

Although minor, the observed shortfalls on verbal episodic memory tests and even the perception of memory difficulties may have implications for tasks of everyday living for pregnant women. Pregnant women may lack confidence in their memory abilities and benefit from the use of compensatory techniques such as making lists and using pictorial aids. Differences in verbal memory between the pregnant and nonpregnant women were mostly due to a reduced immediate memory span, so those who feel their memory is below par may want to avoid overwhelming themselves with too much information at one time. Given the inconsistencies in current literature, women should be reassured that significant memory loss is not a proven "side effect" of pregnancy, and they should generally be able to function as per usual. On this note, visual memory, repetitive learning, and procedural memory remain unaffected. Approaching motherhood, the pregnant woman has much to learn and many new skills to master, so her ability to improve learning with repetition and to master "how to" tasks without difficulty is important.

A limitation of the current study is its cross-sectional rather than longitudinal design, mostly as a consequence of the broader study that involves overnight sleep studies. Longitudinal memory research is also difficult due to a paucity of rigorous memory tests with multiple equivalent forms (Lezak et al., 2004). In this study, the delay period for memory testing was approximately 9 hours compared to 30 min for standardized testing. Our results therefore may be difficult to compare to previous and future research in this area. However, even with a lengthy delay period, performances were generally within the normal ranges, and it could be argued that a longer delay period is more realistic to real-world demands than the standard 30 minutes. Recruitment difficulties due to the broader study requirements resulted in a reduced sample size. The sample size in this study had less than a 50% chance of finding a medium effect of .06 at a significance level of .05. There is potential that small differences in visual memory may have been undetected due to insufficient power.

Future research is needed to disentangle the discrepant findings on research into memory during pregnancy. If pregnancy can be associated with a particular pattern of memory dysfunction, then ways to overcome their impact on everyday functioning can be developed. The cause of memory differences during pregnancy such as those found in this study still remains to be discovered.

The current study has demonstrated that early and late pregnancy is associated with reduced verbal memory performance compared to nonpregnant woman, mostly as a consequence of a reduced immediate span. On the other hand, visual and procedural memory remains intact. Attention difficulties and mood disturbance were ruled out as possible contributors to these findings, but progesterone was found to play a small role. The implications of this research are important for prenatal health and education, in that pregnant women can be reassured that any memory difficulties experienced should be minor, and that those with actual or even perceived memory problems can be taught compensatory techniques to improve confidence in their abilities.

Original manuscript received 5 June 2010
Revised manuscript accepted 20 December 2010
First published online 14 March 2011

REFERENCES

Andersson, L., Sundström-Poromaa, I., Bixo, M., Wulff, M., Bondestam, K., & åström, M. (2003). Point prevalence of psychiatric disorders during the second trimester of pregnancy: A population-based study. *American Journal of Obstetrics and Gynecology, 189*(1), 148–154.

Barrash, J., Suhr, J., & Manzel, K. (2004). Detecting poor effort and malingering with an expanded version of the Auditory Verbal Learning Text (AVLTX): Validation with clinical samples. *Journal of Clinical and Experimental Neuropsychology, 26*, 125–140.

Bearden, C. E., Glahn, D. C., Monkul, E. S., Barrett, J., Najt, P., Villarreal, V., et al. (2006). Patterns of memory impairment in bipolar disorder and unipolar major depression. *Psychiatry Research, 142*(2–3), 139–150.

Bernard, L. C., Houston, W., & Natoli, L. (1993). Malingering on neuropsychological memory tests: Potential objective indicators. *Journal of Clinical Psychology, 49*, 45–53.

Berry, D. T. R., & Schipper, L. J. (2008). Assessment of feigned cognitive impairment using standard neuropsychological tests. In R. Rogers (Ed.), *Clinical assessment of malingering and deception* (3rd ed.). New York, NY: The Guilford Press.

Brett, M., & Baxendale, S. (2001). Motherhood and memory: A review. *Psychoneuroendocrinology, 26*, 339–362.

Brindle, P. M., Brown, M. W., Brown, J., Griffith, H. B., & Turner, G. M. (1991). Objective and subjective memory impairment in pregnancy. *Psychological Medicine, 21*, 647–653.

Buckwalter, J. G., Stanczyk, F. Z., McCleary, C. A., Bluestein, B. W., Buckwalter, D. K., Rankin, K. P., et al. (1999). Pregnancy, the postpartum, and steroid hormones: Effects on cognition and mood. *Psychoneuroendocrinology, 24*, 69–84.

Casey, P. (2000). A longitudinal study of cognitive performance during pregnancy and new motherhood. *Archives of Women's Mental Health, 3*, 65–76.

Casey, P., Huntsdale, C., Angus, G., & Janes, C. (1999). Memory in pregnancy. II: Implicit, incidental, explicit, semantic, short-term, working and prospective memory in primigravid, multigravid and postpartum women. *Journal of Psychosomatic Obstetrics and Gynaecology, 20*, 158–164.

Christensen, H., Leach, L. S., & Mackinnon, A. (2010). Cognition in pregnancy and motherhood: Prospective cohort study. *The British Journal of Psychiatry, 196*, 126–132.

Christensen, H., Poyser, C., Pollitt, P., & Cubis, J. (1999). Pregnancy may confer a selective cognitive advantage. *Journal of Reproductive and Infant Psychology, 17*(1), 7–25.

Crawley, R. A. (2002). Self-perception of cognitive changes during pregnancy and the early postpartum: Salience and attentional effects. *Applied Cognitive Psychology, 16*, 617–633.

Crawley, R. A., Dennison, K., & Carter, C. (2003). Cognition in pregnancy and the first year post-partum. *Psychology and Psychotherapy, 76*, 69–84.

Crawley, R. A., Grant, S., & Hinshaw, K. (2008). Cognitive changes in pregnancy: Mild decline or societal stereotype? *Applied Cognitive Psychology, 22*, 1142–1162.

de Groot, R. H. M., Hornstra, G., Roozendaal, N., & Jolles, J. (2003). Memory performance, but not information processing speed, may be reduced during early pregnancy. *Journal of Clinical and Experimental Neuropsychology, 25*(4), 482–488.

de Groot, R. H. M., Vuurman, E. F. P. M., Hornstra, G., & Jolles, J. (2006). Differences in cognitive performance during pregnancy and early motherhood. *Psychological Medicine, 36*, 1023–1032.

Dohanich, G. (2003). Ovarian steroids and cognitive function. *Current Directions in Psychological Science, 12*(2), 57–61.

Flowers, K. A., Sheridan, M. R., & Shadbolt, H. (1996). Simulation of amnesia by normals on the Rey Auditory Verbal Learning Test. *Journal of Neurolinguistics, 9*, 147–156.

Freeman, E. W., Weinstock, L., Rickels, K., Sondheimer, S. J., & Coutifaris, C. (1992). A placebo-controlled study of effects of oral progesterone on performance and mood. *British Journal of Clinical Pharmacology, 33*, 293–298.

Greiffenstein, M. F., Baker, J., & Gola, T. (1996). Comparison of multiple scoring methods for Rey's malingered amnesia measures. *Archives of Clinical Neuropsychology, 11*(4), 283–293.

Greiffenstein, M. F., Greve, K. W., Bianchini, K. J., & Baker, W. J. (2008). Test of Memory Malingering and Word Memory Test: A new comparison of failure concordance rates. *Archives of Clinical Neuropsychology, 23*, 801–807.

Greve, K. W., Ord, J., Curtis, K. L., Bianchini, K. J., & Brennan, A. (2008). Detecting malingering in traumatic brain injury and chronic pain: A comparison of three forced-choice symptom validity tests. *The Clinical Neuropsychologist, 22*(5), 896–918.

