MATERNAL COGNITIVE FUNCTIONING IN PREGNANCY AND ITS ASSOCIATION WITH GESTATION, ENDOCRINE FACTORS AND FETAL SEX: A LONGITUDINAL STUDY IN WOMEN FROM EARLY PREGNANCY TO THE POSTPARTUM PERIOD

by

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ABSTRACT

Research addressing the effects of maternal cognitive changes during pregnancy has yielded equivocal findings with both confirmatory and negative results appearing fairly equally in the literature. In an attempt to evaluate and further test this phenomena, 45 women where tracked from early pregnancy until postnatal resumption of menses. An age and education matched control group of 45 non-pregnant women were tested concurrently. At each of the five test sessions participants completed a battery of cognitive tests. Results showed no effect of pregnancy on any of the dependent measures, with pregnant women performing no worse than control women on the nine cognitive tasks administered. One possible explanation for this negative finding (and the research ambiguity in this area) could be linked to the sex of the fetus. When fetal sex was considered, a selective and persistent effect on maternal cognitive function was observed. Those women pregnant with sons consistently outperformed women pregnant with daughters on the tests of working memory. On several other cognitive tests fetal sex was unrelated to maternal performance. This effect was evident from the first test session and persisted until the final session and was unrelated to sleep, mood and demographic measures. This result suggests either a fetal-derived factor that differs in type or concentration between male and female fetuses may influence the mothers' cognition both during pregnancy and into the postnatal phase. Or, alternatively, qualities inherent to the mother may be related to both her propensity to deliver a specific sex and her cognitive profile. Both possible explanations are discussed.

DEDICATION

Research is Me-search

To Bianca, whom I find wholly responsible for my inability to remember the definition of "rate limiting factor" on the Neuroscience 500 final exam at UBC, and my lousy grade in the course. You would be delivered at Royal Columbian Hospital just three short weeks later.

And to my Alex, who with a degree dedication already under your belt, despite what I may say, I promise I will never give you away in the supermarket checkout line.

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ꕥ

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ANALYSIS 1: INTRODUCTION

Sex Hormones and Cognition

When Voltaire was asked why no woman has even written a tolerable tragedy,

"Ah (said the Patriarch) the composition of a tragedy requires testicles."

Letter from Byron to John Murray
2 April 1817

Mammalian Gonadal Hormones

"As the French say, there are three sexes – men, women and clergymen..."

Rev. Sydney Smith
(1771-1845)

Steroid hormones represent a distinct hormonal subclass. These fat-soluble secretory products are derived from a cholesterol precursor by selective enzymatic action. The estrogens, androgens, corticosteroids and progesterone represent the four major classes of steroids, biochemically identified by a characteristic four ring molecular structure (Nelson, 2000).

In mammals, the gonads, adrenals and placenta are the major steroidogenic organs, differentially secreting the sex hormones. The adrenals primarily synthesize and secrete corticosteroids and the androgens androstenedione and dehydroepiandrosterone (DHEA), while the gonads secrete the remaining three steroids in this class. Although steroidogenesis of androgens, progesterone and estrogens occurs in both the male and female gonads, they are differentially secretory for these

hormones. The testes primarily produce the androgen testosterone, and to a lesser extent dihydrotestosterone and androstenedione. The estrogens and progesterone are the major products of the ovaries (Resko, 1985).

Although ovaries secrete the estrogens, androgens are their obligate precursors. By the process of aromatization, specific enzymes present in the ovaries convert testosterone and androstenedione to one of the three estrogen subtypes: estriol, estradiol or estrone (Clemens & Weaver, 1985). Thus, although the ovaries synthesize significant quantities of androgens, these are generally converted to estrogens prior to release. 17β-estradiol is the most potent estrogen in the vertebrate nervous system (Whalen, Yahr & Luttge, 1985). Progesterone is secreted both by the ovaries and the placenta (Bazer, 1998).

