UNIVERSITY OF CALIFORNIA, SAN DIEGO

SAN DIEGO STATE UNIVERSITY

Cognitive Performance of Pregnant and Postpartum Women With and Without Major Depression

A dissertation submitted in partial satisfaction of the requirements of the degree Doctor of Philosophy

in

Clinical Psychology

by

Sara Nowakowski

Committee in Charge:

University of California, San Diego

Professor Barbara L. Parry, Chair
Professor Sonia Ancoli-Israel
Professor Sean P.A. Drummond
Professor Charles J. Meliska

San Diego State University

Professor Claire Murphy
Professor V. Robin Weersing

2010

The Dissertation of Sara Nowakowski is approved, and it is acceptable in quality and form for publication on microfilm and electronically:

_____

_____

_____

_____

_____

_____,

Chair

University of California, San Diego

San Diego State University

2010

DEDICATION

I would like to dedicate this manuscript to my husband, John. Without your love and support I would have never made it through the past five years of graduate school. From moving cross county with me several times, attending boring professional functions, to proofing so many of my papers and manuscripts (including this one), you truly deserve an honorary degree! Thank you for everything. You mean more to me than words can express.

TABLE OF CONTENTS

LIST OF TABLES

LIST OF FIGURES

ACKNOWLEDGEMENTS

I would like to acknowledge Dr. Barbara L. Parry her support throughout my graduate training and as chair of my dissertation committee. She has provided invaluable guidance from assisting with methodological design, grant preparation, to the many iterations of this manuscript.

I would also like to acknowledge the rest of my dissertation committee (Drs. Sonia Ancoli Israel, Sean P.A. Drummond, Claire Murphy, V. Robin Weersing, and Charles J. Meliska) and express my extreme gratitude for all of their support and guidance throughout this process.

I would also like to give a special thank you to the members of Dr. Parry's laboratory, Diane Sorenson, Ana Lopez, and L. Fernando Martinez. Their support has helped me in an immeasurable way.

Finally, I would like to acknowledge Kelly Cavanaugh and Emerson Posadas, research assistants who helped with recruitment, data collection and entry.

Support for this project was provided by National Institute of Health grant R01 MH070788-01A2 (B. Parry) and UCSD Block Grant Dissertation Research Award (S. Nowakowski).

CURRICULUM VITAE

UNIVERSITY EDUCATION

2009-Present Clinical Psychology Intern
Alpert Medical School of Brown University, Providence, Rhode Island
Specialty Track: Behavioral Medicine
Advisors: Donn Posner, Ph.D. and Mary A. Carskadon, Ph.D.

2010 Doctorate of Philosophy, Clinical Psychology
San Diego State University/ University of California, San Diego
Joint Doctoral Program in Clinical Psychology
Specialty Track: Experimental Psychopathology
Dissertation: Cognitive performance of pregnant and postpartum women with and without major depression
Dissertation Chair: Barbara L. Parry, M.D.
Anticipated date of graduation: June 2010

2006 Master of Science, Clinical Psychology
San Diego State University/ University of California, San Diego
Joint Doctoral Program in Clinical Psychology
Thesis: Neuropsychological performance of menopausal women with and without major depression
Advisor: Barbara L. Parry, M.D.

2002 Bachelor of Science, Psychology, Summa Cum Laude
State University of New York at Brockport College

HONORS AND AWARDS

2007 UCSD Dissertation Research Award; $5,000
2007 SDSU Dorathe Frick Memorial Award – Student of the Year
2007, 09 Sleep Research Society Abstract Excellence Award
2006 Phi Kappa Phi National Honor Society (top 10% of all majors)
2002, 03, 05 Sleep Research Society Meritorious Abstract Award
2001 Alpha Chi National Honor Society (top 10% of all majors)
2001 National Scholars Honor Society
2001 SUNY Brockport Psychology Department Scholar Award
2000 New York Scholarship for Academic Achievement
2000 Psi Chi National Honor Society (top 10% of psychology majors)

RESEARCH EXPERIENCE

2009-Present Brown University, EP Bradley Sleep and Chronobiology Research Laboratory

Psychology Intern Research Assistant
Advisor: Mary A. Carskadon, Ph.D.
Responsibilities include assisting with collection and management of data, data analysis and manuscript preparation for a prospective study examining sleep, mood, and genetic vulnerability in a sample of adolescents transitioning to college.

2004-09 University of California, San Diego Chronobiology and Mood Disorders Laboratory
Graduate Research Associate
Academic Advisor: Barbara L. Parry, M.D.
Responsibilities include conducting intake and structured clinical interviews (SCIDs), mood assessments using Hamilton Rating Scale for Depression (HRSD), neuropsychological assessments, managing and analyzing data, supervising undergraduate research assistants, ad hoc co-reviews, and grant and manuscript preparation.

2002-04 University of Rochester Sleep and Neurophysiology Laboratory
Clinical Research and Project Coordinator
Supervisor: Michael L. Perlis, Ph.D.
Responsibilities include telephone screening, clinical intake interviews, assisting with grant and manuscript preparation, ad hoc co-reviews, phlebotomy, neuropsychological evaluations, coordinating clinical trials and NIH sponsored projects to ensure integrity of protocols and procedures, training clinical technicians, personnel issues related to students.

2001-02 University of Rochester Sleep and Neurophysiology Laboratory
Clinical Technologist specializing in polysomnography
Supervisor: Michael L. Perlis, Ph.D.
Responsibilities include electrode placement, biocalibrations, electroencephalograph sleep scoring, phlebotomy, manuscript reviews, literature searches, maintaining data base and laboratory supplies.

2001-02 State University of New York at Brockport College
Research Assistant
Supervisor: Susan Shonk, Ph.D.
Responsibilities include coding video recordings of care giver and child for attachment and emotion self-regulation, article reviews, operating audio/video equipment for purposes of recording data, setting up developmental laboratory, recruitment.

2000 State University of New York at Brockport College
Research Assistant
Supervisor: David Abwender, Ph.D.

Responsibilities include neuropsychological test administration and scoring, literature reviews, and data entry using SPSS.

CLINICAL EXPERIENCE

2009 Alpert Medical School at Brown University
The Miriam Hospital, Rhode Island Hospital, Hasbro Children's Hospital, Butler Hospital
Predoctoral Intern, Psychiatry and Behavioral Medicine
Supervisors: Ron Thebarge, Ph.D., Kevin McKay, Ph.D., Lucy Rathier, Ph.D., John Wincze, Ph.D., Jeff Burock, M.D., Donn Posner, Ph.D., Julie Boergers, Ph.D., Judy Owens, M.D., and Richard Brown, Ph.D.
Responsibilities include bariatric surgery evaluations, weight and lifestyle evaluations, leading weight management groups, providing individual therapy in behavioral medicine, psychiatry consultation/liaison for medical in-patients, smoking cessation therapy, men's health assessments, behavioral assessment and follow-up in primary care, anxiety, adult and pediatric sleep disorders, substance abuse.

2008-09 University of California, San Diego and Veterans Affairs San Diego Healthcare System
J. Christian Gillin Sleep and Chronobiology Laboratory
Psychometrist
Supervisor: Sonia Ancoli-Israel, Ph.D. and Barton Palmer, Ph.D.
Responsibilities include neuropsychological test administration, scoring, interpretation, and report writing in research subjects with breast cancer undergoing chemotherapy and Parkinson's
Disease.

2007-08 University of California, San Diego Sleep Medicine Center
and Veterans Affairs San Diego Healthcare System Psychiatry Sleep Disorders Clinic
Supervisor: Sonia Ancoli-Israel, Ph.D. and José Loredo, M.D.
Orientation: Multi-modal behavioral and medical approaches to various sleep disorders.
Responsibilities include intake assessments, diagnosing sleep disorders, developing and implementing treatment plans, report writing, and presenting cases to a multidisciplinary team. Patients, ranging from adolescence to elderly adults, were seen in an outpatient VA and university-based setting.

2006-07 Veterans Affairs San Diego Healthcare System
Cognitive Behavioral Interventions Program
Supervisors: Sean P.A. Drummond, Ph.D. and John McQuaid, Ph.D.

Orientation: Cognitive Behavioral Therapy (CBT), CBT-Insomnia, and Imagery Rehearsal Therapy for nightmares
Responsibilities include intake assessments and structured clinic interviews (SCIDs), developing and implementing treatment plans, report writing, presenting cases to multidisciplinary team, co-leading CBT group for veterans with bipolar disorder, and individual psychotherapy for veterans presenting primarily with mood disorders (depression, bipolar, and psychoses related to mood) and sleep disturbances (insomnia and nightmare disorder) with or without medical or psychiatric co-morbidities.

2005-06 San Diego State University Psychology Community Clinic
Supervisors: Rick Schulte, Ph.D. & Brenda Johnson, Ph.D.
Orientation: Cognitive Behavioral Therapy and Interpersonal Therapy
Responsibilities include intake assessments and structured clinic interviews (SCIDs), developing and implementing treatment plans, report writing, and individual and group psychotherapy with outpatients seeking treatment at a university-based community psychology clinic. Patients (aged 18-68 years) presented with various psychological difficulties, including depression, bipolar, anxiety, borderline personality disorders, substance abuse, self-injurious behaviors, and acculturative stress.

2004-2009 University of California, San Diego
Chronobiology and Mood Disorders Laboratory
Supervisor: Barbara L. Parry, M.D.
Responsibilities include psychodiagnositic and neuropsychological assessment, structured clinical interviews (SCIDs) to diagnose Axis I disorders in NIH-funded research studies examining chronobiology of mood disorders associated with the reproductive cycle – premenstrual dysphoric disorder, pregnancy-, postpartum-, and menopausal-related depression.

TEACHING EXPERIENCE

2009 University of California, San Diego
Guest Lecturer – Sleep, Sleep Disorders and Biological Rhythms
School of Medicine (Medical students)

2008 San Diego State University
Instructor
Statistical Methods in Psychology (Undergraduate level)

2008 University of California, San Diego
Guest Lecturer – Choosing a career path

Undergraduate seminar

2007-2008 San Diego State University
Teaching Assistant
Cognitive Assessment (Doctoral level)

2006-2007 San Diego State University
Guest Lecturer – Sleep and Sleep Disorders
Abnormal Psychology (Undergraduate level)

2006 San Diego State University
Teaching Assistant
Interventions (Doctoral level)

2005-2007 San Diego State University
Guest Lecturer – Successfully applying to graduate school
Research Orientation Seminar (Master's level)

EDITORIAL SERVICES

Ad Hoc Co-Reviews

2001	Sleep
2001, 02, 05	Journal of Health Psychology
2002, 03	Behavioral Sleep Medicine
2003	Archives of General Psychiatry
2003, 06	Journal of Affective Disorders
2005	Psychoneuroendocrinology
2006, 08	Journal of American Medical Association (JAMA)
2006	Journal of Fertility and Sterility
2007	Journal of Women's Health
2007	The Lancet
2007, 08, 09	Journal of Sleep Research
2008	Chronobiology International
2009	American Journal of Physiology

PROFESSIONAL SERVICE

2009	Brown University Training Committee
2009	Sleep Research Society Trainee Member-At-Large, Trainee Education and Advisory Committee
2008	Sleep Research Society Trainee Member-At-Large Elect, Trainee Educ and Advisory Committee
2007	Sleep Research Society Trainee Subcommittee to Trainee Education and Advisory Committee

2006-08	Sleep Research Society Communications Committee, Trainee Representative
2007	APPIC conference, San Diego - Student Volunteer
2007	SDSU/UCSD Joint Doctoral Program Selection Committee
2005-08	SDSU/UCSD JDP Interview & Host Graduate Student Applicants
2005	SDSU Undergraduate Research Symposium - Judge

PROFESSIONAL SOCIETY MEMBERSHIPS

2009-Present	Association for Behavioral and Cognitive Therapies – Student Affiliate
2001-Present	Sleep Research Society – Student Affiliate
1999-Present	American Psychological Association – Student Affiliate

PUBLICATIONS

Manuscripts:

1. **Nowakowski, S.**, Meliska, C.J., & Parry, B.L. (In sub). Neuropsychological performance in menopausal women with and without major depression. *Menopause.*

2. **Nowakowski, S.**, Meliska, C.J., Martinez, L.F., & Parry, B.L. (2009). Sleep and Menopause. *Current Neurology and Neuroscience Reports, 9(2), 165-172.*

3. Parry, B.L., Meliska, C.J., Sorenson, D.L., Lopez, A.M., Martinez, L.F., **Nowakowski, S.**, Hauger, R.L., Elliot, J.A., & Kripke, D.F. (2008). Plasma Melatonin Circadian Rhythms During Pregnancy and Postpartum in Depressed Women and Women With Personal or Family Histories of Depression. *American Journal of Psychiatry, 165(12),* 1551-8.

4. **Nowakowski, S.**, Meliska, C.J., & Parry, B.L. (2008). Menopause and Sleep Disorders. *The Female Patient, 33(9),* 30-32.

5. Parry, B.L., Meliska, C.J., Sorenson, D.L., Lopez, A.M., Martinez, L.F., **Nowakowski, S.**, Hauger, R.L.,& Elliot, J.A. (2008). Increased Melatonin and Delayed Offset in Menopausal Depression: Role of Years Past Menopause, FSH, Sleep End Time and Body Mass Index, *Journal of Clinical Endocrinology and Metabolism, 93(1),* 54-60.

6. Orff, H.J., Drummond, S.P., **Nowakowski, S.**, & Perlis, M.L. (2007) Discrepancy between subjective symptomology and objective neuropsychological performance in insomnia, *Sleep, 30(9),*
1205-1211.

7. Perlis, M.L., Orff, H.J., Smith, M.T., Enright, T., **Nowakowski, S.**, Jungquist, C.R., & Plotkin, K. (2004). The effects of modafinil and cognitive behavior

therapy on sleep continuity in patients with primary insomnia. *Sleep*, 27(4), 715-725.

8. Perlis, M.L., Smith, M.T., Cacialli, D.O., **Nowakowski, S.**, & Orff, H.O. (2003). On the comparability of pharmacotherapy and behavior therapy for chronic insomnia: Commentary and implications. *Journal of Psychosomatic Research, 54(*1), 51-59.

Book Chapters:

1. **Nowakowski, S**. & Ancoli-Israel, S. (In press) Acute and Emergent Sleep Events in Older Adults. In Acute and Emergent Events in Sleep Disorders, Oxford University Press.

2. Parry, B.L., **Nowakowski, S.**, Martinez, L.F., & Berga, S.L. (2009). Premenstrual Dysphoric Disorder. In Donald W. Pfaff, Arthur P. Arnold, Anne M. Etgen, Susan E. Fahrbach, and Robert T. Rubin, editors. Hormones, Brain, and Behavior, 2nd edition, Vol 5. pp. 2945-2971. San Diego: Academic Press.

3. Parry, B.L., Meliska, C.J., Martinez, L.F., Lopez, A.M., Sorenson, D.L., & **Nowakowski, S.** (2008). Premenstrual Dysphoric Disorder and Postpartum Major Depression: Chronobiology. In Larry R. Squire, Editor-in-Chief, Encyclopedia of Neuroscience, Academic Press, Oxford.

4. **Nowakowski, S.**, Haynes, T., & Parry, B.L. (2007). Premenstrual Dysphoric Disorder. In The Encyclopedia of Stress-2nd edition , Volume 3, pp.173-179. Elsevier.

5. Parry, B.L., Meliska, C.J., Martinez, L.F., Lopez, A.M., **Nowakowski, S.**, & Loving, R.L. (2007). Melatonin Circadian Rhythms in Women with Depression: Relationships to the Reproductive Cycle. In S.R. Pandi-Perumal, D.P. Cadinali (Eds.). Melatonin: From Molecules to Therapy. New York: Nova Publishers.

6. Perlis, M.L., Smith, M.T., Jungquist, C.R., **Nowakowski, S.**, Orff H.J., & Soeffing, J.P. (2004). The definition of Insomnia. The Clinical Handbook of Insomnia. Ed. Hrayr Attarian. Humana Press.

7. Smith, L.J., **Nowakowski, S**, Soeffing, J.P., Orff, H.J., & Perlis, M.L. (2002). The Measurement of Sleep. In Perlis M.L. & Lichstein K. Eds. Treating Sleep Disorders: Principles and Practice of Behavioral Sleep Medicine.

8. Smith, M.T., Smith, L.J.**, Nowakowski, S.**, & Perlis M.L. (2002). Primary Insomnia: Diagnostic Issues, Treatment, and Future Directions. In Perlis ML & Lichstein K, eds. Treating Sleep Disorders: Principles and Practice of Behavioral Sleep Medicine.

Published Abstracts:

1. **Nowakowski, S.,** Bond, T.L., Raffray, T., Sharkey, K.M. , & Carskadon, M.A. (In sub). Subjective Sleep and Daytime Functioning in Older Adolescents: Preliminary Results from an Online Questionnaire, *Sleep.*

2. **Nowakowski, S.**, Meliska, C.J., & Parry, B.L. (2009). Ambient Daylight Influences Polysomnographic Sleep in Healthy and Depressed Menopausal Women. *Sleep, 32 (Supp),* A349. (*) (#)

3. **Nowakowski, S.**, Meliska, C.J., & Parry, B.L. (2009). Ambient Daylight Influences Polysomnographic Sleep in Healthy and Depressed Pregnant and Postpartum Women. *Sleep, 32 (Supp),* A349-50. (*) (#)

4. Parry, B.L., Meliska, C.J., Sorenson, D.L., Lopez, A.M., Martinez, L.F., **Nowakowski, S**. (2009). Plasma Melatonin Circadian Rhythms in Pregnancy and Postpartum Depression. *Archives of Women's Mental Health, 12(Supp1),* S1-S40.