Henry, J. D., & Rendell, P. G. (2007). A review of the impact of pregnancy on memory function. *Journal of Clinical and Experimental Neuropsychology, 29*(8), 793–803.

Janes, C., Casey, P., Huntsdale, C., & Angus, G. (1999). Memory in pregnancy. I: Subjective experiences and objective assessment of implicit, explicit and working memory in primigravid and primiparous women. *Journal of Psychosomatic Obstetrics and Gynaecology, 20*, 80–87.

Kampen, D. L., & Sherwin, B. B. (1994). Estrogen use and verbal memory in healthy postmenopausal women. *Obstetrics and Gynecology, 83*(6), 979–983.

Keenan, P. A., Yaldoo, D. T., Stress, M. E., Fuerst, D. R., & Ginsburg, K. A. (1998). Explicit memory in pregnant women. *American Journal of Obstetrics and Gynecology, 179*, 731–737.

Killgore, W. I. S., & DellaPietra, L. (2000). Using the WMS–III to detect malingering: Empirical validation of the Rarely Missed Index (RMI). *Journal of Clinical and Experimental Neuropsychology, 22*(6), 761–771.

Knowlton, B. J., Mangels, J. A., & Squire, L. R. (1996). A neostriatal habit learning system in humans. *Science*, 273(5280), 1399–1402.

Lee, A. M., Lam, S. K., Sze Mun Lau, S. M., Chong, C. S., Chui, H. W., & Fong, D. Y. (2007). Prevalence, course and risk factors for antenatal anxiety and depression. *Obstetrics and Gynecology, 110*(5), 1102–1112.

Lezak, M. D., Howieson, D. B., & Loring, D. W. (2004). *Neuropsychological assessment* (4th ed.). New York, NY: Oxford University Press.

Lovibond, S. H., & Lovibond, P. F. (1995). *Manual for the Depression Anxiety Stress Scales* (2nd ed.). Sydney, Australia: Psychology Foundation.

McDowall, J., & Moriarty, R. (2000). Implicit and explicit memory in pregnant women: An analysis of data-driven and conceptually driven processes. *The Quarterly Journal of Experimental Psychology, 53A*(3), 729–740.

Milner, B. (1965). Visually-guided maze learning in man: Effects of bilateral hippocampal bilateral frontal, and bilateral cerebral lesions. *Neuropsychologia, 3*, 317–338.

Parsons, C., & Redman, S. (1991). Self-reported cognitive change during pregnancy. *The Australian Journal of Advanced Nursing, 9*(1), 20–29.

Parsons, T. D., Thompson, E., Buckwalter, D. K., Bluestein, B. W., Stanczyk, F. Z., & Buckwalter, J. G. (2004). Pregnancy history and cognition during and after pregnancy. *International Journal of Neuroscience, 114*, 1099–1110.

Priest, S. R., Austin, M. P., Barnett, B. B., & Buist, A. (2008). A psychosocial risk assessment model (PRAM) for use with pregnant and postpartum women in primary care settings. *Archives of Women's Mental Health, 11*(5–6), 307–317.

Psychological Corporation. (1999). *Wechsler Abbreviated Scale of Intelligence (WASI)*. San Antonio, TX: Author.

Reitan, R. (1979). *Manual for administration of neuropsychological test batteries for adults and children*. Tucson, AZ: Reitan Neuropsychological Laboratory.

Rey, A. (1964). *L'examen clinique on psychologie* [clinical tests in psychology]. Paris, France: Presses Universitaires de France.

Sharp, K., Brindle, P. M., Brown, M. W., & Turner, G. M. (1993). Memory loss during pregnancy. *British Journal of Obstetrics and Gynaecology, 100*, 209–215.

Sherwin, B. (1997). Estrogen effects on cognition in menopausal women. *Neurology, 48*(Suppl. 7), S21–S26.

Shetty, D. N., & Pathak, S. S. (2002). Correlation between plasma neurotransmitters and memory loss in pregnancy. *The Journal of Reproductive Medicine, 47*, 494–496.

Silber, M., Almkvist, O., Larsson, B., & Uvnas-Moberg, K. (1990). Temporary peripartal impairment in memory and attention and its possible relation to oxytocin concentration. *Life Sciences, 47*, 57–65.

Smith, C. (2001). Sleep states and memory processes in humans: Procedural versus declarative memory systems. *Sleep Medicine Reviews, 5*(6), 491–506.

Smithson, M. (2003). *Confidence intervals*. Belmont, CA: Sage.

Sweeney, J. A., Kmiec, J. A., & Kupfer, D. J. (2000). Neuropsychologic impairments in bipolar and unipolar mood disorders on the CANTAB neurocognitive battery. *Biological Psychiatry, 48*, 674–685.

Tabachnick, B. G., & Fidell, L. S. (2007). *Using multivariate statistics* (5th ed.). Boston, MA: Pearson Education.

Tombaugh, T. N. (1996). *Test of memory malingering (TOMM)*. New York, NY: Multi Health Systems.

Walker, M. P., Brakefield, T., Morgan, A., Hobson, J. A., & Stickgold, R. (2002). Practice with sleep makes perfect: Sleep-dependent motor skill learning. *Neuron, 35*, 205–211.

Walsh, K. (1985). *Understanding brain damage. A primer of neuropsychological evaluation*. London, UK: Churchill Livingstone.

Wechsler, D. (1997). *Wechsler Memory Scale. Third edition manual*. San Antonio, TX: The Psychological Corporation.

Appendix H

Copy of Published Manuscript – Chapter 3

Wilson, D. L., Barnes, M., Ellett, L., Permezel, M., Jackson, M., & Crowe, S. F. (2011). Decreased sleep efficiency, increased wake after sleep onset and increased cortical arousals in late pregnancy. *Australian and New Zealand Journal of Obstetrics and Gynaecology, 51,* 38-46. DOI: 10.1111/j.1479-828X.2010.01252.x

Original Article

Decreased sleep efficiency, increased wake after sleep onset and increased cortical arousals in late pregnancy

Danielle L. WILSON,[1,2] Maree BARNES,[2,3] Lenore ELLETT,[4] Michael PERMEZEL,[4,5] Martin JACKSON[1] and Simon F. CROWE[1]

[1]*School of Psychological Science, La Trobe University, Bundoora,* [2]*Institute for Breathing and Sleep, Austin Health, Heidelberg,* [3]*Department of Medicine, University of Melbourne, Parkville,* [4]*Department of Obstetrics and Gynaecology, Mercy Hospital for Women, Heidelberg, and* [5]*Department of Obstetrics and Gynaecology, University of Melbourne, Parkville, Victoria, Australia*

Background: Anecdotal reports of sleep disturbance during pregnancy are abundant; however, objective measurement of sleep changes has so far produced conflicting results.
Aims: To objectively measure sleep architecture and investigate subjective sleep quality in the first and third trimester of pregnancy, when compared to the nonpregnant state.
Methods: Twenty-seven women in the third trimester of pregnancy, 21 women in the first trimester of pregnancy and 24 nonpregnant control women underwent overnight polysomnography and completed questionnaires regarding sleep quality and mood.
Results: Women in the third trimester of pregnancy had poorer sleep efficiency, more awakenings, less stage 4 sleep, more stage 1 sleep and fewer minutes in rapid eye movement sleep when compared to the control group. Cortical arousals were seen more often during pregnancy, particularly in response to respiratory events and limb movements. Sleep during the first trimester was affected to a lesser extent, with more wake time after sleep onset and less stage 4 sleep when compared to the controls.
Conclusions: Sleep during pregnancy is compromised by higher amounts of wake and cortical arousals leading to sleep fragmentation, with greater amounts of light sleep and less deep sleep. Mood state did not have an effect on sleep. Given the impact of sleep on well-being, this study increases our understanding of the characteristics of sleep during pregnancy, to help recognise when severe sleep disruption may warrant referral to a specialist for appropriate diagnosis and treatment.