Steroid Hormones and Cognition

It is generally agreed the same sex hormones that are responsible for prenatal physical sexual differentiation and pubertal changes in mammals also influences brain development and neural sexual differentiation (Breedlove, 1992; Nelson, 2000). The effects of gonadal sex hormones have been loosely categorized into two developmental stages: (1) Organizational effects of sex hormones are those effects that permanently change physiological structure and function. They are dependent on early developmental critical periods and serve to coordinate sexual differentiation of neural and somatic tissues. (2) Activational effects are more transient. These effects are generally seen in adulthood and come and go, dependent on the presence or absence of a particular gonadal hormone. Activational effects are also reliant on earlier

organizational effects, where prenatal prior exposure determines the range of potential activational options (Nelson, 2000). While adhering to a rigid dichotomization of steroidal action has been questioned (Stewart, 1988; Williams, 1986) it remains a useful heuristic in understanding steroidal mechanisms of action.

Sex Differences in Behaviour

Behavioural sex differences have been observed across a number of species including humans (Bachevalier, Hagger & Bercu, 1989; Beatty, 1984; Collins & Kimura, 1997; Gaulin & Fitzgerald, 1986; Maccoby & Jacklin, 1974; Michael & Zumpe, 1998; Roof & Haverns, 1992). To evaluate the contributions of sex steroids in these differences, research has addressed how men and women perform on tasks that emphasize cognitive and problem solving skills. Performance on these types of tasks has been shown to vary with circulating changes in gonadal steroid profiles (Hampson, 1990b; Hampson & Kimura, 1988; Kampen & Sherwin, 1994; Van Goozen, Cohen-Kettenis, Gooren, & Frijda, 1995).

Cognitive Tasks Performed Better by Men

Some of the largest sex differences are seen in tasks related to spatial skills and abilities. The concept of "spatial cognition" is a broad term with multiple components and various interpretations (Eliot & Smith, 1983). This has made it difficult to formally define, but it does seem to be related to the ability of an individual to perform mental operations on features, phenomena or locations distributed in external and/or cognitive space. This

would include any cognitive or physical manipulation of real or imagined objects such as map navigation, targeting abilities and object orientation/visualization.

Factor-analytic studies of psychometrically measured spatial abilities have suggested two broad classes: Spatial visualization and spatial orientation (McGee, 1979). Visualization is the ability to manipulate objects in cognitive space resulting in configurational changes to the object. Folding, turning and twisting of an object would be examples of this. Orientation refers to the ability to correct for, and remain unconfused by spatial configurational changes. Mental rotation tasks and route learning tests are examples of spatial orientation tasks.

Research addressing sex differences in spatial abilities has been carried out since at least the middle of the last century (Maccoby, 1966; Witkin, 1949). The largest and most reliable sexual dimorphisms in spatial abilities are seen in tasks of targeting accuracy (such as throwing) and spatial orientation (Kimura, 1999). When compared to women, men are significantly more accurate when required to toss a small Velcro-covered ball (Hall & Kimura, 1995) or dart (Watson & Kimura, 1989) at a bulls eye target. Males are also better at intercepting and deflecting projectiles launched at them from multiple locations (Watson & Kimura, 1991). Despite the inherent differences in these two types of tasks (targeting and deflecting), they do share similar spatial processing loads, since good performance on both tasks requires the accurate localization of a point in space. Moreover, it has been suggested the spatial tests that directly involve a motor output may have superior ecological validity over paper and pencil tasks since the ultimate role of spatial abilities would be to guide and modify overt behaviour (Watson & Kimura, 1991). The effect of superior male spatial processing persists even when

height, weight, reaction time and sports history variables are all held constant (Hall & Kimura, 1995; Watson & Kimura, 1991).

Like targeting and intercepting tasks, spatial orientation skills also show a significant male advantage (Collins & Kimura, 1997; Watson & Kimura, 1991; Wilson, De Fries, McClearn & Vandenberg, 1975). Both pencil and paper and "real world" versions have been developed. One of the more common paper and pencil tasks requires a participant to identify from a set of choices, the new orientation of a complex figure that has been rotated on its axis (Vandenberg & Kuse, 1978). The Viewfinding test is a novel "real world" example of spatial orientation (Watson & Kimura, 1991). This test requires the subject to look at a photograph of a small object and decide on the location of the camera that took the photo. Men outperform women on both versions of these spatial orientation tasks (Collins & Kimura, 1997; Watson & Kimura, 1991; Wilson, De Fries, McClearn & Vandenberg, 1975).