5. Parry, B.L., Meliska, C.J., Sorenson, D.L., Lopez, A.M., Martinez, L.F., **Nowakowski, S**., Elliot, J.A., Hauger, R.L., Kripke, D.F. (2008). Plasma Melatonin Circadian Rhythms in Pregnancy and Postpartum Depression. *Marce Society International Biennial Scientific Meeting.*

6. Parry, B.L., Meliska, C.J., Sorenson, D.L., Lopez, A.M., Martinez, L.F., **Nowakowski, S**., Hauger, R.L., Elliot, J.A., Kripke, D.F. (2007). Sleep and Biological Rhythms in Depressive Disorders During the Menstrual Cycle, Pregnancy, Postpartum and Menopause. *Archives of Women's Mental Health.*

7. **Nowakowski, S**., Meliska, C.J., & Parry, B.L. (2007). Effects of estrogen therapy on sleep in healthy and depressed menopausal women. *Sleep, 30 (Supp),* A333-4. (*)

8. Parry, B.L., Meliska, C., **Nowakowski, S.**, Lopez, A., Martinez, F., Sorenson, D., Lien, M.L. (2007). Sleep in postpartum depression. *Sleep and Biological Rhythms, 5,* 184.

9. Parry, B.L., Meliska, C.J., Lopez, A.M., Martinez, L.F., Sorenson, D.L., Loving, R.L., & **Nowakowski, S**. (2007). Biological dimensions – hormonal and sleep quality predictors of postpartum depression. *Archives of Women's Mental Health, 10,* XXV.

10. Parry, B.L., Meliska, C.J., Lopez, A.M., Martinez, L.F., Sorenson, D.L., Loving, R.L., & **Nowakowski, S**. (2007). Neuroendocrine effects of wake therapy in

pregnant and postpartum depression. *Archives of Women's Mental Health, 10,* XII.

11. **Nowakowski, S.,** Meliska, C.J., & Parry B.L. (2006). Associations between mood and melatonin-sleep phase angles in healthy and depressed pregnant and postpartum women. *Sleep, 28(*Supp), A323. (#)

12. Orff, H.J., Drummond, S.P., **Nowakowski, S.,** & Perlis, M.L. (2006). Subjective and objective measures of sleep and daytime performance in patients with primary insomnia compared to normal controls. *Sleep, 28(*Supp), A264.

13. **Nowakowski, S.,** Meliska, C.J., & Parry, B.L. (2005). Associations between cortisol and sleep variables in healthy and depressed postpartum women combined. *Sleep, 27*(Supp), A317. (*)

14. **Nowakowski, S.,** Soeffing, J.P., Ilniczky, N.K., Orff, H.J., Soeffing, J.P., Smith, M.T., & Perlis, M.L. (2003) . Neuropsychological functioning of patients with primary insomnia as compared to good sleeper controls. *Sleep, 26*(Supp), A302. (*)

15. Sandoval, T., **Nowakowski, S.**, Soeffing, J.P., Christensen, A., Aloia, M., Smith, L.J., & Perlis, M.L. (2003). Gender effects on treatment outcome in patients with primary insomnia. *Sleep,* 26(Supp), A312. (#)

16. Smith, L.J., Lyness, J., **Nowakowski, S.**, Soeffing, J.P., Orff, H.J., Giles, D.E., & Perlis M.L. (2003). Insomnia as a risk factor for depression in the elderly. *Sleep,* 26(Supp), A290.

17. Perlis, M.L., Orff, H.J., Enright, T., Smith, M.T., **Nowakowski, S.**, Plotkin, K.E., & Jungquist, C. (2003). Effect of modafinil on sleep continuity, daytime sleepiness, and treatment adherence in subjects with primary insomnia. *Sleep,* 26(Supp), A300.

18. Perlis, M.L., Ryan, N., Orff, H.J., Soeffing, J.P., **Nowakowski, S.**, Plotkin, K., & Jungquist, C. (2003). Do patients with primary insomnia have a preferred medication use schedule? *Sleep,* 26(Supp), A302.

19. Ilniczky, N.K., Orff, H.J., Soeffing, J.P., **Nowakowski, S.**, Enright, T., Smith, M.T., & Perlis, M.L. (2002). Neuropsychological functioning of patients with primary insomnia. *Sleep,* 25(Supp), A477. (#)

20. Orff, H.J., Heverly, J., **Nowakowski, S.**, Cacialli, D.O., & Perlis, M.L. (2002). Is hypothyroidism a potential risk factor for development of insomnia? *Sleep,* 25(Supp), A480.

21. Smith, L.J., Cacialli, D.O., Ilniczky, N.K., Pennington, J.Y., **Nowakowski, S.**, & Perlis, M.L. (2002). Autobiographic memory and its association with REM sleep in patients with MDD and good sleeper controls. *Sleep,* 25(Supp), A388.

22. Soeffing, J.P., Cacialli, D.O., **Nowakowski, S.**, Pennington, J.Y., Smith, M.T., & Perlis, M.L. (2002). Determining sleep onset: Is there a definition that will minimize subjective vs. objective discrepancies? *Sleep,* 25(Supp), A482.

23. Heverly, J., Smith, L.J., Ilniczky, N.K., **Nowakowski, S.** Pennington, J.Y., Soeffing, J.P., Smith, M.T. & Perlis, M.L. (2002). Latency and rate of discharge of slow wave sleep in patients with primary insomnia and good sleeper controls. *Sleep,* 25(Supp), A481. (#)

(*) Oral Conference Presentation (n = 5); (#) Poster-only Presentation (n = 6)

ABSTRACT OF THE DISSERTATION

Cognitive Performance of Pregnant and Postpartum Women

With and Without Major Depression

by

Sara Nowakowski

Doctor of Philosophy in Clinical Psychology

University of California, San Diego, 2010

San Diego State University, 2010

Professor Barbara L. Parry, Chair

Keenan and colleagues (1998) have demonstrated that episodic memory is diminished during pregnancy and returns to baseline in the postpartum period. Given that memory deficits may occur in major depression, possible memory deficits during pregnancy could be exacerbated by major depression. The present study examined

memory performance in 37 pregnant women, 14 of whom met clinical criteria for a Major Depressive Episode (MDE) as defined in the Diagnostic and Statistical Manual 4th Edition (*DSM-IV*), and 23 normal control (NC) pregnant women who had no current or prior history of depression. Additionally, postpartum groups consisted of 21 postpartum women, 11 of whom met clinical criteria for a MDE, and 10 NC postpartum women. The study utilized a 2 x 2 Multivariate Analysis of Variance design to compare memory performance and sleep of pregnant and postpartum women with and without major depression. The study demonstrated that pregnancy and major depression were both associated with poorer performance in a task involving verbal learning and memory. Specifically, on the California Verbal Learning Test (CVLT), pregnant women learned significantly fewer words from trials one through five; recalled significantly fewer words on trial one, short delay free and cued recall, and long delay free and cued recall; and utilized a semantic clustering strategy significantly fewer than postpartum women. Depressed patients learned significantly fewer words from trials one through five, recalled significantly fewer words on CVLT long delay free recall, and utilized a semantic clustering strategy significantly fewer than NC women. No alterations in outcomes of the above analyses were found when age, education, weeks pregnant/postpartum, or circadian preference were applied as covariates. The present results are consistent with previous investigations of memory functioning of major depressive disorder and healthy pregnant and postpartum women. That is, pregnant and depressed women exhited poorer performance in tasks involving verbal learning and memory compared with postpartum and NC women.

INTRODUCTION

In the early 20th century, Bleuler introduced the notion of "endocrine depression," postulating a relationship between the endocrine system and psychiatric diseases. In the late 1970's higher rates of depression were noted in women as compared with men (Weissman & Klerman, 1977) and these results have since been replicated (Kessler, McGonagle, Swartz, Blazer, & Nelson, 1993; Weissman et al., 1996). According to the Women's Health Organization and World's Bank Global Burden of Disease, depression is the most common disease worldwide in women (Murray & Lopez, 1996). Weissman and colleagues (1993) found that women are particularly vulnerable to depression during times of reproductive hormonal change.

Perinatal Pregnancy

Pregnancy is a period of great reproductive hormone fluctuation (Bloch, 2003; Halbreich, 2000; Parry et al., 2003; Zonana, 2005). Historically, pregnancy was thought to safeguard against mental illness. However, there is increasing evidence to challenge this notion, and to suggest that depressed mood is common during pregnancy (Evans, Heron, Francomb, Oke, & Golding, 2001; Johanson, Chapman, Murray, Johnson, & Cox, 2000), with estimates indicating 10-20% of women experience depression during pregnancy (Gotlib, Whiffen, Mount, Milne, & Cordy, 1989; Marcus, 2009; Marcus, Barry, Flynn, Tandon, & Greden, 2001). Gotlib and colleagues (1989) were among the first to point out a possible continuum of depression through pregnancy into the postpartum period. Despite their observation, research during the past 25 years has focused on postpartum depression, rendering

pregnancy-related depression a secondary issue. While Diagnostic and Statistical Manual – Fourth Edition (*DSM-IV; American Psychiatric Association*, 1994) recognizes postpartum onset mood disorders, it does not make reference to depression during pregnancy. The present study characterizes pregnancy-related depression, focusing on memory functioning that could potentially impact a pregnant woman's ability to care for herself and her fetus.

Postpartum Depression

Negative mood and mild-to-moderate depression are common in the postpartum period (Cohen & Altshuler, 1997; Dalton, 1996; Diket & Nolan, 1997; Kendell, Chalmers, & Platz, 1987; Nott, Franklin, Armitage, & Gelder, 1976; O'Hara, 1986). Under a mandate from Congress, the NIH Office of Research has targeted postpartum depression as an area for increased research on women's health. It is also a priority area for World Health Organization and American Psychiatric Association (APA). The incidence of postpartum depression has been reported from 8% to 23% (Cooper & Murray, 1997; O'Hara, Neunaber, & Zekoski, 1984). Inadequate treatment of depression may have severe consequences for the mother, her child, the family and society (Parry, 2003). Untreated depression puts women at risk for the sequelae of increased severity of affective illness (i.e., the depression may become chronic, recurrent, and/or refractory; Cooper & Murray, 1997). Evidence is now accruing that postpartum depression also can adversely affect the neurocognitive and emotional development of children whose mothers were depressed after giving birth (Beck, 1998; Goodman & Gotlib, 1999; Murray, 1992; Murray et al., 1999). Exposure to mothers suffering from postpartum depression, in the early months after birth may have lingering effects on children's

psychological adjustment and intellectual development (Goodman & Gotlib, 1999; Halligan, Murray, Martins, & Cooper, 2007; Murray, Cooper, & Hipwell, 2003; Murray, Halligan, Adams, Patterson, & Goodyer, 2006; Murray, Woolgar, Cooper, & Hipwell, 2001; Weissman et al., 2006). In addition, it has been demonstrated that persons with MDD and maternal depression have significantly higher levels of disability than those with any of the disorders, causing a greater public health burden (Gureje, Ademola, & Olley, 2008), and greater workplace costs (Kessler et al., 1999); Webb et al., 2008).

Postpartum depression is defined as a moderate-to-severe mood disorder comparable to a major depressive episode in the *DSM-IV* (*American Psychiatric Association. Diagnostic and Statistical Manual of Mental Disorders*, 1994). The criteria for major depression include (a) depressed mood or diminished interest or pleasure and (b) at least four of the following symptoms: weight loss/gain or appetite increase/decrease, insomnia/hypersomnia, psychomotor agitation/retardation, fatigue, neurocognitive impairment, inappropriate guilt/feelings of worthlessness, and suicidal ideation. The criteria specify including only affective episodes whose onset is within four weeks postpartum, which is in contrast to the criteria specified by the Marcé Society, an international organization for the study of mental illness related to childbearing that includes episodes occurring within a year postpartum. Most epidemiologic studies have not used the strict criteria of onset within 4 weeks, as stipulated by the *DSM-IV* (*American Psychiatric Association*, 1994). The inconsistencies in the time frame used for diagnosing postpartum depression make the literature difficult to interpret. Several published reports suggest the highest risk for onset of postpartum depression is during 3-4 months postpartum (Cooper & Murray, 1997; O'Hara et al., 1984). Postpartum

depression is often characterized as an irritable, severely depressed mood and the most common symptoms reported by new mothers include crying spells, insomnia, agitation, irritability, and confusion (Sugawara, Sakamoto, Kitamura, Toda, & Shima, 1999). In *DSM-II* (*American Psychiatric Association*, 1968) postpartum depression was noted as a separate diagnostic category. Some researchers hold the position that postpartum depression has a biological basis, which distinguishes it from Major Depressive Disorder (MDD; Steiner, 1990).

Neurocognitive Functioning in Major Depression

Diminished ability to think or concentrate and psychomotor slowing are identified as symptoms of major depressive disorder in the *DSM-IV* (*American Psychiatric Association*, 1994). Women with major depression often report a subjective sense of altered neurocognitive functioning; decreased concentration, motor inefficiency, forgetfulness, and indecisiveness are among the most frequent complaints. MDD is associated with objective neurocognitive deficits in attention (Mialet, Pope, & Yurgelun-Todd, 1996), psychomotor speed (Sobin & Sackeim, 1997), memory (Burt, Zembar, & Niederehe, 1995; Cohen, Weingartner, Smallberg, Pickar, & Murphy, 1982; Golinkoff & Sweeney, 1989; Ilsley, Moffoot, & O'Carroll, 1995), sustained attention (Cornblatt, Lenzenweger, & Erlenmeyer-Kimling, 1989) and executive functioning (Merriam, Thase, Haas, Keshavan, & Sweeney, 1999; Sweeney, Strojwas, Mann, & Thase, 1998). Cassens, Wolfe, and Zola (1990) reviewed literature from 1975 to 1990 and found a scattered pattern of dysfunction with impairments in memory, visuo-spatial and visuo-motor skills in patients with major depression. A more recent and stringent meta-analysis conducted by Veiel (1997) documents a global-diffuse impairment of executive functioning.

Neurocognitive Functioning in Pregnancy

Interest in the effects of a variety of reproductive states on brain functioning has dramatically increased in recent years. Several anecdotal reports can be found in the literature specifying “maternal amnesic syndrome” or “benign encephalopathy of pregnancy” (Baildam, 1991; Welch, 1991). Similar neurocognitive difficulties are also reported in a number of more systematic studies that have examined the subjective experience of neurocognitive change during and after pregnancy (Brindle, Brown, Brown, Griffith, & Turner, 1991; Casey, Huntsdale, Angus, & Janes, 1999; Crawley, Dennison, & Carter, 2003; Janes, Casey, Huntsdale, & Angus, 1999; Jarrahi-Zadeh, Kane, Van de Castlf, Lachenbruch, & Ewing, 1969; McDowall & Moriarty, 2000; Parsons & Redman, 1991; Poser, Kassirer, & Peyser, 1986; Sharp, Brindle, Brown, & Turner, 1993). Forgetfulness, reading difficulties, confusion, absent-mindedness, disorientation, distractibility, poor concentration, cognitive slowing, and word finding difficulties are among the subjective complaints, with poor memory being the greatest complaint across studies. In addition to these neurocognitive changes, Parsons and Redman (1991) found women reported poor co-ordination resulting in significantly more accidents around the home (dropping/spilling things, minor burns, etc.) during their pregnancies. With few exceptions, studies that examined subjective reports of neurocognitive change during pregnancy suggest a substantial proportion of women experience some degree of neurocognitive disturbance with estimates ranging from 50-80%.

Despite subjective reports, there are no systematic data on objective measures of neurocognitive functioning during pregnancy. The majority of studies report decreased

performance on neurocognitive tasks during pregnancy (Brindle et al., 1991; Buckwater, 2001; de Groot, Hornstra, Roozendaal, & Jolles, 2003; de Groot, Vuurman, Hornstra, & Jolles, 2006; Eidelman, Hoffmann, & Kaitz, 1993; Sharp et al., 1993), but some have demonstrated no effect of pregnancy (Casey et al., 1999; Crawley et al., 2003; Janes et al., 1999; McDowall & Moriarty, 2000; Morris, Toms, Easthope, & Biddulph, 1998) or even positive effects on some neurocognitive functions (Christensen, 1999; Schneider, 1989). Methodological limitations, such as limited measures of neurocognitive domains and lack of standardized measures hinder the interpretation and integration of findings. Discrepant findings in neurocognitive performance may also be due to differences in stage of pregnancy, subjects investigated, mood, hormones, and other variables.