Key words: awakenings, cortical arousal, polysomnography, pregnancy, sleep efficiency.

Introduction

Pregnancy is marked by considerable physiological changes and a multitude of symptoms, many of which are likely to disrupt sleep. Research utilising self-reported questionnaires has demonstrated that sleep complaints are more frequent during pregnancy when compared to the nonpregnant state[1] and that sleep disturbance increases as pregnancy progresses.[2–5] Frequent night awakenings are reported by as many as 90% of women by the end of pregnancy,[3] owing to general discomfort and pain, urinary frequency, nausea and vomiting, foetal movements and shortness of breath.[2,3] However, self-report methodologies are limited by their subjective nature and may be prone to bias, as the pregnant women may be more aware of changes in sleeping habits owing to cultural expectations of sleep deprivation during pregnancy. Furthermore, people who believe they have a sleeping problem will tend to overestimate the extent of their sleep disruption.[6,7]

Polysomnography (PSG) has been utilised to objectively measure sleep changes during pregnancy. The use of electroencephalography (EEG) together with the use of electromyogram and electrooculogram (EOG) allows sleep to be classified into different stages according to objective criteria.[8] Rapid eye movement (REM) sleep is characterised by cortical activation, the presence of rapid eye movements and a global abolition of muscle tone,[9] and is often associated with dreaming. Non-REM (NREM) sleep is subdivided into four stages; stages 1 and 2 correspond to light sleep and stages 3 and 4 are often referred to as slow wave sleep (SWS) or deep sleep and show an increase in

Correspondence: Prof Simon F. Crowe, School of Psychological Science, La Trobe University, Bundoora, Victoria 3086, Australia. Email: s.crowe@latrobe.edu.au or Ms Danielle Wilson, Ground Floor Bowen Centre, Austin Health, Studley Rd, Heidelberg, Victoria 3084, Australia.
Email: danielle.wilson@austin.org.au

The authors indicate no conflicts of interest.

Received 28 April 2010; Accepted 14 September 2010.

slow oscillations and decreased muscle tone as sleep deepens.[9]

Alterations in REM sleep associated with pregnancy have ranged from a reduction compared to nonpregnant controls,[10,11] a reduction from early to late pregnancy,[12] through to showing no significant differences.[9,13,14] Slow wave sleep changes during pregnancy vary from a decrease in comparison with prepregnancy baseline measures[13] and nonpregnant women,[11,14,15] to no consistent changes across trimesters[12] and even to an increase in SWS.[10] Documented changes in stage 1 sleep associated with pregnancy have also been inconsistent.[11,12,14]

Sleep efficiency (defined as time spent sleeping as a percentage of time spent in bed) is often reduced during pregnancy and declines further as pregnancy advances,[12,13] mostly as a result of increased time spent awake after sleep onset.[10–12] Earlier PSG studies found longer sleep latencies (the time taken to fall asleep) during the last month of pregnancy;[15] however, more recent studies have failed to support this observation.[10,11,14] Cortical arousals from sleep are characterised by brief abrupt changes in EEG frequency (suggestive of an awake state), which results in sleep fragmentation;[16] the occurrence of these during pregnancy has yet to be reported on.

This lack of consistent findings may be because of generally small sample sizes and differences in methodology such as cross-sectional versus longitudinal design and laboratory-based versus home-based PSG. Furthermore, the effect of parity is rarely considered or reported upon.[17]

Pregnancy is accompanied by dramatic hormonal changes, which have significant potential to impact on sleep quality. One of the most responsive hormones is progesterone,[10] with previous research suggesting it has a soporific or sedative effect,[18,19] and may induce significant increases in Non-REM sleep.[20] However, knowledge of the effects of progesterone on human sleep mostly comes from the study of the application of exogenous hormones,[21] and clinical studies tend to limit their samples to men or postmenopausal women.[20,22] It remains uncertain how the substantial increase in progesterone during pregnancy may affect sleep.

Depressive symptomatology in the prenatal period is a significant problem with reported prevalence rates between 14 and 37%.[23–25] Pregnant women identified as being depressed report poorer sleep quality than their nondepressed counterparts,[26,27] and researchers have also begun to assess sleep deprivation as a contributor to both prenatal[27,28] and postnatal mood changes.[29,30] There is potential that mood disturbance may account for some of the variation in altered sleep patterns during pregnancy, and vice versa.

Additionally, primary sleep disorders may be more prevalent during pregnancy and impact on sleep quality. Several studies show reported increases in snoring during pregnancy,[31–35] and although the prevalence of obstructive sleep apnoea during pregnancy is unknown there is strong suggestion that this condition may be more common during pregnancy.[34,36] Restless legs syndrome affects around a quarter of women during pregnancy,[37,38] and many people with restless legs syndrome also suffer from a distinct condition known as periodic limb movements during sleep. The prevalence of periodic limb movements during sleep during healthy singleton pregnancy is unknown; however, Dzaja *et al.*[39] recently showed that restless legs syndrome during pregnancy is associated with increased amounts of periodic limb movements during sleep.

The potential for sleep disruption to impact on quality of life may be particularly detrimental to the pregnant woman who is preparing for the important task of child-rearing. Previous PSG studies during pregnancy have focussed on changes in sleep efficiency and sleep stage architecture without attempting to account for these changes. These studies have also neglected to investigate cortical arousals during sleep and the potential causes of these. The purpose of this study was to investigate both objective and subjective changes in sleep patterns associated with early and late pregnancy when compared to the nonpregnant state and to address limitations in previous PSG studies by investigating cortical arousals and accounting for possible influences on sleep such as hormonal change, mood state and parity.

Methods

The Human Research Ethics Committees at Austin Health, Mercy Hospital for Women and La Trobe University in Melbourne, Victoria, Australia approved this study, and informed consent was obtained from all participants. Four hundred and thirty pregnant women from the Outpatient Obstetrics Clinic at the Mercy Hospital for Women were consecutively approached to participate in the study, of these 58 agreed. The reasons for declining participation were typically an unwillingness to have a sleep study and inability to be away from home overnight because of family responsibilities. Ten pregnant women withdrew from the study prior to data collection because of pregnancy-related complications or inability to attend the sleep laboratory. Nonpregnant control women were recruited from advertisements in the Austin Health newsletter and from friends of the pregnant participants. The participant exclusion criteria were multiple or complicated pregnancy, significant medical, psychological or psychiatric disorder diagnosed by a health professional, a previously diagnosed sleep disorder (eg obstructive sleep apnoea, insomnia, hypersomnolence), or current use of anti-depressant medication. During the recruitment phase, only one pregnant woman was excluded from participation because of depression, and one nonpregnant woman was excluded because of a prior history of encephalopathy. In total, 27 women in the third trimester of pregnancy (T3; 30–38 weeks gestation), 21 women in the first trimester of pregnancy (T1; 9–14 weeks gestation) and 24 nonpregnant women (control group) participated in the study.