Consistent with male spatial superiority, men also outperform women on tasks of spatial navigation. When required to manoeuvre a stylus through a two-dimensional maze drawing, men perform the task faster and more accurately than women (Galea & Kimura, 1993). Additional "real world" evidence comes from a more recent study that evaluated spatial performance using a 3-dimensional computer generated maze as the testing apparatus. Participants were required to escape from this virtual reality maze with the escape latency being the dependent measure. On average, the men in this study escaped the maze in two minutes and 22 seconds, while it took women an average of three minutes and 16 seconds to find their way out (Gron, Wunderlich, Spitzer, Tomczak & Riepe, 2000).

Research suggests the navigational aspects of the male spatial advantage may be due in part to differential strategies used by men and women when solving spatial tasks. When presented with a test that required a participant to traverse a route or deliver directions, men and women use different spatial cues. Women tend to use landmarks such as buildings, structures or landscape features as referents, while men use compass cardinal points or geometric directions. This suggests men and women employ different cognitive strategies for solving spatial tasks (Galea & Kimura, 1993; Moffat, Hampson & Hatzipantelis, 1998).

Individuals with naturally occurring endocrinological anomalies provide researchers with the opportunity to further examine the cognitive effects of specific gonadal hormones. Congenital Adrenal Hyperplasia (CAH) is a genetic disorder characterized by excessive adrenal steroidogenesis. Serum levels of the androgen androstenedione dramatically exceed normal titers in children with this disorder (New 1995). Due to androgenic organizational effects affected girls are often born with masculinized genitalia provoking early postnatal diagnosis. Once identified, these girls generally undergo corrective surgery as infants and are placed on remedial hormone therapy, which reduces androstenedione levels (Baskin, 1987). These prenatally masculinized girls provide researchers with a unique opportunity to evaluate the organizational effects of androgens independent of activational effects. Thus, subsequent behaviours that differ from unaffected girls may be, in part causally linked to early androgenic influences (Berenbaum, Duck & Bryk, 2000; Kimura, 1999).

CAH girls show patterns of spatial performance similar to that of their male siblings. When girls with this disorder were tested as children on a variety of tasks including tests of spatial ability, CAH girls scored significantly higher than their sisters on

the spatial tasks. The spatial tests on which these girls show enhanced abilities include imaginal rotation tasks, spatial visualization tasks and disembedding tasks. This latter paper and pencil task requires a subject to find a geometric shape hidden within a complex figure (Kimura, 1999). Intelligence quotient tests did not differ across the groups indicating the superior spatial performance of the CAH girls was not due to higher general intelligence (Hampson, Rovet & Altmann, 1998; Resnick, Berenbaum, Gottesmann & Bouchard, 1986). The enhanced performance of these girls on tasks that generally confer a male advantage suggests to researchers the spatial advantage seen in males may be linked to the early organizational effects of androgens (Berenbaum, Duck & Bryk, 2000; Kimura, 1999).

Cognitive Tasks Performed Better by Women

On tasks requiring fine distal motor skills and speeded dexterity women consistently outperform men, although this statistical effect is smaller than the male spatial advantage (Kimura, 1999). The test that has often been used to test this skill is the Purdue pegboard. This task requires a subject to place as many wooden pegs as possible into small linearly arranged holes within a specific time frame. Thus, number of pegs inserted is the dependent variable (Purdue Pegboard Examiners Manual, (1987), NCS: London House). A variation of this task requires the participant to place a small ring over each inserted peg. Women outperform men on both versions of this task (Purdue Pegboard Examiners Manual, (1987), NCS: London House). In addition, when required to make fine distal motor movements such as bending only one finger from the middle knuckle (Kimura & Vanderwolf, 1970), or performing a sequence of finger

movements at once (Nicholson & Kimura, 1996), women are also superior; an effect that persists even when finger size is controlled for (Hall & Kimura, 1995; Nicholson & Kimura, 1996).