Neurocognitive Functioning in the Postpartum Period

Neurocognitive impairments may extend beyond pregnancy into the postpartum period (Baildam, 1991; Jarrahi-Zadeh et al., 1969; Welch, 1991). The effect of parturition on mental state and function is not fully understood. Surveys of new mothers have noted that many women report confusion, forgetfulness, and “fogginess” in the immediate postpartum period (Robinson, 1987; Stein, 1980). These anecdotal reports have been corroborated by studies examining subjective neurocognitive impairment (Casey et al., 1999; Janes et al., 1999; Jarrahi-Zadeh et al., 1969; Kane, Harman, Keeler, & Ewing, 1968; Swain, O'Hara, Starr, & Gorman, 1997). However, not all investigators reported impairments in the postpartum period (Harris, 1996), and measures have generally only extended to a few days or weeks postpartum. Objective studies of neurocognitive function have again yielded contradictory results. Robinson (1987) documented poor conceptual functioning on the eighth postpartum day; and Treadway, Kane, Jarrahi-

Zadeh, and Lipton (1969) noted poor functioning on the Trailmaking test 3 days after delivery. The findings from other studies support neurocognitive deficits during the postpartum period (Buckwalter, Buckwalter, Bluestein, & Stanczyk, 2001; Eidelman et al., 1993). In contrast, other investigators have failed to document deficits in neurocognitive functioning (Freedman, Redlich, Eron, & Jackson, 1952; Jarrahi-Zadeh et al., 1969; Rofe & Algom, 1985; Swain et al., 1997; Yalom, Lunde, Moos, & Hamburg, 1968). In a longitudinal study of explicit memory, Keenan and colleagues (1998) found a pregnancy-related decline in memory in the third trimester and improvement in memory function postpartum. In general, cognition during pregnancy has received more attention than the postpartum period, and the few studies that have continued investigation beyond pregnancy have not systematically examined the time course of neurocognitive effects. Some studies do not extend very far beyond parturition, measuring performance up to three days (Eidelman et al., 1993; Jarrahi-Zadeh et al., 1969), four weeks (Harris, 1996), six weeks postpartum (Buckwalter et al., 2001), while other studies combine postpartum and pregnancy data (Casey et al., 1999; Janes et al., 1999). A strength of the present study is the ability to examine memory functioning in women during pregnancy and the postpartum period cross-sectionally, which allowed us to make comparisons across these two periods (albeit not longitudinally).

Memory Functioning in Maternal Depression

Depressed mood experienced by some women during pregnancy and the postpartum period may impact memory or other cognitive processes. Depressed mood may be a moderator of memory deficits found during pregnancy and postpartum; however, few studies on memory functioning in pregnancy and postpartum have

simultaneously evaluated mood (Buckwalter et al., 2001; Casey et al., 1999; Treadway et al., 1969). Buckwalter and colleagues (1999) examined memory functioning of 19 women during their last 2 months of pregnancy and 2 months after delivery. When compared with performance in the postpartum period, women displayed more impairment of verbal memory and reported greater mood disturbance during pregnancy. However, depressed mood did not appear to explain memory deficits. It is noteworthy that Buckwater and colleagues sampled "healthy" pregnant women and measured depression using self-report instruments, such as the BDI and Profile of Mood States, not using Diagnostic and Statistical Manual (*DSM*) criteria. Mean BDI score was 10.2, indicating a minimally depressed mood. In another study by examining sleep, mood, and neurocognitive functioning in postpartum and non-postpartum women, Swain and colleagues (1997) observed few differences in multiple assessments of neurocognitive functioning. Swain et al., again, examined nonclinical postpartum women. Daily mood was measured using a visual analog scale. The authors concluded that new mothers differed on negative mood rating only during the first week, consistent with the time course of the "blues." Self-reported mood predicted neurocognitive functioning for both postpartum mothers and non-postpartum controls. Thus, these studies suggest mood fluctuations may influence neurocognitive performance in healthy, non-clinically depressed women. In contrast, it remains largely unknown whether clinically diagnosable depression affects memory functioning in pregnancy and the postpartum period. It remains largely unknown whether women diagnosed with major depression during the perinatal and postpartum periods have diminished memory functioning. Therefore, the present study examined the effects of pregnancy and the postpartum period on mood and

memory functioning. According to previous literature, the overlap of impaired neurocognitive functioning among patients with major depressive disorder and among healthy pregnant and postpartum women are deficits found in episodic memory, with a predominance in verbal/semantic memory. No published studies have focused on memory of a major depressive episode diagnosed during pregnancy and/or the postpartum period. The present study will contribute to the larger literature by exploring the effects of perinatal and postpartum depression on verbal learning memory performance, and examine subjective sleep as a potential moderating variable. We expect to find deficits in verbal memory in pregnant and depressed women (see Figure 1).

Memory Functioning and Sleep

Discrepant findings in neurocognitive performance may also be due to differences in sleep. For example, Janes and colleagues (1999) found sleep disruption was a significant predictor of level of subjective memory complaints. The authors concluded that self-reports of memory change during pregnancy and postpartum were related to life changes such as changes in sleep pattern. Further, Naismith and colleagues (2009) found late insomnia in older people with major depression may be independently and aetiologically linked to neuropsychological performance, particularly verbal fluency and memory. The authors concluded that sleep and circadian disturbance may indicate underlying structural and neurochemical changes, may serve as a biomarker for ongoing cognitive decline, and may be a potentially modifiable risk factor.

In addition, daytime consequences of sleep disturbance and motherhood, such as fatigue, may contribute to diminished neurocognitive performance. Although individuals of all ages and both genders are at risk for developing fatigue, pregnant and postpartum

fatigue is particularly challenging, because of biological and hormonal changes and the new mother has demanding life tasks to accomplish during this period of time. Postpartum fatigue may impact postpartum maternal role attainment and may place a woman at increased risk for postpartum depression (Corwin & Arbour, 2007). Fatigue is an unrelenting condition that affects physical and mental health, and it has implications for everyday activities, motivation, and social interactions. In order to examine sleep as well as fatigue as a potential moderating variable, several subjective sleep and one fatigue measure will be administered in the present study (see Measures).

Finally, there is a well-established diurnal variation found in depressed patients. In *DSM-IV* one of the criteria for the melancholic subtype of depression is diurnal variation of mood, with a pattern of being worse in the morning. Typical diurnal mood variations with a morning low and afternoon high (evening type) have long been considered a classical characteristic of endogenous depression or melancholia (Wefelmeyer & Kuhs, 1996). However, diurnal variation is not specific to endogenous or melancholic depression (Leibenluft & Wehr, 1992), and is not dependent of severity of depression (Haug & Fahndrich, 1990). Moffoot et al. (1994) examined 20 melancholic depressed patients and 20 NC subjects, matched for age and intelligence, on a battery of neuropsychological tests administered at 08:00 and 20:00 and found that melancholics performed significantly worse than NC on cognitive tests in the morning, but not in the evening. Melancholic patients showed marked deficits in attention/concentration/working memory, episodic memory, psychomotor speed, speed of recognition memory, and grip strength in the morning. However, marked improvement of cognitive performance was found in the evening along with improvement in mood. Similarly, tests of executive

function and verbal fluency (Porterfield, Cook, Deary, & Ebmeier, 1997) and sustained attention (Schmidt et al., 2009) are sensitive to homeostatic pressure and diurnal variation. Therefore, Horne-Östberg Morningness Eveningness Questionnaire (Horne & Ostberg, 1976) was administered in the present study to measure and control for circadian preference.

Significance and Long-Term Impact

Investigation of the effects of mood disorders during the pregnancy and postpartum periods, with the ultimate aim of developing new treatment strategies, is urgently needed, particularly given the limitation on the safe and effective treatment options documented in pregnant and lactating women. Selective serotonin reuptake inhibitor (SSRI) use during pregnancy incurs a low absolute risk for major malformations; however, other adverse outcomes have been reported. Wisner and colleagues (2009) investigated the impact of major depression versus antidepressant treatment on pregnancy and neonatal outcomes in 238 women. The authors found that infants exposed continuously to either SSRI or major depression were more likely to be born preterm (>20%rate) than were unexposed or partially exposed infants. However, in a prospective naturalistic investigation using longitudinal psychiatric assessments on a monthly basis across pregnancy, Cohen and colleagues (2006) found women who discontinued antidepressant medication relapsed significantly more frequently over the course of their pregnancies (68%) when compared with women who maintained their medication (21%). Furthermore, studies demonstrated failing to treat these disorders has disabling effects on the mother and family, and impairs the neurocognitive development of the child. The most serious consequence of untreated maternal depression is increased

mortality from suicide. For example, Appleby (1998) found severe post-partum psychiatric disorder is associated with a high rate of deaths from natural and unnatural causes, particularly suicide. The risk is especially high for women suffering from psychosis in the first postnatal year, when the suicide risk is increased 70% and infanticide 4%. Thus, new and expecting mothers and their doctors are faced with a difficult decision to risk harm of fetus/newborns by continuing medication to treat depression or to discontinue use and risk relapse of depression. At the present time, there is general consensus that untreated major depression outweighs the risk of effects of SSRI treatment on neonatal outcomes (Parry, 2009).

Clearly, maternal depression has deleterious effects on mother and child and requires unique treatment considerations. Potential teratologic effects of some pharmacotherapies or the mismatch of other therapies to symptoms of patients with pregnancy-related and postpartum depression complicates treatment. Research on the characteristics of maternal depression will aid in developing better therapy in the long-term. Identifying and delineating specific memory deficits in pregnant and postpartum women with major depression can serve as the first step towards augmenting treatment to enhance benefit. Tailoring treatment to level of memory may aid in comprehension and compliance of treatment.

Specific Aims and Hypotheses

Aim 1: Compare verbal learning and memory performance and subjective sleep quality of healthy pregnant and postpartum control women with pregnant and postpartum women with major depression.

Hypothesis 1a: Pregnant and postpartum depressed women will exhibit diminished

verbal learning and memory when compared with healthy control pregnant and postpartum women.

Hypothesis 1b: Pregnant and postpartum depressed women will report poorer subjective sleep quality (as measured by Pittsburgh Sleep Quality Index and sleep diaries) and greater fatigue (as measured by Multidimensional Fatigue Inventory) when compared with healthy control pregnant and postpartum women.

Aim 2: Investigate the association between depression severity and memory performance, and depression severity and sleep quality.

Hypothesis 2a: Depression severity and memory performance will be inversely correlated; i.e., as depression increases, memory performance decreases in all women.

Hypothesis 2b: Poor subjective sleep quality is expected to be associated with diminished mood, while improved sleep quality is expected to be associated with increased mood in all women.

Aim 3: Compare verbal learning and memory performance and subjective sleep quality in pregnant and postpartum women.

Hypothesis 3a: Based on findings by Keenan and colleagues (1998), pregnant (both healthy and depressed) women will display diminished verbal learning and memory performance compared with healthy and depressed postpartum women. The effects of depression status and child bearing status are expected to be additive, such that women who are both pregnant and clinically depressed will exhibit the greatest memory performance deficits and healthy postpartum women will display the smallest memory performance deficits.

Hypothesis 3b: Postpartum (both healthy and depressed) women will report poorer

subjective sleep quality (as measured by Pittsburgh Sleep Quality Index and sleep diaries) and greater fatigue (as measured by Multidimensional Fatigue Inventory) when compared with healthy and depressed pregnant women.

METHODS

Participants

Participants (N=62) of reproductive age (18-45 years) were recruited from the San Diego area. Four women were excluded from the study because they did not meet inclusion/exclusion criteria (2 women had other concurrent psychiatric disorders, one women had gestational diabetes, and one women was currently being treated with antidepressant medication). Of the remaining 58 women, 37 were pregnant women, 14 (mean age of 27.1 ± 5.4) of whom met clinical criteria for a MDE as defined in the *DSM-IV* and 23 who were normal control (NC) pregnant women (mean age of 28.1 ± 5.3), who had no current or prior history of depression. In 21 postpartum women, 11 met clinical criteria for a MDE as defined in the *DSM-IV* (mean age of 27.3 ± 3.3) and 10 were NC postpartum women (mean age of 28.4 ± 6.8) who had no current or prior history of depression. Groups were relatively balanced in terms of age, education, ethnicity, weeks pregnant/postpartum, and trimester (see Table 1).

Participants were recruited primarily from online advertisements placed on www.craigslist.org, flyers hung around the local community, at University of California, San Diego obstetrics and gynecology office and Outpatient Psychiatric Clinic, and from participants in Dr. Barbara Parry's chronobiology of pregnancy and postpartum depression study. Abstinence from medication (including hormonal contraception in postpartum women and antidepressant medication in all women) was required for at least one month prior to the study.

Postpartum depression was determined by patient report during clinical interview, where depression must have been present at time of testing; and onset must have occurred within 1 month of delivery (by *DSM-IV* criteria). In addition, postpartum women were excluded if they delivered greater than 12 months prior to the study. Depression during pregnancy was determined by patient report during clinical interview, where depression must have been present at time of testing; and depression must have occurred during the pregnancy period. In order to rule out organic conditions or other factors that can influence cognition, individuals with a history of head injury involving loss of consciousness, significant learning problems, and/or learning disabilities were excluded from the study. A history of head injuries or learning difficulties was inquired about during the intake assessment in order to make the determination of possible exclusion. In addition, women with serious medical conditions (e.g., cancer, diabetes, thyroid disease), concurrent psychiatric diagnosis (except anxiety disorders), or who were imminently suicidal or in current need of hospitalization for treatment of depression were excluded from the study.

Procedures

All procedures conducted were approved by University of California, San Diego and San Diego State University Committees for Protection of Human Subjects, and participation in the study was voluntary. All information provided by each participant was strictly confidential, and each participant was informed that information was "de-identified" and not be shared outside of the laboratory, as documented in the consent form. Further, all data is stored under highly secure procedures, compliant with HIPPA

regulations. Since all information is confidential and is not collected as part of any clinical service, we did not share diagnostic information with any participants.

Screening Phase. All potential participants were evaluated via brief telephone screen interview in which interested participants were asked about inclusion/exclusion criteria. Participants were given the option for home or laboratory visits and the opportunity to reschedule missed appointments to ensure the completion of the protocol. After meeting initial screening criteria, a 1-3 hour interview was completed during which participants signed the informed consent form; and were provided information explaining the importance of the research, the safety of the protocol, confidentiality of the study and contact information for psychiatric assistance should it be needed. Additionally, psychiatric and medical symptoms were documented. The Structure Interview Guide for the Hamilton Depression Rating Scale (SIGH-SAD; Hamilton, 1967), Beck Depression Inventory (BDI; Beck, Ward, Mendelson, Mock, & Erbaugh, 1961), Beck Anxiety Inventory (BAI; Beck & Steer, 1990) and Edinburgh Postnatal Depression Scale (EPDS; Cox, Holden, & Sagovsky, 1987) were administered to assess mood. The Multidimensional Fatigue Inventory (MFI) was also administered to assess fatigue at intake. Finally, a structured clinical interview for *DSM-IV* diagnoses (SCID-I/NP; First, Spitzer, Gibbon, & Williams, 1995) was used to obtain a complete psychiatric history from each potential subject, to determine whether she had the requisite symptoms to meet diagnostic criteria for major depressive episode (MDE), and to ensure that there is no concurrent Axis I diagnoses (see Diagnostic measures). A concurrent diagnosis of anxiety (with depression) did not preclude women from the study. Depressed patients (DP) were required to meet *DSM-IV* criteria for MDE and have a mean SIGH-SAD objective score

of ≥ 15 and BDI and EPDS subjective scores ≥ 10 during screening. NC women were excluded if they met *DSM-IV* criteria for MDE or if they scored ≥ 10 on the SIG-SAD, BDI, BAI, or EPDS. The following variables were also recorded: age, educational history, work status, handedness, number of weeks pregnant/postpartum, breast feeding status, and number of children. Participants were asked to complete a sleep diary for approximately one week, at home between screening and the experimental phase in order to track subjective sleep prospectively (see Measures).

Experimental Phase. Following screening and diagnostic classification, each participant completed a second visit approximately 1 week later to complete a 1.5 - 2 hour battery of neuropsychological tests consisting of measures of verbal learning and memory, psychomotor speed, verbal fluency, attention, and executive functioning/working memory that have been standardized and well-normed. Research assistants that were blind to subjects' diagnoses administered neuropsychological tests. In addition, SIGH-SAD, BDI, BAI, EPDS, and MFI were administered both at the time of intake and at memory testing. See Table 2 for the study timeline.

Measures

Mood and Diagnostic measures. As part of screening of mood, participants were evaluated using several mood questionnaires.

Hamilton Depression Rating Scale (HDRS). HDRS is an objective 21-item scale assessing affective and physical depressive symptomology. Each item is rated on a scale ranging from either 0 to 2 or 0 to 4 with a maximum of 64 points (Hamilton, 1967).

Addendum to Hamilton Depression Rating Scale. As part of SIGH-SAD, HDRS addendum was implemented in order to assess atypical depressive symptoms (i.e. fatigue,

weight gain, social withdrawal, carbohydrate craving, and hypersomnia) with a maximum of 26 points. (Williams, Link, Rosenthal, Amira, & Terman, 1994)

Hypomania Rating Scale. The hypomania scale was used to rule out patients with mania, assessing expansive and irritable mood, decreased need for sleep, increased work and activities, activation, speech, flight of ideas, creativity, impulsive behavior, libido, or social activities. Each item is rated on a scale ranging from 0-2 to 0-5 with a maximum of 40 points (Rosenthal, 1986).

Beck Depression Inventory (BDI). Subjective mood was assessed using the BDI, a 21-item scale with items ranging from 0-3 with a maximum of 63 points (Beck et al., 1961).

Beck Anxiety Inventory (BAI). Subjective anxiety was assessed using the BAI, a 21-item scale with items ranging from 0-3 with a maximum of 63 points (Beck, Epstein, Brown, & Steer, 1988; Beck & Steer, 1990).

Edinburgh Postnatal Depression Scale (EPDS). EPDS is a 10-item self-report mood scale designed to predict depression specifically in pregnant and postpartum women (Cox et al., 1987).