Polysomnography

Overnight PSG was conducted in-laboratory to control for variations in potential external disruptions in the home environment. PSG was performed using the Somté

(Compumedics, Abbotsford, Australia) portable sleep-monitoring device to provide greater comfort to the participants. Portable sleep-monitoring systems are commonly used in clinical settings and have been shown to have a high level of agreement with standard laboratory-based systems.[40,41] Signals measured included EEG, EOG, nasal airflow measured via nasal cannula, arterial oxygen saturation, thoracic and abdominal respiratory effort, snore, body position, leg movements and heart rate. PSG recordings were sleep staged by a single experienced sleep technologist who was blinded to pregnancy status, in accordance with standard criteria.[8] Variables of sleep included total sleep time, sleep efficiency (defined as total sleep time/total dark time), sleep latency (defined as 3 epochs of stage 1 sleep or 1 epoch of any other sleep stage), REM sleep latency, number of awakenings during sleep and wake after sleep onset. In addition, sleep stage 1, 2, 3, 4 and REM were expressed in minutes as well as a percentage of total sleep time. Arousals were measured in accordance with the rules set out by the American Sleep Disorders Association (ASDA) Atlas Task Force[16] and were categorised as to whether they were associated with a respiratory event, a limb movement or were spontaneous. Participants were woken eight hours after lights out time and asked whether they had slept worse, the same or better than usual. Morning blood was taken for serum progesterone levels. All but two of the control participants were in the follicular phase of the menstrual cycle.

Subjective sleep quality and mood

Participants completed a questionnaire developed for this study, rating their current (over the past fortnight) and general (or when not pregnant) sleep quality on a scale of 1–10, and answered questions pertaining to usual sleep duration, sleep latency, difficulties falling asleep and reasons for overnight awakenings. Reasons for overnight awakenings such as discomfort or back pain were rated for how frequently they occurred, on a scale of 'always', 'often', 'rarely' or 'never'. For statistical analysis, 'always' and 'often' responses were combined and 'rarely' and 'never' responses were combined to create a dichotomous variable.

Current state of depression, anxiety and stress was measured with the Depression Anxiety Stress Scale – Short version (DASS21).[42] Each of the three scales has seven items that are scored on a 4-point severity/frequency scale to rate the extent to which they have experienced each state over the past week. The scores for the short version are then doubled; the score range for each scale is 0–42. Internal consistency of the DASS21 using Cronbach's alpha has been shown to range from 0.88 to 0.94 for the Depression scale, from 0.82 to 0.87 for the Anxiety scale and from 0.90 to 0.91 for the Stress scale.[43,44] The DASS21 evidences good convergent and discriminant validity when compared with other validated measures of depression and anxiety.[44,45]

Statistical analysis

All statistical analyses were performed with the Statistical Package for Social Sciences 15.0 (SPSS Inc., Chicago, IL, USA). Data were tested for linearity and normality and non-normally distributed variables were log transformed apart from progesterone level which was subjected to inverse transformation. Chi-square tests, multivariate analysis of variance and univariate analysis of variance were conducted on the variables of interest. As progesterone is strongly linked to trimester of pregnancy, its influence on sleep needed to be investigated separately for each group with regression analyses. Effect sizes were calculated using partial eta squared (n^2). Effect sizes of 0.01, 0.09 and 0.25 are considered small, medium and large in magnitude.[46] To determine which groups differed on ANOVA, *post hoc* Tukey tests were set at a significance level of $P < 0.05$. All values are given in means with standard deviations (M ± SD) for normally distributed variables and median (*Mdn*) and interquartile range (*IQR*) for non-normally distributed variables.

Results

Participants

Participants were approximately 30 years old and were within a healthy weight range according to prepregnancy

Table 1 Demographic variables

	Control (n = 24)	T1 (n = 21)	T3 (n = 27)	P
Age*	29.3 ± 5.9	29.6 ± 3.4	32.3 ± 3.5	0.06
Prepregnancy BMI*	23.9 ± 3.2	25.4 ± 5.4	23.4 ± 2.5	0.22
Married/De Facto (%)	37.5	85.7	92.6	<0.001**
Nulliparous (%)	75.0	42.9	55.6	0.09
Tertiary educated (%)	87.5	100.0	77.7	0.07
Employed (%)				
Full time	50.0	42.9	40.7	0.06
Part time	50.0	52.4	37.0	
Not employed	0.0	4.8	22.2	

Data are mean ± SD. T1, first trimester; T3, third trimester; BMI, body mass index.
*P values associated with univariate ANOVA. All other P values associated with chi-square tests.
**$P < 0.01$.

Table 2 Means (±SD) for sleep variables for each group

	Control (n = 24)	T1 (n = 21)	T3 (n = 27)	Partial n^2	P
Sleep efficiency (%)	90.0 ± 6.4	84.9 ± 8.0	80.1 ± 13.5	0.15	0.004*
Sleep latency (min)	17.0 ± 19.1	19.9 ± 16.6	17.5 ± 12.8	0.01	0.82
REM latency (min)	133.3 ± 43.3	118.3 ± 60.9	126.1 ± 55.0	0.01	0.65
WASO (mins)	28.0 ± 19.5	49.4 ± 35.5	62.2 ± 36.8	0.18	0.001†
Arousals/h‡	8.8 (7.2–10.9)	10.6 (7.6–15.8)	14.6 (10.7–18.9)	0.23	<0.001§
Resp Arousals/h‡	0.9 (0.5–2.3)	1.3 (0.4–2.0)	2.4 (1.3–4.7)	0.13	0.009§
Limb Arousals/h‡	1.2 (0.5–2.4)	0.8 (0.5–2.4)	2.1 (1.3–4.8)	0.13	0.009§
Spont Arousals/h	5.9 ± 2.2	7.9 ± 3.4	8.1 ± 5.1	0.07	0.10
No. of awakenings	15.3 ± 4.1	16.0 ± 4.7	18.8 ± 6.8	0.08	0.053
Stage 1 (min)	27.8 ± 12.2	30.3 ± 15.7	35.3 ± 15.4	0.05	0.18
Stage 2 (min)	167.1 ± 39.4	165.7 ± 43.7	161.7 ± 40.8	0.003	0.89
Stage 3 (min)	77.8 ± 27.7	84.9 ± 38.1	66.9 ± 28.3	0.06	0.14
Stage 4 (min)	79.6 ± 20.0	61.6 ± 27.0	54.5 ± 23.8	0.18	0.001*
REM sleep (min)	75.0 ± 18.1	64.4 ± 15.5	60.1 ± 22.5	0.10	0.02*
%TST supine	33.1 ± 23.0	41.0 ± 23.6	19.1 ± 15.3	0.17	0.002§
Progesterone (nmol/L)‡	4.2 (2.6–7.9)	68.5 (58.6–82.3)	415 (316.3–538.4)	0.92	<0.001*

*Control vs T3 – $P < 0.05$; †control vs T1 and T3 – $P < 0.05$; §control and T1 vs T3 – $P < 0.05$.
‡Values given as *Mdn* (*IQR*) as variable was transformed.
Effect size and probability associated with univariate ANOVA with *post hoc* Tukey tests set at $P < 0.05$.
WASO, Wake after sleep onset; REM, rapid eye movement; Resp, Respiratory; Spont, Spontaneous; %TST, Percentage of total sleep time.

body mass index (BMI) and there was a high prevalence of tertiary educated women (Table 1). The three participant groups did not differ in terms of employment status or parity; however, a significantly higher percentage of pregnant women were partnered compared to the control group.

Objective sleep measurement

Multivariate analysis of variance revealed that measures of sleep fragmentation [sleep efficiency, wake after sleep onset (WASO), number of awakenings and arousals/h] differed significantly across the groups (*Wilks* = 0.69, $F(8,132) = 3.43$, $P = 0.001$, see Table 2). In particular, women in the third trimester of pregnancy had significantly poorer sleep efficiency than the controls and significantly more cortical arousals per hour than either the first-trimester women or controls. Wake after sleep onset was significantly less in the control group when compared to both pregnancy groups.