Of the spatial skills studied which generally show a male advantage, one type of spatial skill seems to consistently favour women. Tests designed to evaluate spatial location memory require subjects to recall the position of objects previously laid out in a large array. Women can locate the prior position of the object with greater accuracy than their male counterparts. (Eals & Silverman, 1994; James & Kimura, 1997). The same female advantage was also evident when participants were required to locate and match pairs of cards previously scrambled and laid out facedown in a large array (McBurney, Gaulin, Devineni & Adams, 1997).

A reliable female favouring sex difference is found on tests of verbal function. These types of tasks include verbal fluency tests, which require subjects to complete a word in the presence of some linguistic constraint. For example, "Name all the words you can think of beginning with f." In addition, women are also better spellers (Feingold, 1988; Hyde & Lynn, 1988) and tend towards a better memory for verbal material. This is true when both recalling the content of a previously read paragraph (Owen & Lynn, 1993) or a spoken list of unrelated words (Kramer, Delis & Daniel, 1988). These effects although reliable, are not nearly as large as the sex differences seen in spatial and motor tasks (for a review see Kimura, 1999; Maccoby, 1966).

Steroid Hormones and Cognitive Function Within Each Sex

Another, perhaps more direct approach to evaluate the influence of sex hormones on behaviour is to examine the effects of differing hormone levels within each sex. Among women cognitive performance appears to vary with hormonal levels, with some abilities declining with increased gonadal steroids while other abilities improve (Hampson, 1990a; Hampson, 1990b; Hampson & Kimura, 1988). Testing women at different stages of the menstrual cycle, thereby sampling different hormonal states, results in differential scores on tasks of spatial and verbal performance. Hampson and Kimura (1988) found that women tested during the midluteal phase, when ovarian steroid levels are high, scored better on tasks of verbal fluency and fine motor skill than when steroid hormones are low (during the menstrual phase). Recall these are the tasks in which women generally have been demonstrated to excel. Conversely, when the same women were tested during the menstrual phase when ovarian steroid levels are low, scores were better on the male-favouring spatial tasks than when in the midluteal phase. This finding suggests high levels of estrogen and progesterone seem to enhance performance on tests at which females excel, but are detrimental to performance on tests at which males excel. Similarly, surgically and naturally menopausal women treated with synthetic estrogen replacement show improved cognitive performance when compared to controls without estrogen replacement on tests of verbal skills (Kampen & Sherwin, 1994; Sherwin, 1988).

Additional evidence suggesting a beneficial cognitive effect of endogenously- or exogenously-derived estrogens and progesterone/progestins comes from studies related to the amount of lifetime steroid exposure a woman might receive (Smith, McCleary,

Murdock, Wilshire, Buckwalter & Bretsky, 1999). Women with greater exposure to natural (i.e. produced by their own ovaries) or synthetic (i.e. hormone replacement therapy) cyclic gonadal hormones throughout their lives were shown to have higher cognitive test scores for verbal memory when compared to women with shorter exposures. To reach this conclusion researchers evaluated menarche and menopausal age along with synthetic hormone use in a large sample of women. Those women with histories of longer steroid hormone contact, caused either by early menarche or late menopause, showed superior verbal memory scores when their results were compared to women who had shorter exposures. Similarly, women who had hysterectomies earlier in life, and thus were exposed to estrogen and progesterone for shorter lifetime periods, performed significantly worse than women who had their hysterectomies later in life (Richards, Kuh, Hardy & Wadsworth, 1999). There is also evidence that synthetic estrogens may have a neuroprotective effect against the debilitating memory loss associated with Alzheimers disease (Paganini-Hill & Henderson, 1994). Moreover, a meta-analytic review of 16 prospective, placebo-controlled human studies suggests synthetic hormone replacement therapy (HRT) seems to be able to maintain verbal memory and prevent or avert normal age-related memory loss in women (Sherwin, 1999). This finding was recently challenged however, when a large randomized, double-blind clinical study was terminated early due to significant evidence than estrogen plus progestin HRT not only did not prevent mild cognitive impairment, it actually seemed to increase the risk of probable dementia in postmenopausal women (Shumaker et al, 2003).