Structured Clinical Interview of DSM-IV (SCID). The SCID-I/NP was used to diagnose *DSM-IV* Axis I disorders in persons not identified as psychiatric patients. Segal and colleagues (Segal, Hersen, & Van Hasselt, 1994) reported kappas from .70 to .93 for depressive disorders. Most investigators recommend using the SCID in lieu of clinical interviews (Shear et al., 2000). The SCID-I/NP is regarded among the most valid standardized instruments, and has often been used as the “gold standard” in evaluating

screening tools (Broadhead et al., 1995). In the present study the SCID-I/NP was used to evaluate lifetime Axis I psychiatric diagnosis in all subjects.

Neuropsychological measure. *California Verbal Learning Test (CVLT).* CVLT is a test designed to assess verbal learning and memory and has well-documented sensitivity and specificity (Delis, Kramer, Kaplan, & Ober, 1987). Participants are required to learn a 16-item list of shopping items, administered over five trials. Participants are then asked to learn and recall a distractor list. Subsequent to the distractor list, they are asked to recall the original list and recall words by category. Following a 20-minute delay period, participants are asked to recall these words, recall items by category, and recognize the words from a list including distracters. The CVLT yields information concerning strategies employed in encoding verbal stimuli, rapidity of verbal learning, spontaneous and cued recall and recognition. Verbal memory factors included in analyses were number of items recalled after the first and fifth presentation of the list, short-term and long-term cued and free recall, perseveration errors, and the degree to which items are semantically clustered upon recall.

Sleep measures. To evaluate the impact of sleep and circadian preference on memory performance, participants were asked to complete several sleep questionnaires.

Pittsburgh Sleep Quality Index (PSQI). The PSQI is a standardized self-rated questionnaire developed to assist in measuring retrospective global sleep quality over a one-month period. The 24-item questionnaire generates seven component scores, ranging from subscale scores 0 to 3: sleep quality, sleep latency, sleep duration, habitual sleep efficiency, sleep disturbances, use of sleep medications and daytime dysfunction. The addition of these seven components yields a global score of subjective sleep quality. The

global score ranges from 0 to 21, and a higher score is indicative of poorer subjective sleep quality. A score of > 5 identifies clinically significant sleep disturbance with 89.6% sensitivity and 86.5% specificity (Buysse, Reynolds, Monk, Berman, & Kupfer, 1989).

Sleep diary. The sleep diary was created in-house based on other validated sleep diaries (Monk et al., 1994), and was used to measure prospective sleep. Women were asked to complete the sleep diary upon rising to provide an estimate of lights out, sleep latency, rise time, time in bed, quality of sleep, number of nocturnal awakenings, wake after sleep onset, and total sleep time each night; and nap time each day for one week prior to memory testing. Using a ratio of total sleep time to time in bed provided a calculation for subjective sleep efficiency. Conventional sleep assessment procedures, such as sleep diaries, can complement depression scales by providing additional information about specific aspects of sleep in depression (Manber et al., 2005).

Horne-Östberg Morningness-Eveningness Questionnaire (MEQ). The MEQ is a self-report instrument that contains 19 questions aimed at determining when during the daily temporal span the respondent's maximum propensity to be active lies. Most questions are preferential, in the sense that the respondent is asked to indicate when, for example, he/she would prefer to wake up or start sleep, rather than when he/she actually does. Questions are multiple choice, with each answer being assigned a value. Their sum gives a score ranging from 16 to 86, with lower values corresponding to evening types (Horne & Ostberg, 1976).

Multidimensional Fatigue Inventory (MFI). A 20-item self-report instrument designed to measure fatigue, the MFI measures five dimensions independently: general fatigue, physical fatigue, mental fatigue, reduced motivation and reduced activity. There

are four items in each dimension. The score on each item ranges from 1 (no fatigue) to 5 (very fatigued). The score in each dimension ranges from 4 to 20. Total possible scores range from 20 (no fatigue) to 100 (very fatigued). The instrument was found to have good internal consistency, with an average Cronbach's alpha coefficient of 0.84 and construct validity (Schneider, 1998; Smets, 1995).

Data Analytic Plan

Examination of Covariates. Demographics and sleep variables were analyzed for group differences using Analysis of Variance (ANOVA). If significant group differences are found at a p-value of .10, variables were added as covariates in the analyses below.

Outcome Measure. The CVLT is a neuropsychological measure that is standardized, and well normed (Heaton, 2004). The CVLT was scored using CVLT manual and electronic scoring software. Standardized scores were normed for sex, age and African American ethnicity.

Aim 1 & 3. Memory data was analyzed using a 2 x 2 Multivariate Analysis of Variance (MANOVA), where the categorical independent variables (IV) was diagnosis (DP vs. NC) and reproductive status (pregnant vs. postpartum) and the continuous dependent variables (DV) were scores of CVLT and subjective sleep measures (PSQI, sleep diaries, and MFI). Wilks' criterion (Λ) was used to examine the omnibus test statistics. If overall main effects or the interaction were significant for the omnibus MANOVA, univariate ANOVAs were subsequently examined.

Main effects are expected for mood and child bearing status, where DP and pregnant women will exhibit diminished verbal learning and memory compared with NC and postpartum women. An interaction between child bearing status and depression

status will also be examined. An interaction is not expected to occur. In addition, main effects are expected for mood and child bearing status, where DP and postpartum women will exhibit diminished subjective sleep quality and greater fatigue when compared to NC and pregnant women.

Aim 2. To examine the relationship between measures of mood (i.e., HDRS, atypical items, BDI, BAI, and EPDS scores at time of memory testing) and memory performance Pearson Bivariate Correlations were conducted. A negative association between mood and memory performance was expected for all subjects. That is, as depression increases, memory performance will decrease.

Additionally, in order to examine the association between subjective sleep (measured by PSQI) and mood (measured by HDRS, BDI, BAI, and EPDS), bivariate correlations were conducted. A positive association is expected for PSQI score and mood scores. That is, as PSQI increases (indicating poorer sleep quality), mood scores will increase (indicating greater severity of depressed mood and/or anxiety).

Power Analysis. To determine what sample size was necessary to detect significant group differences in memory performance, a power analysis was conducted using nQuery software. Medium effect sizes were extrapolated from studies examining memory functioning of healthy pregnant/postpartum women. The power is based on a one-sided test; since we hypothesized that the memory performance would be diminished in maternal depression. At power of 80%, a sample of 60 (i.e., 15 per group) was determined to be necessary to detect significant differences for aims one and three. Thus, the projected sample size was 15 for each subgroup. Due to time constraints of the study, goal for sample sizes were not met in all of the groups

RESULTS

Preliminary Analyses

Variables were assessed for normality, homogeneity of variance, and linearity. Using an alpha level of .001 to evaluate homogeneity assumptions, Box's M test of homogeneity of covariance was non-significant ($p > .05$). Therefore, the assumption of homogeneity of covariance was met. Levene's homogeneity of variance test was not statistically significant ($p > .05$). Therefore, the assumption of homogeneity of variance was met.

Covariates

A 2 x 2 ANOVA indicated that diagnostic groups (NC vs. DP) were equivalent in age $F(1,57) = 0.82$, $p = .317$, education $F(1,57) = 0.44$, $p = .834$, weeks pregnant or postpartum $F(1,57) = 0.01$, $p = .922$, circadian preference determined by Horne-Östberg (H-O) Morningness Eveningness Scale $F(1,57) = 1.73$, $p = .202$; on reproductive status (pregnant vs. postpartum) groups were also equivalent in age $F(1,57) = 1.54$, $p = .221$, education $F(1,57) = 0.24$, $p = .877$, weeks pregnant or postpartum $F(1,57) = 0.30$, $p = .587$, circadian preference determined by H-O score $F(1,56) = 0.05$, $p = .831$; and diagnosis x reproductive status interactions were not significant for age $F(1,57) = 2.69$, $p = .107$, education $F(1,57) = 0.19$, $p = .891$, weeks pregnant or postpartum, $F(1,57) = 0.13$, $p = .720$, or circadian preference determined by H-O score $F(1,56) = 1.42$, $p = .246$ (see Table 1).

Age, education, weeks pregnant/postpartum, H-O and MFI scores were used in subsequent analysis as covariates. With respect to these covariates in the statistical

tests, no alterations in outcomes of the analyses were found when age, education, weeks pregnant/postpartum, circadian preference, or fatigue were applied as covariates.

Mood Measures

The HDRS, HDRS atypical measure (SIGH-SAD), hypomania scale, BDI, BAI, and EPDS were administered during the intake visit and during the time of neuropsychological evaluation. A 2 x 2 MANOVA was conducted for mood measure (for scores at intake and time of memory testing). As expected, there were significant group differences (see Figure 2) for diagnosis on measures of both subjective and objective depression at the time of intake (see Table 4) and memory testing (see Table 5).

Neuropsychological Measure

The verbal memory domain consisted of one test (California Verbal Learning Test) with multiple subtests/variables. The 2 x 2 omnibus MANOVA revealed no overall significant main effects for diagnosis $F(7, 47) = 1.57$, $p = .176$, reproductive status $F(7,47) = 1.86$, $p = .105$, or diagnosis x reproductive status interaction $F(7, 47) = 0.46$, $p = .855$. Due to close trends for main effects, and for exploratory purposes, univariate analyses were examined (see Table 6).

Aim 1a. For diagnosis, NC women learned significantly more words than DP on CVLT trials one through five $F(1,53) = 4.06$, $p = .05$ ($m = 39.65$ vs. 31.90), recalled significantly more words on long delay free recall $F(1,53) = 5.86$, $p = .019$ ($m = -1.12$ vs. -2.30), and exhibited a significantly greater amount of semantic clustering on the CVLT versus DP $F(1,53) = 5.87$, $p = .022$ ($m = -0.57$ vs. -1.05) and a trend towards significance for fewer CVLT perseveration errors $F(1,53) = 2.89$, $p = .096$ ($m = -0.39$ vs. 0.11).

Aim 3a. For reproductive status, postpartum women learned significantly more words than pregnant women on CVLT trials one through five $F(1,53) = 5.61$, $p = .037$ ($m = 39.71$ vs. 31.67), and recalled significantly more words on short delay free recall $F(1,53) = 6.00$, $p = .018$ ($m = -0.71$ vs. -1.70), short delay cued recall $F(1,53) = 10.61$, $p = .002$ ($m = -0.64$ vs. -1.67), long delay free recall $F(1,53) = 6.32$, $p = .016$ ($m = -1.43$ vs. -2.78), long delay cued recall $F(1,53) = 5.31$, $p = .026$ ($m = -1.07$ vs. -2.12). In addition, postpartum women were also able to use semantic clustering strategy significantly more that pregnant women $F(1,53) = 6.18$, $p = .017$ ($m = -0.43$ vs.-0.91). Of note, all group standardized scores were negative values (see Figures 3-5)

Sleep Measures

Pittsburgh Sleep Quality Index. To measure subjective sleep quality over the past month, PSQI was administered at the time of intake. A 2 x 2 MANOVA revealed a significant overall main effect for diagnosis $F(7,48) = 6.91$, $p < .001$ and reproductive status $F(7,48) = 4.47$, $p = .002$, however diagnosis x reproductive status interaction was not significant $F(7,48) = 0.77$, $p = .615$. Due to significant overall main effects, univariate analyses were also examined.

Aim 1b. For diagnosis, groups were significantly different for Index 1 – Sleep Quality ($p = .030$), Index 2 – Sleep Latency ($p = .030$), Index 5 – Sleep Disturbance ($p < .001$), Index 6 – Use of Sleep Medications ($p = .030$), Index 7 – Daytime Dysfunction ($p = .004$), and PSQI Global Score ($p < .001$). For all indices and the global score, DP scored significantly higher on the PSQI, indicating poorer subjective sleep quality.

Aim 3b. For reproductive status, there was a trend towards significance on group difference for Index 1 – Sleep Quality ($p = .083$), Index 3 – Sleep Duration ($p = .072$),

and significant group differences on Index 5 – Sleep Disturbance (p = .009), Index 6 – Use of Sleep Medications (p = .053). For all indices postpartum women scored significantly higher than pregnant women on the PSQI, indicating poorer subjective sleep quality (see Figure 6).

Sleep Diary. To measure prospective sleep, a sleep diary was administered the week between intake and memory testing. A 2 x 2 MANOVA was conducted for mean sleep diary variables (lights out, rise time, sleep latency, number of awakenings, wake after sleep onset, sleep efficiency, total sleep time, and time napping) and revealed no significant group differences. For exploratory purposes, sleep diary data for the night prior to memory testing was also examined. A 2 x 2 MANOVA revealed the overall main effects were not significant for diagnosis $F(6, 49) = 0.71$, p = .646 or reproductive status $F(6, 49) = 0.77$, p = .604; however, the omnibus diagnosis x reproductive status interaction was significant $F(6, 49) = 5.72$, p = .002. Univariate interactions were examined and revealed significant diagnosis x reproductive interactions for lights out $F(6, 49) = 5.10$, p = .034, rise time $F(6, 49) = 5.36$, p = .030, and number of awakenings $F(6, 49) = 6.79$, p = .016.

Analyses of simple effects showed a trend towards significance in DP (but not NC), where postpartum women attempted to go to sleep earlier, recorded as “lights out” on the sleep diary on the night prior to memory testing versus pregnant women (21:06 vs. 23:22 *h*, p= .096). The difference between NC and DP was not significant for lights out for both pregnant (p = .599) and postpartum women (p = .223). The difference between pregnant and postpartum women was nonsignificant for rise time recorded on the sleep diary on the night prior to memory testing for both NC women (p = .316) and DP (p =

.110). The difference between NC and DP was nonsignificant for rise time for both pregnant (p = .647) and postpartum women (p =.130). In NC (but not DP), postpartum women reported significantly more nocturnal awakenings on the night prior to memory testing versus pregnant woman (3.00 vs. 0.91, p = .002). In pregnant (but not postpartum) women, DP versus NC reported significantly more nocturnal awakenings (2.25 vs. 0.91, p =.022; see Figure 7).

Multidimensional Fatigue Inventory. Multidimensional Fatigue Inventory (MFI) was administered during the intake visit and at the time of memory testing to examine fatigue. A 2 x 2 ANOVA revealed a trend towards significance on level of fatigue as measured by MFI at the time of intake $F(1,57) = 3.20$, p = .085, where DP reported feeling more fatigued m=55.9 (10.20) versus NC women m=47.7 (9.66).

Aim 1b. A significant main effect for diagnosis was revealed for MFI at time of memory testing $F(1,57) = 7.41$, p = .011, where DP scored significantly higher on MFI (indicating feelings of greater fatigue) m=58.3 (3.20) versus NC women m=45.9 (3.25).

Aim 3b. Notably, no significant differences were found for the main effect of reproductive status $F(1,57) = 0.92$, p = .346 or the diagnosis x reproductive status interaction $F(1,57) = 0.16$, p = .694 for MFI at intake or at time of memory testing $F(1,57) = 0.36$, p = .556 and $F(1,57) = 0.12$, p = .271, respectively. See Table 7 for means and standard deviations of sleep measures (see Figure 8).

Correlations

Mood and Memory Performance. Pearson bivariate correlations were calculated for all subjects between measures of mood (i.e., HDRS, atypical items, hypomania, EPDS, BDI, and BAI scores) at time of testing and memory performance.

Aim 2a. A positive correlation was found between CVLT preservations and HDRS ($r = 0.39$, $p = .007$), hypomania scale ($r = 0.37$, $p = .011$), BDI ($r = 0.32$, $p = .038$), and BAI ($r = 0.30$, $p = .041$). As mood scores increased (indicating greater severity of depressed mood), women made more perseveration errors (i.e., perseverating on the same word when recalling CVLT items).

Sleep and Mood. Pearson bivariate correlations were calculated for all subjects between measures of mood (i.e., HDRS, atypical items, hypomania, EPDS, BDI, and BAI scores) at intake and time of testing and PSQI (7 indices + global score).

Aim 2b. As expected, a positive correlation was found on most mood and PSQI scores, ranging between $r = 0.30$, $p = .093$ to $r = 0.69$, $p < .001$. As mood scores increased (indicating greater severity of depressed mood), PSQI index and global scores increased (indicating poorer subjective sleep quality; see Figure 9).

DISCUSSION

The present study examined memory performance in pregnant and postpartum women with and without major depression to investigate whether depressed mood affects performance on short- and long-term verbal memory. Several investigators have demonstrated that cognition, and more specifically, verbal memory, is diminished during pregnancy (Brindle et al., 1991; de Groot et al., 2006) and, to a lesser degree, during the postpartum period (Buckwalter et al., 2001; Eidelman et al., 1993; Robinson, 1987). Given that memory deficits occur in major depression, major depression could exacerbate memory deficits during pregnancy. Therefore, we hypothesized both depressed and pregnant women would exhibit diminished verbal memory relative to normal control and postpartum women.

Summary of Findings

Overall, the results confirm this hypothesis and are consistent with previous investigations of memory functioning of major depressive disorder and healthy pregnant and postpartum women. That is, DP exhibited greater deficits in tasks involving verbal memory. In addition, pregnant women exhibited more deficits with respect to verbal memory versus postpartum women.