Further analysis of cortical arousals revealed that women in the third trimester of pregnancy had significantly more respiratory and limb movement-related arousals per hour when compared to the nonpregnant and first-trimester women, whereas spontaneous arousals did not differ across groups (see Table 2). It was subsequently found that significantly more third-trimester pregnant women had an Apnoea/Hypopnoea Index per hour >5 when compared to the first-trimester women and controls (30.8% vs 23.8% vs 4.2%, $P < 0.05$). Similarly, significantly more third-trimester women had a Periodic Leg Movement index of >5 per hour when compared to the first-trimester women and controls (29.6% vs 9.5% vs 4.2%, $P = 0.03$).

Multivariate analysis of variance on minutes spent in each stage of sleep (stage 1, 2, 3, 4 and REM) showed that sleep architecture differed significantly across the three groups (*Wilks* = 0.65, $F(10,130) = 3.08$, $P = 0.002$; see Table 2). Women in the third trimester of pregnancy spent significantly less time in REM sleep and stage 4 sleep when compared to the control group. Multivariate analysis of variance on the percentage of total sleep time spent in each stage of Non-REM sleep (stage 1, 2, 3 and 4) also differed significantly across the groups (*Wilks* = 0.73, $F(8,132) = 2.86$, $P = 0.006$; see Fig. 1). Women in the third trimester of pregnancy spent a significantly greater proportion of total sleep time in stage 1 sleep but a significantly smaller proportion in stage 4 sleep when compared to the first-trimester or control groups. There was no difference

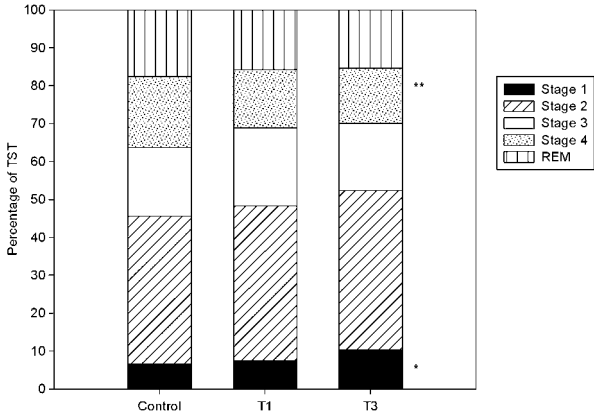

Figure 1 Mean percentage of total sleep time (TST) in each sleep stage for the control (n = 24), T1 (n = 21) and T3 (n = 27) groups. The T3 group had a significant increase in stage 1 sleep (*$P = 0.02$) compared to the T1 and control groups, and the T3 and T1 groups had a significant reduction in stage 4 sleep (**$P = 0.02$) compared to the control group.

between groups in the percentage of total sleep time spent in REM sleep.

As shown in Table 2, sleep latency and REM sleep latency were comparable across groups. Sleeping position differed significantly, with third-trimester women spending less time in the supine position when compared to the first-trimester or control groups.

In terms of perceived sleep quality for the PSG study, 71% of the third-trimester group said they slept similar to usual, compared to 43% of the first-trimester group and only 25% of the control group. Alternately, 70% of the control group said they slept worse than usual, compared to 57% of the first-trimester group and 29% of the third-trimester group. This difference in perceived sleep quality was significant ($P = 0.03$).

Nulliparas vs multiparas

As shown in Table 3, nulliparous women in the third trimester had significantly poorer sleep efficiency than multiparous women in the third trimester of pregnancy. This appears mostly because of more time in stage 2 sleep in the multiparous women. No other measures of sleep differed across the groups.

Progesterone

Progesterone level differed across the groups in accordance with pregnancy state (see Table 2). Within the control group, higher progesterone levels were associated with fewer awakenings during sleep ($r = -0.51$, $F(1,21) = 7.48$, $P = 0.01$). Progesterone was unrelated to sleep quality within the first-trimester group. Within the third-trimester group and after accounting for gestational age, progesterone significantly explained an additional 18.3% of the variance in the percentage of time in stage 2 sleep ($r = -0.50$, $F(1,23) = 5.63$, $P = 0.03$), 17.1% in number of awakenings ($r = 0.34$, $F(1,23) = 4.77$, $P = 0.04$) and 15.9% in wake after sleep onset ($r = 0.40$, $F(1,23) = 4.43$, $P = 0.046$).

Mood state

On average, all groups scores within the normal range for depression (Control – *Mdn* (*IQR*) = 2.0 (0.0–4.0), T1 = 2.0 (2.0–5.5), T3 = 2.0 (0.0–3.5), anxiety (Control – *Mdn* (*IQR*) = 1.0 (0.0–4.0), T1 = 2.0 (0.0–4.0), T3 = 4.0 (0.0–6.0) and stress (Control – *Mdn* (*IQR*) = 9.0 (6.0–12.0), T1 = 7.0 (2.0–13.0), T3 = 6.0 (4.0–12.0). A multivariate analysis of variance showed no differences in mood status across the groups (*Wilks* = 0.86, $F(6,126) = 1.67$, $P > 0.1$) and depression and stress were not associated with any sleep variables. Anxiety showed a significant but weak negative correlation with minutes spent in stage 1 sleep ($r = -0.26$, $P = 0.03$).

Subjective sleep quality

Women in the third trimester of pregnancy reported a significantly greater reduction in sleep quality over the past six months when compared to the control group (T3: 2.6 ± 1.7; control: 1.0 ± 1.0; $F(2,69) = 7.02$, $P = 0.002$). As shown in Table 4, reported average sleep duration, sleep latency, and daytime tiredness did not differ between the groups. There was a trend for more third-trimester women to report difficulty falling asleep when compared to first-trimester women or controls. Pregnant women reported significantly more overnight awakenings compared to the controls and were more likely to report difficulty falling back asleep. Third-trimester pregnant women were more likely to report frequently waking during the night because of discomfort, back pain and leg cramps when compared to controls or first-trimester women. Awakening because of urinary frequency was reported often for both pregnant groups.

Table 3 Means (±SD) for sleep variables by pregnancy trimester and parity

	First trimester		Third trimester			
	Nulliparous ($n = 9$)	Multiparous ($n = 12$)	Nulliparous ($n = 15$)	Multiparous ($n = 12$)	Partial n^2	P
Sleep efficiency (%)	83.8 ± 7.2	85.7 ± 8.9	75.2 ± 15.2	86.4 ± 7.6	0.18	0.03⋆
WASO (min)	55.4 ± 36.3	44.9 ± 35.8	77.1 ± 37.9	43.7 ± 26.5	0.16	0.052
No. of awake	15.4 ± 2.2	16.4 ± 6.0	19.3 ± 6.0	18.2 ± 8.0	0.06	0.42
Arousals/h†	10.6 (6.1–15.8)	11.0 (8.8–16.2)	15.0 (12.7–18.9)	13.2 (9.2–19.0)	0.14	0.08
Stage 1 (min)	33.1 ± 15.6	28.2 ± 16.2	32.0 ± 15.4	39.5 ± 14.9	0.07	0.36
Stage 2 (min)	149.6 ± 30.6	177.8 ± 49.1	145.4 ± 43.1	182.2 ± 27.3	0.16	0.04‡
Stage 3 (min)	88.2 ± 42.6	82.5 ± 36.0	66.3 ± 26.8	67.7 ± 31.1	0.08	0.33
Stage 4 (min)	68.8 ± 20.4	56.2 ± 30.8	57.9 ± 25.6	50.3 ± 21.7	0.06	0.43
REM sleep (min)	63.4 ± 13.9	65.0 ± 17.1	53.8 ± 21.1	68.0 ± 22.4	0.09	0.26

⋆T3 nulliparous vs T3 multiparous – $P < 0.05$.