Verbal Learning and Memory. Depressed women learned significantly fewer words from trials one through five, recalled significantly fewer words on long delay free recall, made more perseveration errors, and utilized semantic clustering strategy less often when completing CVLT versus NC women. Several investigators have demonstrated that individuals with MDE exhibit varying degrees of cognitive

dysfunction (Cassens et al., 1990; Veiel, 1997). Specifically, individuals with MDE tend to exhibit a subcortical pattern of verbal memory performance characterized by impaired encoding and retrieval of information, and marked improvement on recognition trails (Dunbar & Lishman, 1984; Massman, Delis, Butters, Dupont, & Gillin, 1992). The results of the present study are consistent with deficits in memory found in MDD (Burt et al., 1995; R. M. Cohen et al., 1982; Golinkoff & Sweeney, 1989; Ilsley et al., 1995).

In addition, pregnant women learned significantly fewer words from trials one through five, recalled fewer words on CVLT immediately and after short- and long-delay, and also utilized semantic clustering strategy less often versus postpartum women. These results of reproductive status group differences support subjective complaints and objective findings of diminshed memory during the pregnancy period (Brindle et al., 1991; Buckwalter et al., 2001; Buckwalter et al., 1999; de Groot et al., 2003; de Groot et al., 2006; Lurie, 2005; Sharp et al., 1993). Of note, a few previous studies found subjective complaints of memory, but failed to detect memory deficits when measuring objectively (Casey et al., 1999; Crawley et al., 2003; Janes et al., 1999; McDowall & Moriarty, 2000; Z. Schneider, 1989). These discrepant findings may be due to methodolical limitations of previous studies, such as small samplie size, different phases of pregnancy, limited measures of neurocognitive domains and lack of standardized measures, or failing to control for potential confounding variables.

Our findings of diminished performance of verbal memory in pregnancy compared to postpartum is consistent with a longitudinal study of explicit memory by Keenan and colleagues (1998), who found a pregnancy-related decline in memory in the third trimester and improvement in memory function postpartum in healthy women

without depression. Our findings also were consistent with other investigators who found no performance decrements in the postpartum period (Freedman et al., 1952; Jarrahi-Zadeh et al., 1969; Rofe & Algom, 1985; Swain et al., 1997; Yalom et al., 1968). Of note, a few studies did find diminished performance in verbal learning and memory during the postpartum period (Buckwalter et al., 2001; Buckwalter et al., 1999; de Groot et al., 2006; Eidelman et al., 1993). These differences, may in part be explained by timing of testing during the postpartum period. That is, several investigators point out that these deficits in verbal memory in the postpartum period may be transient and only occur during the early motherhood (de Groot et al., 2006; Eidelman et al., 1993).

Sleep and Memory Performance. In order to examine the effects of subjective sleep on memory performance, we administered several measures of subjective sleep. When examining PSQI (a measure of subjective sleep quality over the past month), DP reported poorer sleep quality, longer sleep latency, and increased sleep disturbance, and daytime dysfunction versus NC women. In addition, when examining the sleep diary entry on the night prior to memory testing, in pregnant women, DP reported more awakenings. Fatigue was measured in the present study at time of intake and memory testing. We found depressed patients reported feeling more fatigued at intake and at time of memory testing versus NC women. Taken in total, these findings suggest that subjective sleep disturbance, poor sleep quality, and fatigue may be a moderating variable and may contribute to poor memory performance.

However, when reproductive status was examined for differences on the PSQI and sleep diary, postpartum women reported significantly poorer sleep quality and increased sleep disturbance, and awakenings than pregnant women. No significant group

differences were found between pregnant and postpartum women in terms of fatigue. Since postpartum women reported more sleep disturbance, poorer sleep quality, and similar fatigue levels; yet performed significantly better on verbal learning and memory compared with pregnant women, it appears that sleep may not greatly influence memory performance after all.

Implications for Daily Living

So what does this mean in terms of women completing tasks in their daily lives? Studies of major depressive disorder have shown that neurocognitive deficits impact daily living. Memory deficits in maternal depression may also translate into experience related deficits in "real world" functioning and jeopardize care for other children during the pregnancy and early postpartum period. For example, maternal depression may compromise consenting to medical procedures, understanding hospital discharge instructions, transmission of childcare technique instructions, and care for newborn and other children. Specifically, verbal memory deficits may impact the ability to remember medical appointments, medication administration, instructions during medical visits, and other errands and appointments that may occur. When women with maternal depression feel the burden of time constraints, they may make more errors when performing instrumental activities of daily living such as drops, spills, or other accidents in the home. Patients with medical and delivery complications, sick neonates, or low social support may be of greatest concern.

Treatment Implications

In addition, deficits in memory may cloud a new mother's decision-making about treatment options. Deficits in verbal memory in pregnant women with clinical depression

might explain why previous experiences of therapy have not worked well and suggest alternative paths of treatment. For example, Taylor and colleagues (2006) found examining psychomotor speed helped identify a subgroup of depressed patients that were unresponsive to fluoxetine, suggesting that patients may be cognitively profiled to predict treatment response. Tailoring therapy to level of neurcognitive ability may aid in comprehension and compliance of treatment. It may be necessary to tailor existing therapy to memory ability by increasing repetition and check-ins, providing written handouts, or by having patients summarize more often; or it may be necessary to develop new strategies to aid treatment outcome, such as replacing cognitive therapy with more behavioral techniques or utilizing biological interventions (e.g., light treatment, wake therapy).

Possible Strategies to Ameliorate Memory Deficits

Memory deficits may be improved by treating the underlying depression. In addition, clinicians may employ specific techniques to sharpen existing memory and make new information more easily retainable. For example, trying to make new information more meaningful and relevant to the patient by personalizing it will aid in recall. In addition, there are certain organizational habits that patients can be taught in order to perform better, such as sticking to a routine; keeping important, frequently used belongings in the same place; using a calendar or electronic organizer to remember appointment and other important dates; using a daily planner to keep lists of things to do each day, phone calls, bills, errands, medication administration, etc.; using and updating an address book to remember names and phone numbers; and using repetition, grouping, and retracing strategies.

Strengths and Limitations

A strength and limitation of the study is the rich ethnic diversity of the sample. In this sample of 58 women, 25 were Caucasian (43%), 20 were Hispanic (34%), 9 were Asian (16%) and 4 were African American (7%). While ethnic diversity increases ability to genearlize findings, it might be at the expense of internal validity. Previous studies have demonstrated that ethnicity may influence results of neurocogitive testing and results should be interpreted with caution. At first blush, the large sample of ethnic minorities would suggest interpreting these results with caution. However, results of memory testing were normed for sex, age, and ethnicity (in African Americans). It remains largely unknown what the effects of other ethic origins (such as, Hispanic and Asian) have on memory performance. That said, ethnicity was sampled relatively equally across groups. Consequently, ethnicity may not be a confounding variable or influence study results. For percentage of ethnicity per group see Table1.

In addition, to increase enrollment, women were givent the option to test in their home envoirnments. Therefore, the use of enviornmental setting could also be seen as both a strength and limitation. On one side, women were allowed to test in a setting that was more comfortable to them and represented a more “real world” setting, however, all variables outside the laboratory can not be controlled. Study personnel did their best to control the home testing envoirnment, by ensuring a quiet testing area and flat space to work, and allowing breaks when needed. However, more often in the postpartum condition, women had new infants to care for simultaneously to memory testing. While this may be more representative of “real world” by forcing women to multitask and care for infants while completing memory tasks, it may have interfered with performance on

tests. This challenge further supports the findings that postpartum women performed significantly better versus pregnant women, despite the challenge of caring for a infant while completing testing. This finding may suggest that postpartum women have a strength in divided and selective attention, by utilizing these abilities to overcome challenges and perform relatively well on tasks. Despite these limitations, the present study provides an initial exploration into the mood, memory, and sleep in pregnant and postpartum women with and without major depression.

Future Directions

Although this study is limited by it's cross-sectional design and we do not have data on pre-pregnancy baseline performance, it appears that memory performance may increase in the postpartum period and return to baseline/premorbid functioning (at least when compared to pregnant counterparts). Longitudinal studies examing memory performance prior to and during pregnancy through the postpartum period would be necessary to confirm this initial finding. It would also be useful to exmine memory in non-pregnant/postpartum women with and without depression compared to those women experiencing maternal depression to explore effects of reproductive status and delineate major depression from maternal depression. Further, longitudinal studies examining the course of maternal depression after it remits would be useful to examine long-term effects of mood on memory functioning. Finally, the notion of subjective-objective discrepancies in depressed patients is not a new idea and can be found in the sleep literature as well (Argyropoulos et al., 2003; Tsuchiyama et al., 2003; Weiss et al. 1973). Tsuchiyama and colleagues (2003) examined 23 patients with MDD and found that patients tended to inaccurately estimate total sleep time when compared with objective

polysomnographic (PSG) measures of sleep. These misinterpretations were influenced by degree of objective sleep disturbance, severity of depression, age, and personality. Future studies examining objective sleep and daytime sleepiness using polysomnography, multiple sleep latency test, or actigraphy in conjunction with measuring memory performance might be able to determine more accurately sleep effects on memory performance in maternal depression. Although results only partially confirm that sleep is a moderating variable of mood – performance relationship, it is important to continue to explore this issue because of the potential of sleep disturbance as a modifiable risk factor for both depression and memory deficits.

Potential Moderating Effects of Hormones on Memory Functioning

Several investigators have found that ovarian hormones estrogen and progesterone contribute to the higher incidence of major depression (Abou-Saleh, Ghubash, Karim, Krymski, & Bhai, 1998; Asher et al., 1995; Parry et al., 2003). Estrogen receptors in the brain, could mediate estrogen-induced vasodilatation that could affect the blood supply of the brain. Estrogen receptors are located in areas of the brain involved with memory, e.g., cerebral cortex, basal forebrain, and hippocampus. When estrogen levels begin to decline with menopause, there is a decline in various cognitive functions in women, such as memory, attention and language (Ditkoff, Crary, Cristo, & Lobo, 1991; Joffe et al., 2006; Maki, 2002; Sherwin, 1994, 2006). Other research has examined neuropsychological performance across the menstrual cycle (Hampson, 1990; Keenan, Stern, Janowsky, & Pedersen, 1992; Phillips & Sherwin, 1992). Resnick, Perry, Parry, Mostofi, and Udell (1998) examined neurocognitive performance of 37 women with and without premenstrual dysphoric disorder (PMDD) and found psychomotor slowing in the

late luteal phase in women with PMDD compared with the early follicular phase. Buckwalter and colleagues (1999) examined the effects of steroid hormones on cognition in 19 pregnant women followed 2 months postpartum. During pregnancy, higher levels of progesterone were associated with greater mood disturbances and higher levels of dehydroepiandrosterone with better mood. After delivery, testosterone was strongly and consistently associated with greater reported mood disturbances. However, no hormone consistently has been found to be related to memory performance during pregnancy. Buckwalter et al. conclude that peripartal memory deficit could not be explained by the dramatic rise in circulating steroid hormones during pregnancy. However, memory functioning may not be related to the absolute value of reproductive hormones. Rather, it may be the case that memory performance is associated with longitudinal changes in reproductive hormone levels during pregnancy or their interaction with stress.

While clinical manifestations can be very similar, there may be neurocognitive distinctions between MDD and reproductive mood disorders. The similarities and differences between memory performance and pathophysioloical processes of major depression and depressed mood proximate to reproductive hormone change must still be clarified. Further studies examining reproductive hormones (such as estrogen, progestin, and prolactin) and neuroendocrine variables (such as cortisol and follicle stimulating hormone) known to influence memory, in conjunction with measuring memory performance of maternal depression would be useful to determine potential associations.

Summary

In sum, the results confirm hypotheses one and three, and are consistent with previous investigations that found pregnant women and patients with major depression

exhit greater deficits in tasks involving verbal learning memory compared with normal control and postpartum women. As depressed mood increased neurocognitive errors increased. Although women experienced diminished verbal learning and memory during pregnancy, these deficits diminished in the postpartum period. In addition, the effects of sleep disturbance did not influcence memory performance. Although postpartum women reported greater sleep complaints, they exhibited increased peformance on memory tasks when compared with pregnant women. Further studies examinng objective sleep are needed to clarify this issue. Finally, longitudinal studies examining reproductive horomones and neurocognitive performance over the course of pregnancy and the postpartum period are needed to explore changing levels of reproductive hormones and their effects on memory when interacting with stress.

APPENDIX

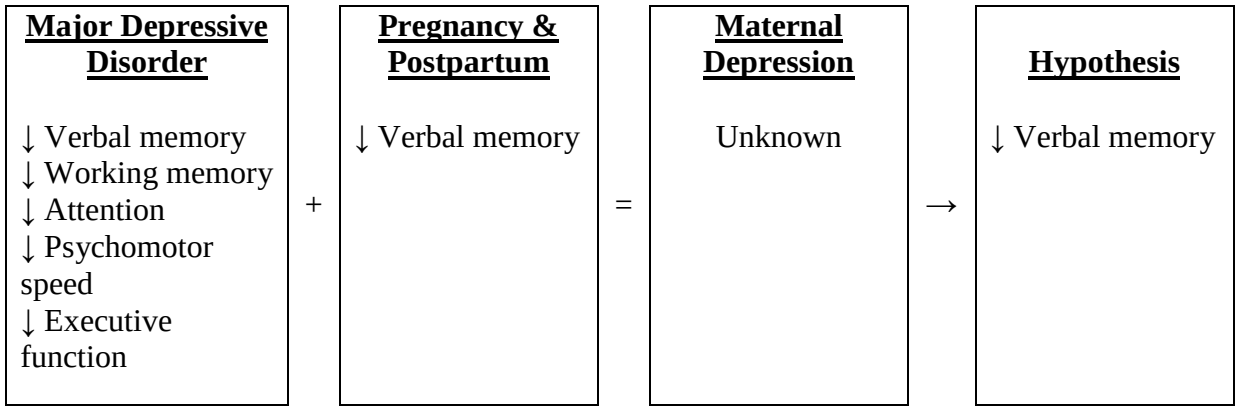

Figure 1: Cognitive deficits found in the literature and proposed hypothesis

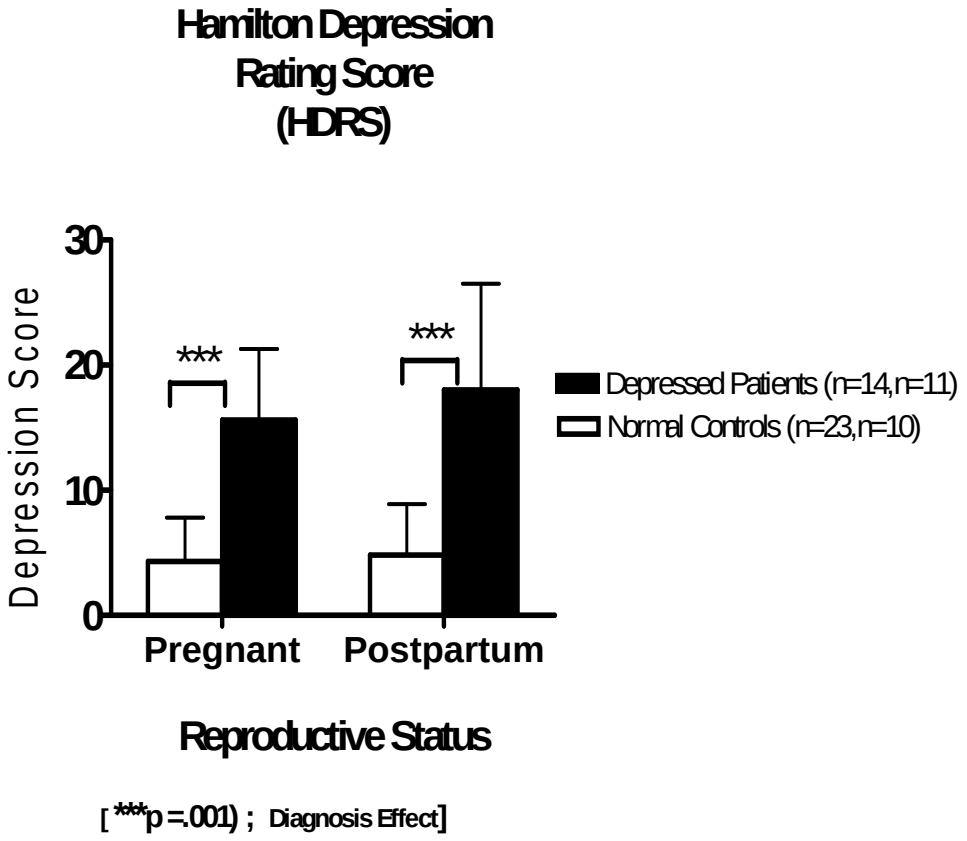

Figure 2: Mean score (± SE) of Hamilton Depression Rating Scale (HDRS) of pregnant and postpartum women with and without major depression. Significant group differences were found for diagnosis, where depressed pregnant and postpartum women exhibited a higher score on HDRS.

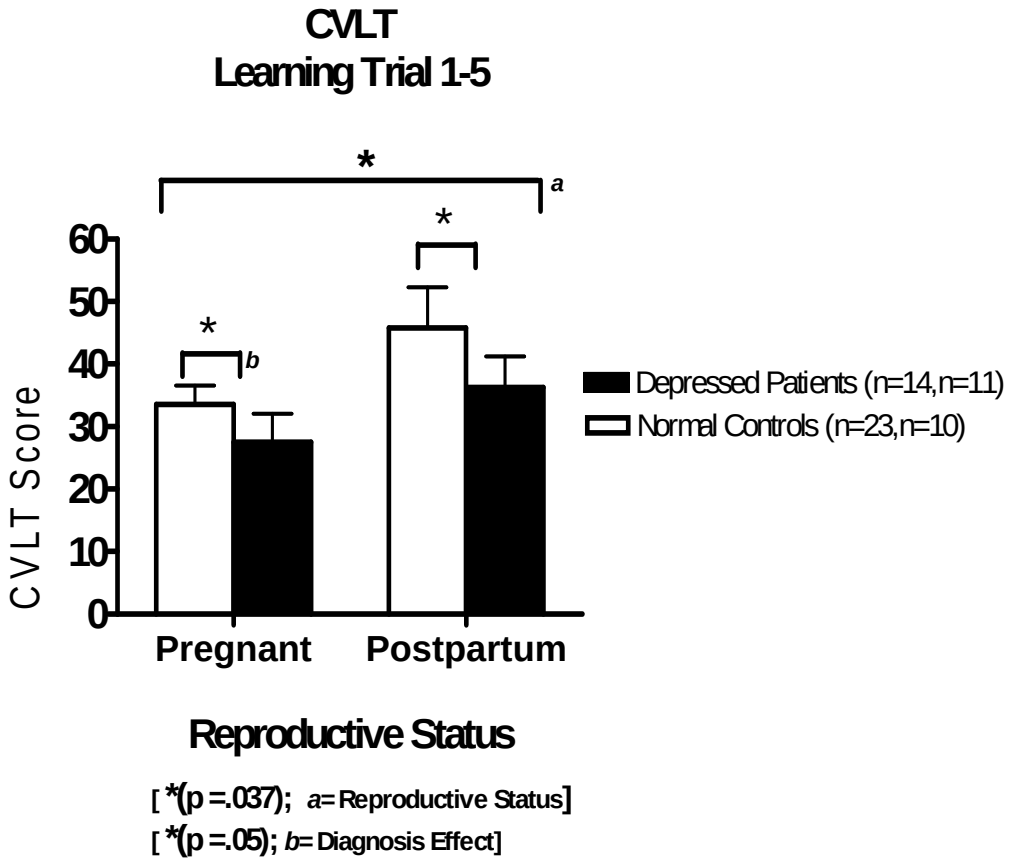

Figure 3: Mean score (± SE) of California Verbal Learning Test Learning Trial (CVLT) 1 -5 in pregnant and postpartum women with and without major depression. Significant group differences were found for diagnosis and reproductive status, where depressed and pregnant women learned fewer words on CVLT than normal control and postpartum women.

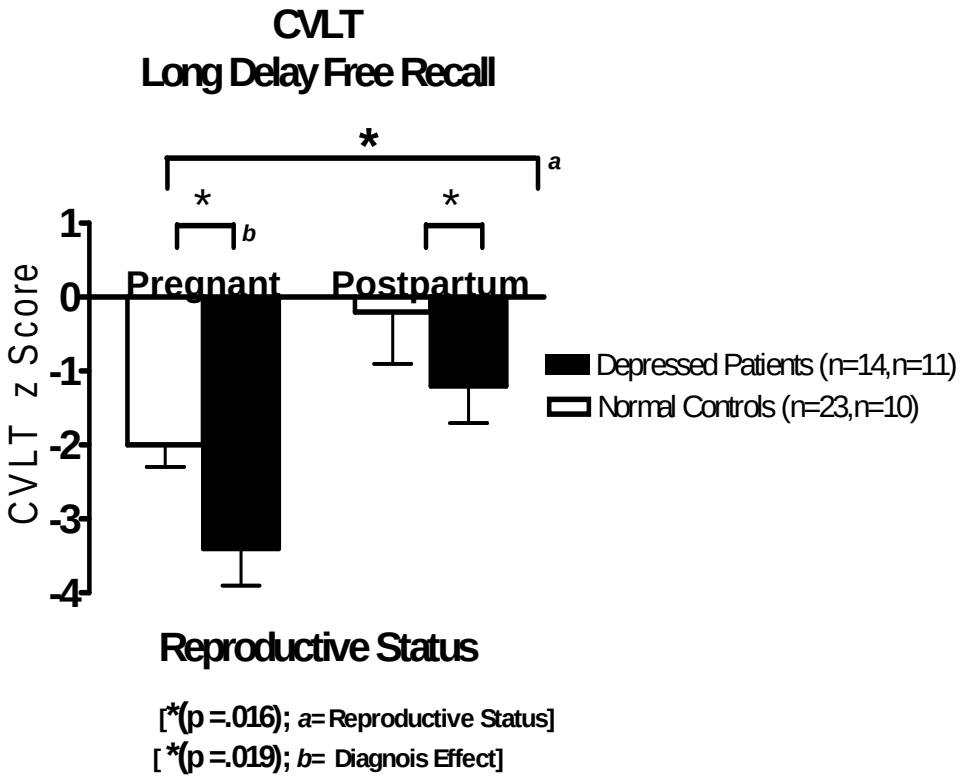

Figure 4: Mean (± SE) of California Verbal Learning Test (CVLT) Long Delay Free Recall (standardized score) in pregnant and postpartum women with and without major depression. Significant group differences were found for diagnosis and reproductive status, where depressed and pregnant women recalled fewer words than normal control and postpartum women.

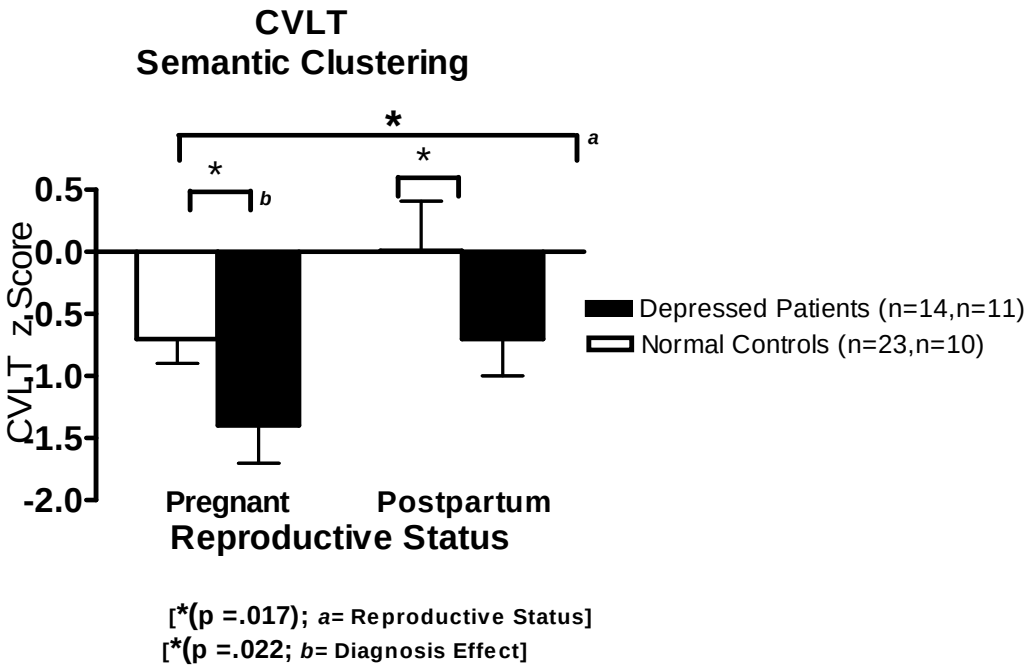

Figure 5: Mean (± SE) of California Verbal Learning Test Semantic Clustering (standardized score) in pregnant and postpartum women with and without major depression. Significant group differences were found for diagnosis and reproductive status, where depressed and pregnant women utilized semantic clustering strategy less often than normal control and postpartum women.

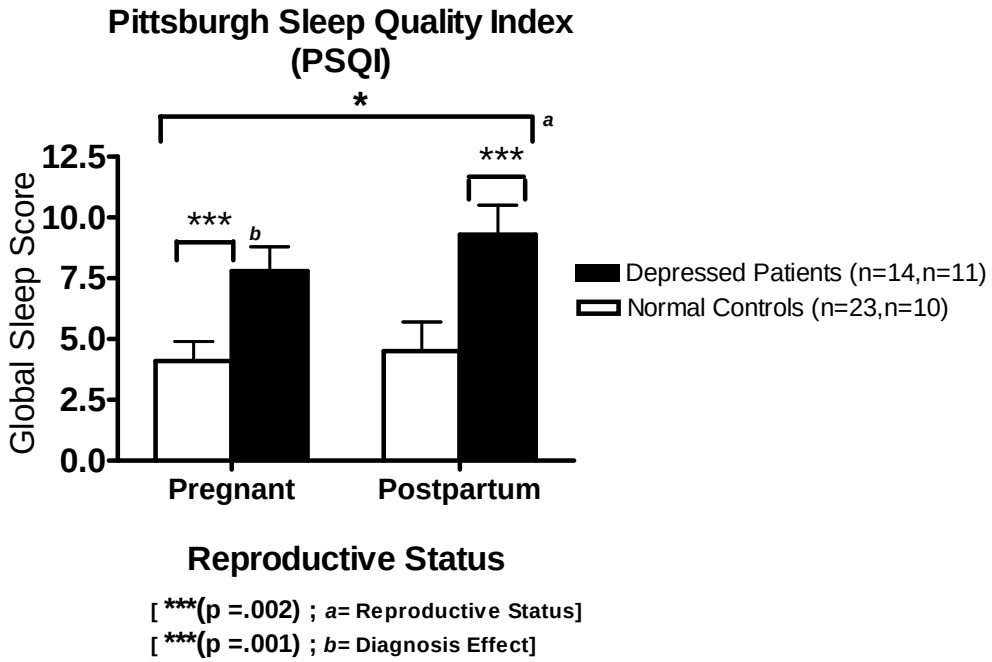

Figure 6: Mean score (± SE) of Pittsburgh Sleep Quality Index (PSQI) in pregnant and postpartum women with and without major depression. Significant group differences were found for diagnosis and reproductive status, where depressed and postpartum women reported poorer sleep quality (indicated by higher score on PSQI) compared to normal control and pregnant women.

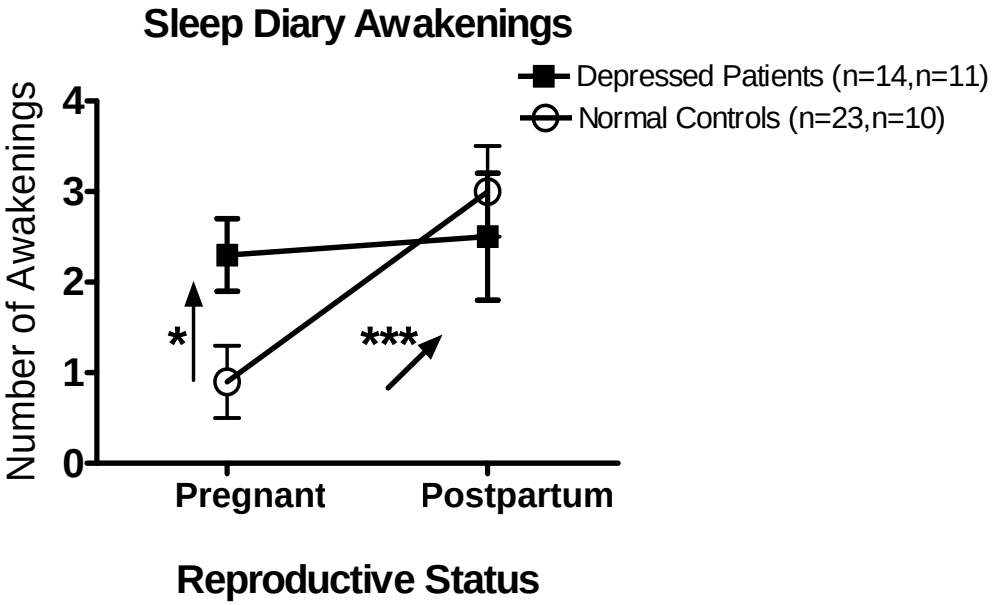

Figure 7: Mean (± SE) of Number of Awakenings on Sleep Diary on night prior to neurocognitive testing. Significant overall interaction and simple effects were found. In pregnant (but not postpartum) women, depressed patients reported more awakenings than normal women. In normal control (but not depressed) women, postpartum women reported more awakenings than pregnant women.

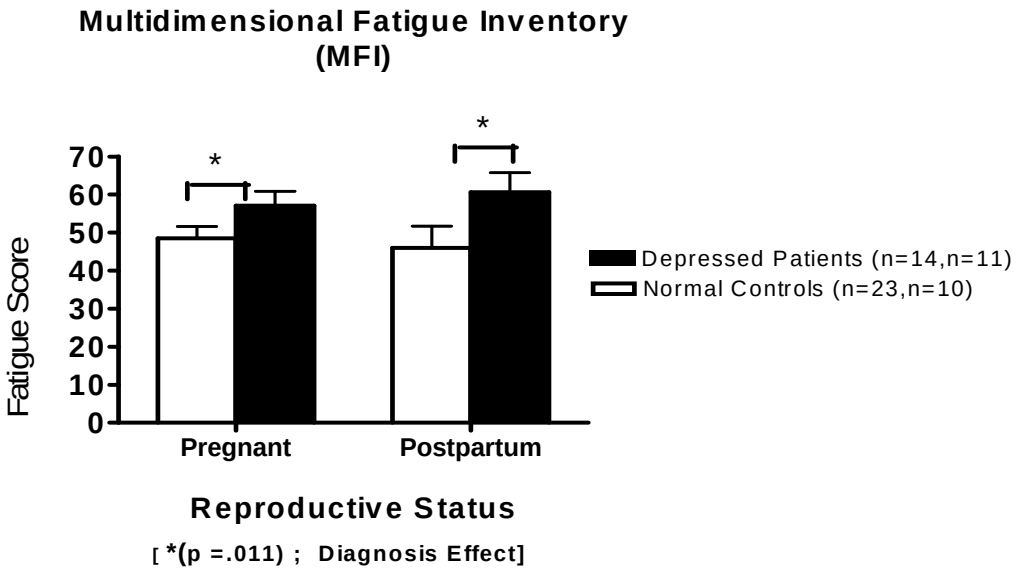

Figure 8: Mean score (± SE) of Multidimensional Fatigue Inventory (MFI) in pregnant and postpartum women with and without major depression. Significant group differences for diagnosis were found, where depressed women reported greater fatigue compared to normal control women.

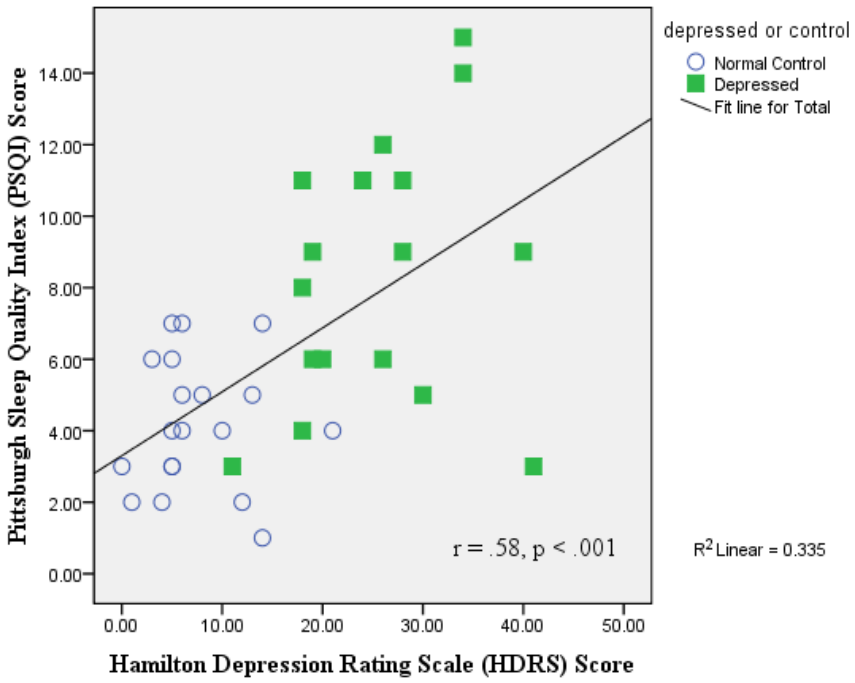

Figure 9: Scatterplot of Hamilton Depression Rating Scale (HDRS) and Pittsburgh Sleep Quality Index (PSQI). A positive association was found. That is, as scores on HDRS increased (indicating greater depression), scores on PSQI increased (indicating poorer subjective sleep quality).

Table 1: Demographic variables for pregnant and postpartum women with and without major depression. Group means (standard deviations) or percentages where indicated.