†Values given as *Mdn* (*IQR*) as variable was transformed.

‡T3 nulliparous vs T3 multiparous – $P < 0.09$

Effect size and probability associated with univariate ANOVA with *post hoc* Tukey tests set at $P < 0.05$.

WASO, Wake after sleep onset; awake, awakenings; REM, Rapid eye movement.

Table 4 Percentage of participants reporting sleep-related problems and reported frequency of causes of night awakenings in each group

Complaint (%)	Control (n = 24)	T1 (n = 21)	T3 (n = 27)	P
Sleep-related problems				
<8 h sleep per night	79.2	71.4	74.1	0.83
Sleep latency >20 mins	25.0	28.6	44.4	0.29
Difficulty falling asleep	12.5	9.5	37.0	0.06
Tiredness	70.8	95.2	92.6	0.11
Difficulty falling asleep after waking	8.3	47.6	63.0	0.001*
No. of awakenings				
None	25.0	4.8	3.7	0.001*
1–2	66.7	57.1	29.6	
3–4	8.3	28.6	44.4	
5+	0.0	9.5	22.2	
Cause of night awakenings				
Uncomfortable	29.2	23.8	66.6	0.009*
Need to urinate	16.7	76.2	70.3	0.001*
Back pain/leg cramps	4.2	10.0	37.0	0.005*
Body temperature	20.8	20.0	18.5	0.98
Shortness of breath	0.0	5.0	3.7	0.28
Children/partner	26.0	45.0	18.5	0.07

*$P < 0.01$.

Chi-square test.

$P < 0.05$ values for causes of night awakenings given as the percentage of participants responding with 'often' or 'always'.

Discussion

The results of our study show that sleep in the third trimester of pregnancy is characterised by decreased sleep efficiency, increased wake after sleep onset and increased cortical arousals. The deepest stage of sleep, stage 4, is reduced and a higher proportion of sleep time is spent in stage 1 sleep when compared to the first-trimester or the nonpregnant state. Furthermore, this study found that third-trimester pregnant women spend less time in REM sleep compared to nonpregnant women, generally as a consequence of their reduced overall sleep efficiency rather than an alteration in the structure of their sleep stages. No differences in sleep latency or REM sleep latency were found. Women in the first trimester of pregnancy also spend more time awake after sleep onset and spend a lesser proportion of their sleep in stage 4 sleep when compared to nonpregnant women. Sleep efficiency and time in REM sleep showed a trend towards the pattern seen in the third trimester of pregnancy.

Reports of frequent awakenings and difficulty returning to sleep, mostly because of discomfort and bodily aches, were regularly made by the pregnant women in this study. The fact that third-trimester pregnant women spent substantially less time sleeping supinely when compared to the other groups also indicates compromised sleeping comfort. Unfortunately, PSG only allows attribution of a specific cause to an awakening if it has a physical source. By examining cortical arousals during sleep, we found that third-trimester women experienced more cortical arousals, especially as a consequence of limb movements or respiratory events, compared to either first-trimester or nonpregnant women. Cortical arousal often results in disrupted sleep with reduced restorative power,[47] as the individual returns to light sleep rather than deep sleep following arousal. This trade-off of more stage 1 sleep for less stage 4 sleep was a key feature of our findings in the late pregnancy group.

Investigation of sleep quality according to parity revealed that in the third trimester of pregnancy, nulliparous women have significantly poorer sleep efficiency than multiparous women, mostly as a result of multiparas spending more time in stage 2 sleep which is considered to be a lighter stage of sleep. Sleep in the first trimester of pregnancy was not affected by parity.

In contrast to the suggestion that progesterone may have sedating properties,[18,19] we found that higher progesterone levels in the third trimester of pregnancy were associated with increased awakenings and more time awake after sleep onset. This finding is unexpected given previous work indicating a positive relationship between progesterone and improved sleep measures, such as improved sleep quality in postmenopausal women following hormone replacement therapy,[48] and the suggestion that progesterone may play a role in protecting premenopausal women from sleep-disordered breathing by stimulating upper airway musculature.[49] However, hormonal influences such as progesterone have been hypothesised to be a cause of restless legs syndrome during pregnancy,[50] which can result in disrupted sleep. In our study, the association between the number of periodic limb movements during sleep and progesterone level in the third trimester was almost significant ($r = 0.39$, $P = 0.056$).

In our sample, current state of depression, anxiety and stress did not differ across the groups and did not show any

significant association with sleep disruption. The women in this study were typically in the normal to mildly affected range, so we can conclude that the differences in sleep quality across the pregnant groups were not the result of differences in mood state.

Our findings of decreased sleep efficiency and increased wake after sleep onset during pregnancy are supported by most previous studies,[10–13,15] as is the reduction in stage 4 sleep during pregnancy.[13–15] Our finding that minutes spent in REM sleep was reduced in the third-trimester pregnant group has previous support,[10–12] as well as opposition.[13,14] Lee *et al.*[13] expressed their results as the percentage of total sleep time in REM rather than total minutes and had a result close to significance, and the study by Schorr *et al.*[14] was limited by its very small sample size. Past findings surrounding stage 1 sleep have so far been discrepant. As with the current study, an increased level of stage 1 sleep has been previously found,[11–14] whereas others find no evidence for this marker of sleep fragmentation.[10–12] Again, many possibilities exist for this and other disparities, including sample sizes of <10 per group,[10,12] laboratory-based sleep studies or home sleep studies, variations in how much time the women were allowed to sleep for and the amount of sleep time included in data analyses. Parity has rarely been considered in past PSG studies, with existing literature suggesting that multiparas have a slightly lower sleep efficiency than nulliparas without a change in REM or SWS.[13,51] In contrast, the current study lends support to previous actigraphy research,[52] which found that nulliparous women had lower sleep efficiency than multiparous women. We may speculate that multiparous women were able to sleep better because of previous experience sleeping through the discomforts of pregnancy, or that sleeping away from home allowed them to catch up on sleep away from usual disruptions caused by their other children.

The high frequency of cortical arousals from sleep during pregnancy has not been previously reported. Frequent cortical arousal typically results in the person continually waking fully or returning to light sleep, leading to sleep fragmentation. Studies of sleep fragmentation commonly find increased objective and subjective sleepiness, decreased psychomotor performance and negative mood changes.[53] More specifically, measures of arousal from sleep have been significantly correlated with objective measures of daytime alertness[54,55] and increases in blood pressure.[56,57] The fact that arousals were also secondary to respiratory events or limb movements suggests that conditions such as sleep-disordered breathing and periodic limb movements during sleep should be considered as a cause of sleep disruption, given that current literature is building to suggest that these conditions may be more common during pregnancy.[34,36,39,58]

Sleep efficiency during the later stages of pregnancy in some studies has been found to be as high as 90%,[10,13,51] similar to that of our control group. The third-trimester pregnant women in this study spent 10% less time asleep on average, and almost a quarter slept for less than six hours in total. As pregnancy stretches over many months, partial sleep deprivation may become chronic and can result in seriously impaired neurobehavioural function.[59] Reduced sleep time in the last month of pregnancy has also been associated with longer labours and a higher likelihood of caesarean delivery.[60] Additionally, the cognitive impact of sleep restriction is frequently underestimated,[59] which may have potentially dangerous implications for activities of daily living, such as driving.

Limitations

This study is limited by the use of a single night of PSG to characterise sleep patterns and its cross-sectional rather than longitudinal nature. However, previous polysomnographic research during pregnancy found no differences in sleep characteristics when including an adaptation night.[13] Undertaking multiple sleep studies at appropriate time points can be a major problem with the study of pregnant women, and they are often unwilling to undergo additional measurements and procedures. This was reflected in the low response rate during recruitment and the high dropout rate because of complications of pregnancy. Although limited by our sample size, it was at least comparable to or larger than many existing PSG studies.[10–12,14,15]

Although recruitment for this study was targeted at consecutive patients at a large public hospital, the nature of the study may have resulted in biased sampling (ie those who believe they have a sleeping problem) and restrict generalisation of results. However, this works both ways, in that some pregnant women declined participation citing poor sleep and not wanting to spend a night away from home. Measuring sleep in an unfamiliar laboratory setting may affect sleep outcomes for some women, but this allows participants in each group to undergo the same sleep-monitoring conditions and any associated discomfort is equivalent across groups. We actually found in this study that pregnant women tended to report sleeping similarly to normal whilst in the laboratory, whereas the control group tended to report poorer sleep quality than usual.

Participants in this study were limited to an eight-hour period for time in bed. Although restricting potential sleep time may appear to limit the generalisability of our findings, it is common for women to continue in the work force until very late into pregnancy (as evidenced by 78% of the third-trimester women in this study who were still working), and daily responsibilities such as child-rearing or home duties may exist regardless of pregnancy status. The ability of the pregnant woman to sleep within certain time constraints therefore remains relevant.

Conclusions

In summary, pregnancy is characterised by decreased sleep efficiency and increased awakenings, with a trade-off of less deep sleep in exchange for increased light sleep and less time in REM sleep. In addition to existing literature, this study provides greater depth by revealing a higher number of cortical arousals during the later stages of pregnancy,

particularly in response to respiratory events and limb movements.

Given the impact sleep has on physical and mental well-being, assessing sleep quality throughout pregnancy is important. The creation of a screening tool that can be administered quickly by a health professional during consultation should be considered. However, as self-report measures can only reveal so much about an individual's sleeping habits, it is important to understand the characteristics of sleep during pregnancy to recognise when referral to a sleep specialist may be required, such as the possible presence of a primary sleep disorder (such as obstructive sleep apnoea or periodic leg movement disorder) or significant sleep deprivation, which would require confirmation via PSG. Only once the cause of sleep disruption is identified can appropriate treatment options be explored.

Acknowledgements

The authors would like to thank the staff at the Austin Health Sleep Laboratory for their support of this project, and we appreciate the valuable contribution made by each of the research participants.

This research was funded by La Trobe University and the Austin Health Medical Research Foundation.

References

1 Lopes EA, Carvalho LB, Seguro PB *et al.* Sleep disorders in pregnancy. *Arq Neuropsiquiatr* 2004; **62**: 217–221.
2 Baratte-Beebe K, Lee KA. Sources of midsleep awakenings in childbearing women. *Clin Nurs Res* 1999; **8**: 386–397.
3 Mindell JA, Jacobson BJ. Sleep disturbances during pregnancy. *J Obstet Gynecol Neonatal Nurs* 2000; **29**: 590–597.
4 Naud K, Ouellet A, Brown C, Pasquier JC, Moutquin JM. Is sleep disturbed in pregnancy? *J Obstet Gynaecol Can* 2010; **32**: 28–34.
5 Facco FL, Kramer J, Ho KH, Zee PC, Grobman WA. Sleep disturbances in pregnancy. *Obstet Gynecol* 2010; **115**: 77–83.
6 Means M, Edinger J, Glenn D, Fins A. Accuracy of sleep perceptions among insomnia sufferers and normal sleepers. *Sleep Med* 2003; **4**: 285–296.
7 Pinto L Jr, Pinto M, Goulart L *et al.* Sleep perception in insomniacs, sleep-disordered breathing patients, and healthy volunteers-an important biologic parameter of sleep. *Sleep Med* 2009; **10**: 865–868.
8 Rechtschaffen A, Kales A. *A Manual of Standardized Terminology, Techniques, and Scoring System for Sleep Stages of Human Subjects*. Los Angeles: Brain Information Service, 1968.
9 Carskadon MA, Dement WC. Normal human sleep: an overview. In: Kryger M, Roth T, Dement WC, eds. *Principles and practice of sleep medicine*, 4th edn. Philadelphia, Pennsylvania: W.B. Saunders Company, 2005; 13–23.
10 Driver HS, Shapiro CM. A longitudinal study of sleep stages in young women during pregnancy and postpartum. *Sleep* 1992; **15**: 449–453.
11 Hertz G, Fast A, Feinsilver SH, Albertario CL, Schulman H, Fein AM. Sleep in normal late pregnancy. *Sleep* 1992; **15**: 246–251.
12 Brunner DP, Münch M, Biedermann K, Huch R, Huch A, Borbély AA. Changes in sleep and sleep electroencephalogram during pregnancy. *Sleep.* 1994; **17**: 576–582.
13 Lee KA, Zaffke ME, McEnany G. Parity and sleep patterns during and after pregnancy. *Obstet Gynecol* 2000; **95**: 14–18.
14 Schorr SJ, Chawla A, Devidas M, Sullivan CA, Naef RW, Morrison JC. Sleep patterns in pregnancy: a longitudinal study of polysomnography recordings during pregnancy. *J Perinatol* 1998; **18**: 427–430.
15 Karacan I, Heine W, Agnew HW, Williams RL, Webb WB, Ross JJ. Characteristics of sleep patterns during late pregnancy and the postpartum periods. *Am J Obstet Gynecol* 1968; **101**: 579–586.
16 Bonnet MH, Carley D, Carskadon MA *et al.* EEG arousals: scoring rules and examples: a preliminary report from the Sleep Disorders Atlas Task Force of the American Sleep Disorders Association. *Sleep.* 1992; **15**: 173–184.
17 Lee K. Alterations in sleep during pregnancy and postpartum: a review of 30 years of research. *Sleep Med Rev* 1998; **2**: 231–242.
18 Herrmann WM, Beach RC. Experimental and clinical data indicating the psychotropic properties of progestogens. *Postgrad Med J* 1978; **54**: 82–87.
19 Söderpalm AH, Lindsey S, Purdy RH, Hauger R, de Wit H. Administration of progesterone produces mild sedative-like effects in men and women. *Psychoneuroendocrinology.* 2004; **29**: 339–354.
20 Friess E, Tagaya H, Trachsel L, Holsboer F, Rupprecht R. Progesterone-induced changes in sleep in male subjects. *Am J Physiol* 1997; **272**: E885–E891.
21 Manber R, Armitage R. Sex, steroids, and sleep: a review. *Sleep.* 1999; **22**: 540–555.
22 Schüssler P, Kluge M, Yassouridis A *et al.* Progesterone reduces wakefulness in sleep EEG and has no effect on cognition in healthy postmenopausal women. *Psychoneuroendocrinology.* 2008; **33**: 1124–1131.
23 Andersson L, Sundström-Poromaa I, Bixo M, Wulff M, Bondestam K, åström M. Point prevalence of psychiatric disorders during the second trimester of pregnancy: a population-based study. *Am J Obstet Gynecol* 2003; **189**: 148–154.
24 Lee AM, Lam SK, Sze Mun Lau SM, Chong CS, Chui HW, Fong DY. Prevalence, course and risk factors for antenatal anxiety and depression. *Obstet Gynecol* 2007; **110**: 1102–1112.
25 Priest SR, Austin MP, Barnett BB, Buist A. A psychosocial risk assessment model (PRAM) for use with pregnant and postpartum women in primary care settings. *Arch Womens Ment Health* 2008; **11**: 307–317.
26 Jomeen J, Martin CR. Assessment and relationship of sleep quality to depression in early pregnancy. *J Reprod Infant Psychol* 2007; **25**: 87–89.
27 Field T, Diego M, Hernandez-Reif M, Figueiredo B, Schanberg S, Kuhn C. Sleep disturbances in depressed pregnant women and their newborns. *Infant Behav Dev* 2007; **30**: 127–133.
28 Skouteris H, Germano C, Wertheim EH, Paxton SJ, Milgrom J. Sleep quality and depression during pregnancy: a prospective study. *J Sleep Res* 2008; **17**: 217–220.
29 Wilkie G, Shapiro CM. Sleep deprivation and the postnatal blues. *J Psychosom Res* 1992; **36**: 309–316.