	Pregnant NC (*n*=23)	**Pregnant DP** (*n*=14)	**Postpartum NC** (*n*=10)	**Postpartum DP** (*n*=11)
Age	28.1 (5.3)	27.1 (5.4)	27.3 (3.3)	28.4 (6.8)
Education	15 (2.7)	14 (3.1)	15 (2.5)	15 (1.8)
Ethnicity (%)				
Caucasian	65	29	20	37
Hispanic	35	21	40	45
African American	0	21	10	0
Asian	0	29	30	18
Weeks preg/pp	24.9 (8.6)	24.8 (10.1)	23.9 (13.2)	22.2 (16.8)
Trimester (%)				
First (1-13 weeks)	20.8	25	28.6	33.3
Second (14-25 weeks)	29.2	25	14.3	33.3
Third (26+ weeks)	50	50	57.1	33.3
No. of children	0 (0.4)	1 (1.0)	2 (1.0)	2 (0.6)

Note. No significant group differences on any demographic variable *p*'s > .05

Table 2: Study Timeline

Week	Appointment	Length	Data Collected
Pre-week 1	Study Overview & Initial Telephone Screen	20-30 minutes	Inclusion/Exclusion criteria
Week 1	Intake Informed consent SCID, questionnaires, sleep log between visits	1-3 hours	Psychiatric & medical history, present diagnoses, mood, sleep, psychosocial, reproductive variables
Week 2	Memory Testing + Mood measures	1.5 - 2 hours	Memory performance, mood and fatigue variables

Table 3: Measures

TEST	DOMAIN(S)	CUT-OFF
Mood measures		
Hamilton Depression Rating Scale (HDRS)	Objective measure of depression	± 15
HDRS Addendum of SIGH-SAD	Atypical symptoms of depression	-
Hypomania Rating Scale	Mania symptoms	± 10
Beck Depression Inventory	Subjective depression	± 10
Beck Anxiety Inventory	Subjective anxiety	± 10
Edinburgh Postnatal Depression Scale	Subjective maternal depression	± 10
Neuropsychological measure		
California Verbal Learning Test	Verbal learning and memory	± 2 S.D.'s
Sleep measures		
Pittsburgh Sleep Quality Index	Global sleep quality	± 5
Sleep diary	Prospective subjective sleep	-
Multidimensional Fatigue Inventory	Fatigue	± 50
Horne-Östberg Questionnaire MEQ	Circadian preference	± 40

Table 4: Group means and standard deviations for mood measures in pregnant and postpartum women with and without major depression at time of intake.

	Pregnant NC (*n*=23)	**Pregnant DP** (*n*=14)	**Postpartum NC** (*n*=10)	**Postpartum DP** (*n*=11)
Hamilton Depression Rating Scale**	4.0 (2.8)	14.3 (5.2)	4.3 (3.7)	16.0 (3.1)
Hamilton Addendum (as part of SIGH-SAD)**	2.9 (1.6)	6.8 (2.1)	2.2 (1.5)	4.9 (3.2)
Hypomania Rating Scale*	1.3 (1.6)	2.2 (1.5)	1.2 (1.5)	4.1 (4.0)
Beck Depression Inventory**	5.9 (4.1)	15.5 (7.8)	4.0 (2.6)	20.9 (10.5)
Beck Anxiety Inventory**	6.6 (6.5)	15.2 (11.0)	2.4 (2.1)	14.1 (5.3)
Edinburgh Postnatal Depression Scale**	3.3 (2.4)	10.8 (4.0)	2.7 (2.3)	13.9 (2.3)

Note. * $p < .01$ and ** $p < .001$ for diagnosis (DP vs. NC)

Table 5: Group means and standard deviations for mood measures in pregnant and postpartum women with and without major depression at time of memory testing.

	Pregnant NC (*n*=23)	**Pregnant DP** (*n*=14)	**Postpartum NC** (*n*=10)	**Postpartum DP** (*n*=11)
Hamilton Depression Rating Scale**	4.3 (3.5)	15.6 (5.7)	4.8 (4.1)	18.0 (8.5)
Hamilton Addendum (as part of SIGH-SAD)**	2.4 (2.3)	7.8 (2.9)	2.3 (1.8)	7.1 (2.8)
Hypomania Rating Scale**	1.2 (1.3)	3.5 (2.5)	1.0 (1.6)	4.0 (3.7)
Beck Depression Inventory**	4.6 (2.7)	15.1 (8.5)	1.8 (2.4)	16.5 (7.4)
Beck Anxiety Inventory**	3.4 (3.3)	13.9 (9.6)	2.8 (3.5)	12.3 (8.5)
Edinburgh Postnatal Depression Scale**	2.1 (2.9)	10.2 (4.1)	3.0 (1.8)	12.4 (5.3)

Note. ** $p < .001$ for diagnosis (DP vs. NC)

Table 6: Group means and standard deviations for memory performance in pregnant and postpartum women with and without major depression.

	Pregnant NC (*n*=23)	**Pregnant DP** (*n*=14)	**Postpartum NC** (*n*=10)	**Postpartum DP** (*n*=11)
Verbal Learning & Memory				
CLVT Learning T1-T5	33.5 (14.8)	27.5 (13.1)	45.8 (19.8)	36.3 (12.5)
CVLT Short-delay free recall	-1.5 (1.4)	-2.1 (1.0)	-0.6 (2.1)	-0.7 (1.2)
CVLT Short-delay cued recall	-1.5 (1.0)	-2.1 (1.0)	-0.4 (1.3)	-0.7 (1.3)
CVLT Long-delay free recall	-2.0 (1.5)	-3.4 (1.3)	-0.2 (1.7)	-1.2 (1.7)
CVLT Long-delay cued recall	-2.0 (1.7)	-2.4 (1.5)	-1.0 (1.2)	-1.1 (0.8)
CVLT Perseveration errors	-0.3 (1.3)	-0.1 (0.9)	-0.8 (0.4)	0.3 (1.4)
CVLT Semantic clustering	-0.7 (0.9)	-1.4 (0.5)	0.0 (1.2)	-0.7 (0.7)

Table 7: Group means and standard deviations for sleep measures in pregnant and postpartum women with and without major depression.

	Pregnant NC (*n*=23)	**Pregnant DP** (*n*=14)	**Postpartum NC** (*n*=10)	**Postpartum DP** (*n*=11)
Pittsburgh Sleep Quality Index (PSQI)				
Index 1 – Sleep quality	0.4 (0.5)	1.3 (1.0)	1.2 (1.2)	1.8 (1.3)
Index 2 – Sleep latency	0.3 (0.5)	0.9 (0.8)	0.0 (0.0)	0.7 (0.5)
Index 3 – Sleep duration	0.5 (0.7)	0.2 (0.7)	0.5 (0.8)	1.3 (1.2)
Index 4 – Sleep efficiency	0.5 (0.5)	0.7 (0.9)	0.5 (0.5)	0.3 (0.8)
Index 5 – Sleep disturbance	1.4 (0.5)	2.1 (0.3)	1.0 (0.0)	1.7 (0.5)
Index 6 – Use of sleep medications	0.8 (0.5)	1.2 (0.4)	1.2 (0.4)	1.7 (1.0)
Index 7- Daytime dysfunction	0.3 (0.5)	1.4 (1.6)	0.2 (0.4)	1.8 (2.1)
PSQI Global Score	4.1 (2.1)	7.8 (2.3)	4.5 (1.5)	9.3 (5.3)
Sleep diary (night prior to testing)				
Lights out	22:54*h*	23:22*h*	23:06*h*	21:06*h*
Rise time	07:36*h*	08:09*h*	08:20*h*	05:54*h*
Sleep latency	20*m* (36)	18*m* (14)	12*m* (5)	46*m* (63)

Table 7: Group means and standard deviations for sleep measures in pregnant and postpartum women with and without major depression, Continued.

	Pregnant NC (*n*=23)	**Pregnant DP** (*n*=14)	**Postpartum NC** (*n*=10)	**Postpartum DP** (*n*=11)
Frequency of awakenings	0.9 (0.9)	2.3 (1.5)	3.0 (1.2)	2.5 (1.3)
Wake after sleep onset	7*m* (13.2)	37*m* (64)	38*m* (24)	40*m* (31)
Total Sleep Time	8*h* 15*m*	7*h* 52*m*	8*h* 24*m*	7*h* 22*m*
Nap time	14 *m* (40)	89 *m* (63)	70*m* (97)	0 m (0)
Multidimensional Fatigue Inventory				
MFI at Intake	45.4 (9.2)	57.0 (11.5)	51.8 (10.5)	57.7 (10.6)
MFI at NP testing	48.5 (12.5)	57.1 (11.4)	46.0 (6.0)	60.6 (14.2)
Horne-Östberg Morningness Eveningness Questionnaire	56.1 (10.0)	56.6 (6.0)	52.5 (10.6)	61.8 (7.0)

References

Abou-Saleh, M. T., Ghubash, R., Karim, L., Krymski, M., & Bhai, I. (1998). Hormonal aspects of postpartum depression. *Psychoneuroendocrinology, 23*(5), 465-475.

American Psychiatric Association. Diagnostic and Statistical Manual of Mental Disorders (4 ed.). (1994). Washington, D. C.: American Psychiatric Association.

American Psychiatric Association. DSM-II: Diagnostic and Statistical Manual of Mental Disorders. (1968). Washington, D. C.: American Psychiatric Association.

Appleby, L., Mortensen, P. B., & Faragher, E. B. (1998). Suicide and other causes of mortality after post-partum psychiatric admission. *The British Journal of Psychiatry, 173*, 209-211.

Asher, I., Kaplan, B., Modai, I., Neri, A., Valevski, A., & Weizman, A. (1995). Mood and hormonal changes during late pregnancy and puerperium. *Clinical and Experimental Obstetrics and Gynecology, 22*(4), 321-325.

Baildam, E. (1991). Doctor as mum. *British Medical Journal, 303*, 424.

Beck, A. T., Epstein, N., Brown, G., & Steer, R. A. (1988). An inventory for measuring clinical anxiety: psychometric properties. *Journal of Consulting and Clinical Psychology, 56*(6), 893-897.

Beck, A. T., & Steer, R. A. (1990). *Beck Anxiety Inventory Manual*. San Antonio, TX: The Psychological Corporation.

Beck, A. T., Ward, C. H., Mendelson, M., Mock, J., & Erbaugh, J. (1961). An inventory for measuring depression. *Archives of General Psychiatry, 4*, 561-571.

Beck, C. T. (1998). The effects of postpartum depression on child development: a meta-analysis. *Archives of Psychiatric Nursing, 12*(1), 12-20.

Bloch, M., Daly, R.C., & Rubinow, D.R. (2003). Endocrine factors in the etiology of postpartum depression. *Comprehensive Psychiatry, 44*, 234-246.

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*(3), 647-653.

Broadhead, W. E., Leon, A. C., Weissman, M. M., Barrett, J. E., Blacklow, R. S., Gilbert, T. T., Keller, M.B., Olfson, M., & Higgins, E.S. (1995). Development and validation of the SDDS-PC screen for multiple mental disorders in primary care. *Archives of Family Medicine, 4*(3), 211-219.

Buckwalter, J. G., Buckwalter, D. K., Bluestein, B. W., & Stanczyk, F. Z. (2001). Pregnancy and post partum: changes in cognition and mood. *Progress in Brain Research, 133,* 303-319.

Buckwalter, J. G., Stanczyk, F. Z., McCleary, C. A., Bluestein, B. W., Buckwalter, D. K., Rankin, K. P., & Goodwin, T.M. (1999). Pregnancy, the postpartum, and steroid hormones: effects on cognition and mood. *Psychoneuroendocrinology, 24*(1), 69-84.

Buckwater, J. G., Buckwater, D.K., Bluestein, B.W., & Stanczyk, F.Z. (2001). Pregnancy and postpartum: Changes in cognition and mood. *Progress in Brain Research, 133*, 303-319.

Burt, D. B., Zembar, M. J., & Niederehe, G. (1995). Depression and memory impairment: a meta-analysis of the association, its pattern, and specificity. *Psychological Bulletin, 117*(2), 285-305.

Buysse, D. J., Reynolds, C. F., 3rd, Monk, T. H., Berman, S. R., & Kupfer, D. J. (1989). The Pittsburgh Sleep Quality Index: a new instrument for psychiatric practice and research. *Psychiatry Research, 28*(2), 193-213.

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*(3), 158-164.

Cassens, G., Wolfe, L., & Zola, M. (1990). The neuropsychology of depressions. *The Journal of Neuropsychiatry and Clinical Neurosciences, 2*(2), 202-213.

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

Cohen, L. S., Altshuler, L. L., Harlow, B. L., Nonacs, R., Newport, D. J., Viguera, A. C., Suri, R., Burt, V.K., Hendrick, V., Reminick, A.M., Loughead, A., Vitonis, A.F., & Stowe, Z.N. (2006). Relapse of major depression during pregnancy in women who maintain or discontinue antidepressant treatment. *JAMA, 295*(5), 499-507.

Cohen, L. S., & Altshuler, L. (1997). Pharmacologic management of psychiatric illness during pregnancy and the postpartum period. *Psychiatry Clinical North America, 4*, 21-59.

Cohen, R. M., Weingartner, H., Smallberg, S. A., Pickar, D., & Murphy, D. L. (1982). Effort and cognition in depression. *Archives of General Psychiatry, 39*(5), 593-597.

Cooper, P., & Murray, L. (1997). Prediction, detection, and treatment of postnatal depression. *Archives of Disease in Childhood, 77*(2), 97-99.

Cornblatt, B. A., Lenzenweger, M. F., & Erlenmeyer-Kimling, L. (1989). The continuous performance test, identical pairs version: II. Contrasting attentional profiles in schizophrenic and depressed patients. *Psychiatry Research, 29*(1), 65-85.

Corwin, E. J., & Arbour, M. (2007). Postpartum fatigue and evidence-based interventions. *MCN The American Journal of Maternal Child Nursing, 32*(4), 215-220; quiz 221-212.

Cox, J. L., Holden, J. M., & Sagovsky, R. (1987). Detection of postnatal depression. Development of the 10-item Edinburgh Postnatal Depression Scale. *The British Journal of Psychiatry, 150*, 782-786.

Crawley, R. A., Dennison, K., & Carter, C. (2003). Cognition in pregnancy and the first year post-partum. *Psychology and Psychotherapy, 76*(Pt 1), 69-84.

Dalton, K. (1996). *Depression after delivery (3rd ed.).* Oxford: Oxford University Press.

de Groot, R. H., 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., Vuurman, E. F., Hornstra, G., & Jolles, J. (2006). Differences in cognitive performance during pregnancy and early motherhood. *Psychological Medicine, 36*(7), 1023-1032.

Delis, D. C., Kramer, J. H., Kaplan, E., & Ober, B. A. (1987). *The California Verbal Learning Test Manual, Research Edition, Adult Version*. San Antonio, Tx: The Psychological Corporation.

Diket, A. L., & Nolan, T. E. (1997). Anxiety and depression. Diagnosis and treatment during pregnancy. *Obstetrics and Gynecology Clinics of North America, 24*(3), 535-558.

Ditkoff, E. C., Crary, W. G., Cristo, M., & Lobo, R. A. (1991). Estrogen improves psychological function in asymptomatic postmenopausal women. *Obstetrics and Gynecology, 78*(6), 991-995.

Dunbar, G. C., & Lishman, W. A. (1984). Depression, recognition-memory and hedonic tone a signal detection analysis. *The British Journal of Psychiatry, 144*, 376-382.

Eidelman, A. I., Hoffmann, N. W., & Kaitz, M. (1993). Cognitive deficits in women after childbirth. *Obstetrics and Gynecology, 81*(5 (Pt 1)), 764-767.

Evans, J., Heron, J., Francomb, H., Oke, S., & Golding, J. (2001). Cohort study of depressed mood during pregnancy and after childbirth. *British Medical Journal, 323*(7307), 257-260.

First, M. B., Spitzer, R. L., Gibbon, M., & Williams, J. B. (1995). *Structured Clinical Interview for DSM-IV Axis I Disorders-Patient Edition (SCID-I/Pm, version 2.0).* Biometerics Research Dept., New York State Psychiatric Institute. New York.

Freedman, L. Z., Redlich, F. E., Eron, L. D., & Jackson, E. B. (1952). Training for childbirth; remembrance of labor. *Psychosomatic Medicine, 14*(6), 439-452.

Golinkoff, M., & Sweeney, J. A. (1989). Cognitive impairments in depression. *Journal of Affective Disorders, 17*(2), 105-112.

Goodman, S. H., & Gotlib, I. H. (1999). Risk for psychopathology in the children of depressed mothers: a developmental model for understanding mechanisms of transmission. *Psychological Review, 106*(3), 458-490.

Gotlib, I. H., Whiffen, V. E., Mount, J. H., Milne, K., & Cordy, N. I. (1989). Prevalence rates and demographic characteristics associated with depression in pregnancy and the postpartum. *Journal of Consulting and Clinical Psychology, 57*(2), 269-274.

Gureje, O., Ademola, A., & Olley, B. O. (2008). Depression and disability: comparisons with common physical conditions in the Ibadan study of aging. *Journal of the American Geriatrics Society, 56*(11), 2033-2038.

Halbreich, U. (2000). Gonadal hormones, reproductive age, and women with depression. *Archives of General Psychiatry, 57*(12), 1163-1164.

Halligan, S. L., Murray, L., Martins, C., & Cooper, P. J. (2007). Maternal depression and psychiatric outcomes in adolescent offspring: a 13-year longitudinal study. *Journal of Affective Disorders, 97*(1-3), 145-154.

Hamilton, M. (1967). Development of a rating scale for primary depressive illness. *The British Journal of Social and Clinical Psychology, 6*(4), 278-296.

Hampson, E. (1990). Estrogen-related variations in human spatial and articulatory-motor skills. *Psychoneuroendocrinology, 15*(2), 97-111.

Harris, N. D., Deary, I.J., Harris, M.B., Lees, M.M., & Wilson, J.A. (1996). Peripartal cognitive impairment: Secondary to depression? *British Journal of Health Psychology, 1*, 127-136.

Haug, H. J., & Fahndrich, E. (1990). Diurnal variations of mood in depressed patients in relation to severity of depression. *Journal of Affective Disorders, 19*(1), 37-41.

Heaton, R. K., Miller, S.W., Taylor, M.J., & Grant, I. (2004). *Revised comprehensive norms for an expanded Halstead-Reitan battery: Demographically adjusted neuropsychological norms for African American and Caucasian adults*. Lutz, FL: Par Psychological Assessment Resources.

Horne, J. A., & Ostberg, O. (1976). A self-assessment questionnaire to determine morningness-eveningness in human circadian rhythms. *International Journal of Chronobiology, 4*(2), 97-110.

Ilsley, J. E., Moffoot, A. P., & O'Carroll, R. E. (1995). An analysis of memory dysfunction in major depression. *Journal of Affective Disorders, 35*(1-2), 1-9.

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*(2), 80-87.

Jarrahi-Zadeh, A., Kane, F. J., Jr., Van de Castlf, R. L., Lachenbruch, P. A., & Ewing, J. A. (1969). Emotional and cognitive changes in pregnancy and early puerperium. *The British Journal of Psychiatry, 115*(524), 797-805.

Joffe, H., Hall, J. E., Gruber, S., Sarmiento, I. A., Cohen, L. S., Yurgelun-Todd, D., & Martin, K.A. (2006). Estrogen therapy selectively enhances prefrontal cognitive processes: a randomized, double-blind, placebo-controlled study with functional magnetic resonance imaging in perimenopausal and recently postmenopausal women. *Menopause, 13*(3), 411-422.

Johanson, R., Chapman, G., Murray, D., Johnson, I., & Cox, J. (2000). The North Staffordshire Maternity Hospital prospective study of pregnancy-associated depression. *Journal of Psychosomatic Obstetrics and Gynaecology, 21*(2), 93-97.

Kane, F. J., Jr., Harman, W. J., Jr., Keeler, M. H., & Ewing, J. A. (1968). Emotional and cognitive disturbance in the early puerperium. *The British Journal of Psychiatry, 114*(506), 99-102.

Keenan, P. A., Stern, R. A., Janowsky, D. S., & Pedersen, C. A. (1992). Psychological aspects of premenstrual syndrome. I: Cognition and memory. *Psychoneuroendocrinology, 17*(2-3), 179-187.

Keenan, P. A., Yaldoo, M.S., Stress, M.E., Fuerst, D.R., & Ginsburgh, K.A. (1998). Explicit memory in pregnant women. *American Journal of Obstetrics and Gynecology, 179*(3), 731-737.

Kendell, R. E., Chalmers, J. C., & Platz, C. (1987). Epidemiology of puerperal psychoses. *The British Journal of Psychiatry, 150*, 662-673.

Kessler, R. C., Barber, C., Birnbaum, H. G., Frank, R. G., Greenberg, P. E., Rose, R. M., Simon , G.E., & Wang, P. (1999). Depression in the workplace: effects on short-term disability. *Health Affairs (Project Hope), 18*(5), 163-171.

Kessler, R. C., McGonagle, K. A., Swartz, M., Blazer, D. G., & Nelson, C. B. (1993). Sex and depression in the National Comorbidity Survey. I: Lifetime prevalence, chronicity and recurrence. *Journal of Affective Disorders, 29*(2-3), 85-96.

Leibenluft, E., & Wehr, T. A. (1992). Is sleep deprivation useful in the treatment of depression? *The American Journal of Psychiatry, 149*(2), 159-168.

Lurie, S., Gidron, Y., Piper, I., Ben-Aroya, Z., Sadan. O., Boaz, M., & Glezerman, M. (2005). Memory performance in late pregnancy and erthrocyte indices. *Journal for Society for Gynecologic Investigation, 12*(4), 293-296.

Maki P.M. & Rosenbaum RS. (2002). Implicit memory varies across the menstrual cycle: estrogen effects in young women. *Neuropsychologica, 40*(5), 518-529.

Manber, R., Blasey, C., Arnow, B., Markowitz, J. C., Thase, M. E., Rush, A. J., Dowling, F., Koscis, J., Trivedi, M., & Keller, M.B. (2005). Assessing insomnia severity in depression: comparison of depression rating scales and sleep diaries. *Journal of Psychiatric Research, 39*(5), 481-488.

Marcus, S. M. (2009). Depression during pregnancy: rates, risks and consequences--Motherisk Update 2008. *The Canadian Journal of Clinical Pharmacology, 16*(1), e15-22.

Marcus, S. M., Barry, K. L., Flynn, H. A., Tandon, R., & Greden, J. F. (2001). Treatment guidelines for depression in pregnancy. *International Journal of Gynaecology and Obstetrics, 72*(1), 61-70.

Massman, P. J., Delis, D. C., Butters, N., Dupont, R. M., & Gillin, J. C. (1992). The subcortical dysfunction hypothesis of memory deficits in depression:

neuropsychological validation in a subgroup of patients. *Journal of Clinical and Experimental Neuropsychology, 14*(5), 687-706.

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 A, Human Experimental Pyschology 53*(3), 729-740.

Merriam, E. P., Thase, M. E., Haas, G. L., Keshavan, M. S., & Sweeney, J. A. (1999). Prefrontal cortical dysfunction in depression determined by Wisconsin Card Sorting Test performance. *The American Journal of Psychiatry, 156*(5), 780-782.

Mialet, J. P., Pope, H. G., & Yurgelun-Todd, D. (1996). Impaired attention in depressive states: a non-specific deficit? *Psychological Medicine, 26*(5), 1009-1020.

Moffoot, A. P., O'Carroll, R. E., Bennie, J., Carroll, S., Dick, H., Ebmeier, K. P., & Goodwin, G.M. (1994). Diurnal variation of mood and neuropsychological function in major depression with melancholia. *Journal of Affective Disorders, 32*(4), 257-269.

Monk, T. H., Reynolds, C. F., Kupfer, D. J., Buysse, D. J., Coble, P. A., Hayes, A. J., Machen, M.A., Petrie, S.R., & Ritenour, A.M. (1994). The Pittsburgh Sleep Diary. *Journal of Sleep Research, 3*(2), 111-120.

Morris, N., Toms, M., Easthope, Y., & Biddulph, J. (1998). Mood and cognition in pregnant workers. *Applied Ergonomics, 29*(5), 377-381.

Murray, C. J. L., & Lopez, A. D. (1996). Alternative visions of the future: projecting mortality and disability, 1990–2020. In C. J. L. Murray & A. D. Lopez (Eds.), *The Global Burden of Disease: A Comprehensive Assessment of Mortality and Disability from Diseases, Injuries, and Risk Factors in 1990 and Projected to 2020* (pp. 325–395). Boston: Harvard University Press.

Murray, L. (1992). The impact of postnatal depression on infant development. *Journal of Child Psychology and Psychiatry, and Allied Disciplines, 33*(3), 543-561.

Murray, L., Cooper, P., & Hipwell, A. (2003). Mental health of parents caring for infants. *Archives of Womens Mental Health, 6 Suppl 2*, S71-77.

Murray, L., Halligan, S. L., Adams, G., Patterson, P., & Goodyer, I. M. (2006). Socioemotional development in adolescents at risk for depression: the role of maternal depression and attachment style. *Developmental Psychopathology, 18*(2), 489-516.

Murray, L., Sinclair, D., Cooper, P., Ducournau, P., Turner, P., & Stein, A. (1999). The socioemotional development of 5-year-old children of postnatally depressed mothers. *Journal of Child Psychology and Psychiatry, and Allied Disciplines, 40*(8), 1259-1271.

Murray, L., Woolgar, M., Cooper, P., & Hipwell, A. (2001). Cognitive vulnerability to depression in 5-year-old children of depressed mothers. *Journal of Child Psychology and Psychiatry, and Allied Disciplines, 42*(7), 891-899.

Naismith, S. L., Norrie, L., Lewis, S. J., Rogers, N. L., Scott, E. M., & Hickie, I. B. (2009). Does sleep disturbance mediate neuropsychological functioning in older people with depression? *Journal of Affective Disorders, 116(1-2)*, 139-43.

Nott, P. N., Franklin, M., Armitage, C., & Gelder, M. G. (1976). Hormonal changes and mood in the puerperium. *The British Journal of Psychiatry, 128*, 379-383.

O'Hara, M. W. (1986). Social support, life events, and depression during pregnancy and the puerperium. *Archives of General Psychiatry, 43*(6), 569-573.

O'Hara, M. W., Neunaber, D. J., & Zekoski, E. M. (1984). Prospective study of postpartum depression: prevalence, course, and predictive factors. *Journal of Abnormal Psychology, 93*(2), 158-171.

Parry, B. L. (2003). Management of depression and psychoses during pregnancy and the puerperium. In R. K. Creasy & R. Resnick (Eds.), *Maternal-Fetal Medicine. Principles and Practice* (5 ed., pp. 1193-1200). Philadelphia PA: Elsevier Science.

Parry, B. L. (2009). Assessing risk and benefit: to treat or not to treat major depression during pregnancy with antidepressant medication. *The American Journal of Psychiatry, 166*(5), 512-514.

Parry, B. L., Sorenson, D. L., Meliska, C. J., Basavaraj, N., Zirpoli, G. G., Gamst, A., et al. (2003). Hormonal basis of mood and postpartum disorders. *Current Womens Health Reports, 3*(3), 230-235.

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

Phillips, S. M., & Sherwin, B. B. (1992). Variations in memory function and sex steroid hormones across the menstrual cycle. *Psychoneuroendocrinology, 17*(5), 497-506.

Porterfield, T., Cook, M., Deary, I. J., & Ebmeier, K. P. (1997). Neuropsychological function and diurnal variation in depression. *Journal of Clinical and Experimental Neuropsychology, 19*(6), 906-913.

Poser, C. M., Kassirer, M. R., & Peyser, J. M. (1986). Benign encephalopathy of pregnancy. Preliminary clinical observations. *Acta Neurologica Scandanavia, 73*(1), 39-43.

Resnick, A., Perry, W., Parry, B., Mostofi, N., & Udell, C. (1998). Neuropsychological performance across the menstrual cycle in women with and without Premenstrual Dysphoric Disorder. *Psychiatry Research, 77*(3), 147-158.

Robinson, G. E., & Stewart, D.E. (1987). Postpartum psychiatric disorders. *Canadian Medical Association Journal, 134*, 31-37.

Rofe, Y., & Algom, D. (1985). Accuracy of remembering postdelivery pain. *Perceptual and Motor Skills, 60*(1), 99-105.

Rosenthal, N. E., & Heffernan, M.M. (1986). Bulimia, carbohydrate craving and depression: A central connection? In W. J. Wurtman RJ (Ed.), *Nutrition and Brain* (Vol. 7). New York: Raven Press.

Schmidt, C., Collette, F., Leclercq, Y., Sterpenich, V., Vandewalle, G., Berthomier, P., Berthomier, C., Phillips, C., Tinquely, G., Darsaud, A., Gais, S., Schabus, M., Desseilles, M., Dan-Vu, T.T., Salmon, E., Balteau, E.., Dequeidre, C., Luxen, A., Maquet, P., Cajochen, C., & Peigneux, P.(2009). Homeostatic sleep pressure and responses to sustained attention in the suprachiasmatic area. *Science, 324*(5926), 516-519.

Schneider, R. A. (1998). Reliability and validity of the Multidimensional Fatigue Inventory (MFI-20) and the Rhoten Fatigue Scale among rural cancer outpatients. *Cancer Nursing, 21*(5), 370-373.

Schneider, Z. (1989). Cognitive performance in pregnancy. *The Australian Journal of Advanced Nursing, 6*(3), 40-47.

Segal, D. L., Hersen, M., & Van Hasselt, V. B. (1994). Reliability of the Structured Clinical Interview for DSM-III-R: an evaluative review. *Comprehensive Psychiatry, 35*(4), 316-327.

Sharp, K., Brindle, P. M., Brown, M. W., & Turner, G. M. (1993). Memory loss during pregnancy. *British Journal of Obstetrics and Gynaecology, 100*(3), 209-215.

Shear, M. K., Greeno, C., Kang, J., Ludewig, D., Frank, E., Swartz, H. A., & Hanekamp, M. et al. (2000). Diagnosis of nonpsychotic patients in community clinics. *The American Journal of Psychiatry, 157*(4), 581-587.

Sherwin, B. B. (1994). Estrogenic effects on memory in women. *Annals of NY Academic Sciences, 743*, 213-230.

Sherwin, B. B. (2006). Estrogen and cognitive aging in women. *Neuroscience, 138*(3), 1021-1026.

Smets, E. M., Garrsen, B., Bonke, B., & De Haes, J.C. (1995). The Multidimensional Fatigue Inventory (MFI) psychometric qualities of an instrument to assess fatigue. *Sleep, 39*(3), 315-325.

Sobin, C., & Sackeim, H. A. (1997). Psychomotor symptoms of depression. *The American Journal of Psychiatry, 154*(1), 4-17.

Stein, G. S. (1980). The pattern of mental change and body weight change in the first post-partum week. *Journal of Psychosomatic Research, 24*(3-4), 165-171.

Steiner, M. (1990). Postpartum psychiatric disorders. *Canadian Journal of Psychiatry, 35*(1), 89-95.

Sugawara, M., Sakamoto, S., Kitamura, T., Toda, M. A., & Shima, S. (1999). Structure of depressive symptoms in pregnancy and the postpartum period. *Journal of Affective Disorders, 54*(1-2), 161-169.

Swain, A. M., O'Hara, M. W., Starr, K. R., & Gorman, L. L. (1997). A prospective study of sleep, mood, and cognitive function in postpartum and nonpostpartum women. *Obstetrics and Gynecology, 90*(3), 381-386.

Sweeney, J. A., Strojwas, M. H., Mann, J. J., & Thase, M. E. (1998). Prefrontal and cerebellar abnormalities in major depression: evidence from oculomotor studies. *Biological Psychiatry, 43*(8), 584-594.

Taylor, B. P., Bruder, G.E., Stewart, J.W., McGrath, P.J., Halperin, J., Ehrlichman, H., & Quitkin, F.M. (2006). Psychomotor slowing as a predictor of Fluoxetine nonresponse in depressed outpatients. *American Journal of Psychiatry, 163*(1), 73-78.

Treadway, C. R., Kane, F. J., Jr., Jarrahi-Zadeh, A., & Lipton, M. A. (1969). A psychoendocrine study of pregnancy and puerperium. *The American Journal of Psychiatry, 125*(10), 1380-1386.

Veiel, H. O. (1997). A preliminary profile of neuropsychological deficits associated with major depression. *Journal of Clinical and Experimental Neuropsychology, 19*(4), 587-603.

Webb, D. A., Bloch, J. R., Coyne, J. C., Chung, E. K., Bennett, I. M., & Culhane, J. F. (2008). Postpartum physical symptoms in new mothers: their relationship to functional limitations and emotional well-being. *Birth, 35*(3), 179-187.

Wefelmeyer, T., & Kuhs, H. (1996). Diurnal mood variation in melancholic patients and healthy controls. *Psychopathology, 29*(3), 184-192.

Weissman, M. M., Bland, R., Joyce, P. R., Newman, S., Wells, J. E., & Wittchen, H. U. (1993). Sex differences in rates of depression: cross-national perspectives. *Journal of Affective Disorders, 29*(2-3), 77-84.

Weissman, M. M., Bland, R. C., Canino, G. J., Faravelli, C., Greenwald, S., Hwu, H. G., Joyce, P.R., Karam, E.G,. Lee, C.K., Lellouch, J., Lépine, J.P., Newman, S.C., Rubio-Stipec, M., Wells, J.E., Wickramaratne, P.J., Wittchen, H., & Yeh, E.K. (1996). Cross-national epidemiology of major depression and bipolar disorder. *JAMA, 276*(4), 293-299.

Weissman, M. M., & Klerman, G. L. (1977). The chronic depressive in the community: unrecognized and poorly treated. *Comprehensive Psychiatry, 18*(6), 523-532.

Weissman, M. M., Wickramaratne, P., Nomura, Y., Warner, V., Pilowsky, D., & Verdeli, H. (2006). Offspring of depressed parents: 20 years later. *The American Journal of Psychiatry, 163*(6), 1001-1008.

Welch, J. (1991). Labouring brains. *British Medical Journal, 303*, 253.

Williams, J. B., Link, M. J., Rosenthal, N. E., Amira, L., & Terman, M. (1994). *Structured Interview Guide for the Hamilton Depression Rating Scale, Seasonal Affective Disorders Version (SIGH-SAD), revised edition*. New York: New York Psychiatric Institute.

Wisner, K. L., Sit, D. K., Hanusa, B. H., Moses-Kolko, E. L., Bogen, D. L., Hunker, D. F., Perel, J.M., Jones-Ivy, S., Bodnar, L.M., & Singer, L.T. (2009). Major depression and antidepressant treatment: impact on pregnancy and neonatal outcomes. *The American Journal of Psychiatry, 166*(5), 557-566.

Yalom, I. D., Lunde, D. T., Moos, R. H., & Hamburg, D. A. (1968). "Postpartum blues" syndrome. A description and related variables. *Archives of General Psychiatry, 18*(1), 16-27.

Zonana, J. G., J.M. (2005). The neurobiology of postpartum depression. *CNS Spectrums, 10*(10), 792-806.