30 Wolfson AR, Crowley SJ, Anwer U, Bassett JL. Changes in sleep patterns and depressive symptoms in first-time mothers: last trimester to 1-year postpartum. *Behav Sleep Med* 2003; **1**: 54–67.
31 Izci B, Riha RL, Martin SE *et al.* The upper airway in pregnancy and pre-eclampsia. *Am J Respir Crit Care Med* 2003; **167**: 137–140.
32 Izci B, Vennelle M, Liston WA, Dundas KC, Calder AA, Douglas NJ. Sleep-disordered breathing and upper airway size in pregnancy and post-partum. *Eur Respir J* 2006; **27**: 321–327.
33 Perez-Chada D, Videla AJ, O'Flaherty ME *et al.* Snoring, witnessed sleep apnoeas and pregnancy-induced hypertension. *Acta Obstet Gynecol Scand* 2007; **86**: 788–792.
34 Pien GW, Fife D, Pack AI, Nkwuo JE, Schwab RJ. Changes in symptoms of sleep-disordered breathing during pregnancy. *Sleep* 2005; **28**: 1299–1305.
35 Ursavas A, Karadag M, Nalci N, Ercan I, Gozu RO. Self-reported snoring, maternal obesity and neck circumference as risk factors for pregnancy-induced hypertension and preeclampsia. *Respiration* 2008; **76**: 33–39.
36 Edwards N, Blyton DM, Hennessy A, Sullivan CE. Severity of sleep-disordered breathing improves following parturition. *Sleep* 2005; **28**: 737–741.
37 Manconi M, Govoni V, De Vito A *et al.* Restless legs syndrome and pregnancy. *Neurology* 2004; **63**: 1065–1069.
38 Tunç T, Karadag YS, Dogulu F, Inan LE. Predisposing factors of restless legs syndrome in pregnancy. *Mov Disord* 2007; **22**: 627–631.
39 Dzaja A, Wehrle R, Lancel M, Pollmacher T. Elevated estradiol plasma levels in women with restless legs during pregnancy. *Sleep* 2009; **32**: 169–174.
40 Churchward T, O'Donoghue F, Rochford D, Pierce R, Barnes M, Higgins S. Diagnostic accuracy and cost effectiveness of home based PSG in OSA (Abstract). *Sleep Biol Rhythms* 2006; **4** (s1): A11.
41 Mykytyn I, Sajkov D, Neill A, McEvoy R. Portable computerized polysomnography in attended and unattended settings. *Chest* 1999; **115**: 114–122.
42 Lovibond SH, Lovibond PF. *Manual for the Depression Anxiety Stress Scales*, 2nd edn. Sydney: Psychology Foundation, 1995.
43 Henry J, Crawford J. The 21-item version of the Depression Anxiety Stress Scales (DASS–21): normative data and psychometric evaluation in a large non-clinical sample. *Br J Clin Psychol* 2005; **44**: 227–239.
44 Antony M, Bieling P, Cox B, Enns M, Swinson R. Psychometric properties of the 42-item and 21-item versions of the Depression Anxiety Stress Scales (DASS) in clinical groups and a community sample. *Psychol Assess* 1998; **10**: 176–181.
45 Crawford J, Henry J. The Depression Anxiety Stress Scales (DASS): normative data and latent structure in a large non-clinical sample. *Br J Clin Psychol* 2003; **42**: 111–131.
46 Cohen J. *Statistical Power Analysis for the Behavioral Sciences*, 2nd edn. Mahwah, NJ: Lawrence Erlbaum Associates, 1988.
47 Bonnet MH. Acute sleep deprivation. In: Kryger M, Roth T, Dement WC, eds. *Principles and Practice of Sleep Medicine*, 4th edn. Philadelphia, Pennsylvania: W.B. Saunders Company, 2005; 51–66.
48 Montplaisir J, Lorrain J, Denesle R, Petit D. Sleep in menopause: differential effects of two forms of hormone replacement therapy. *Menopause* 2001; **8**: 10–16.
49 Driver HS, McLean H, Kumar DV, Farr N, Day AG, Fitzpatrick MF. The influence of the menstrual cycle on upper airway resistance and breathing during sleep. *Sleep* 2005; **28**: 449–456.
50 Manconi M, Govoni V, De Vito A *et al.* Pregnancy as a risk factor for restless legs syndrome. *Sleep Med* 2004; **5**: 305–308.
51 Waters MA, Lee KA. Differences between primigravidae and multigravidae mothers in sleep disturbances, fatigue, and functional status. *J Nurse Midwifery* 1996; **41**: 364–367.
52 Signal TL, Gander PH, Sangalli MR, Travier N, Firestone RT, Tuohy JF. Sleep duration and quality in healthy nulliparous and multiparous women across pregnancy and post-partum. *Aust N Z J Obstet Gynaecol* 2007; **47**: 16–22.
53 Bonnet MH, Arand DL. Clinical effects of sleep fragmentation versus sleep deprivation. *Sleep Med Rev* 2003; **7**: 297–310.
54 Carskadon MA, Brown ED, Dement WC. Sleep fragmentation in the elderly: relationship to daytime sleep tendency. *Neurobiol Aging* 1982; **3**: 321–327.
55 Martin SE, Engleman HM, Kingshott RN, Douglas NJ. Microarousals in patients with sleep apnoea/hypopnoea syndrome. *J Sleep Res* 1997; **6**: 276–280.
56 Davies RJ, Belt PJ, Roberts SJ, Ali NJ, Stradling JR. Arterial blood pressure responses to graded transient arousal from sleep in normal humans. *J Appl Physiol* 1993; **74**: 1123–1130.
57 Morrell MJ, Finn L, Kim H, Peppard PE, Badr MS, Young T. Sleep fragmentation, awake blood pressure, and sleep-disordered breathing in a population-based study. *Am J Respir Crit Care Med* 2000; **162**: 2091–2096.
58 Nikkola E, Ekblad U, Ekholm E, Mikola H, Polo O. Sleep in multiple pregnancy: breathing patterns, oxygenation, and periodic leg movements. *Am J Obstet Gynecol* 1996; **174**: 1622–1625.
59 Van Dongen HP, Maislin G, Mullington JM, Dinges DF. The cumulative cost of additional wakefulness: dose-response effects on neurobehavioral functions and sleep physiology from chronic sleep restriction and total sleep deprivation. *Sleep* 2003; **26**: 117–126.
60 Lee KA, Gay CL. Sleep in late pregnancy predicts length of labor and type of delivery. *Am J Obstet Gynecol* 2004; **191**: 2041–2046.