Progesterone has also been demonstrated to affect cognitive function, however the effects appear to be in the direction of impairment. Elevated serum progesterone

concentrations seem to be related to poorer processing of non-verbal information such a symbol copying. In addition, psychomotor speed tends to be impaired when progesterone levels are high, although these authors suggest this effect may be due to anxiolytic and mildly anesthetic properties of its metabolites allopregnanolone and pregnanolone (Freeman, Purdy, Coutifaris, Rickels, & Paul, 1993). Subsequent research has challenged the study (de Wit, Schmitt, Purdy & Hauger, 2001), contending oral administration results in considerable variability in plasma concentrations due to absorption factors and rapid liver metabolism. When progesterone administration was intramuscular, which is associated with more rapid and consistent absorption, the sedative-like effects, cognitive and psychomotor effects where markedly reduced (de Wit, Schmitt, Purdy & Hauger, 2001).

Like the other steroids, androgens have also been shown to directly affect cognitive function. Research in this area is more equivocal, with some studies linking high testosterone to improved spatial performance (Janowsky, Oviatt & Orwoll, 1994) and others reporting the same effects with lower testosterone levels (Moffat & Hampson, 1996). This is especially true of the research involving men. What is clear however, is the demonstrated relationship between oscillating androgen levels in men and changes in spatial skills. The divergence in the existing literature appears to be related to the age of the male participants in the respective studies.

Lower Testosterone and Improved Spatial Performance in Young Men

In both normal young men and women spatial performance has been shown to systematically change relative to testosterone levels. In women, those with higher levels of testosterone, and in men, those with lower levels of testosterone show the best spatial

performance, suggesting a sexually dimorphic "optimum" level for superior spatial ability (Gouchie & Kimura, 1991). In addition, spatial performance in young men is better during the spring (Kimura & Hampson, 1994) and late in the day (Moffat & Hampson, 1996), both times when testosterone titres are lower relative to the fall and the early morning.

Higher Testosterone and Improved Spatial Performance in Older Men

Age-related decline in testosterone levels is associated with a cluster of normal physiologic changes such as decreased muscle mass and strength, osteoporosis and reduced sexual activity (Swerdloff & Wang, 1993). Along with these changes, age-related drops in testosterone have also been associated with a progressive decline in cognitive function in normal aging men (Barrett-Connor, Goodman-Gruen & Patay, 1999; Yaffe, Lui, Zmuda & Cauley, 2002). However, when supplemented with testosterone to either enhance sexual functioning (Janowsky, Oviatt & Orwoll, 1994) or raise chronically low testosterone levels (Cherrier, 1999) these older men showed improved performance on both verbal and spatial tests. In both studies testosterone levels of the older males were in the low-normal range for their age, and the supplementation raised levels to approximately that of a normal young man. Consistent with these results, longitudinal research has identified a fairly clear relationship between high testosterone levels and improved verbal memory, attention and spatial rotation in elderly men (Moffat, Zonderman, Metter, Blackman, Harman & Resnick, 2002). Finally, when elderly men diagnosed with prostate cancer were treated with androgen deprivation therapy, which reduced endogenous testosterone to castration levels, they also showed a concomitant

decline in general cognitive function (Salminen, Portin, Koskinen, Helenius & Nurmi, 2004).

Although earlier research in this area had linked testosterone levels to cognitive changes, it has been unclear as to whether these effects are due to testosterone *per se* or to that of its aromatized product estradiol. Recall, in women estradiol has been associated with improved cognition especially in the area of verbal memory (Hampson & Kimura, 1988; Kampen & Sherwin, 1994; Sherwin, 1988; Smith, McCleary, Murdock, Wilshire, Buckwalter & Bretsky, 1999). To determine the relative contribution of testosterone and estradiol on cognitive processing in older men, participants in a recent study (Cherrier et al, 2005) were given either testosterone alone (T), which can be readily converted to estradiol; or testosterone combined with anastrozole, a potent aromatase inhibitor (T&A). This combination prevented the conversion of testosterone to estradiol thereby allowing for the evaluation of testosterone alone on cognitive function. After supplementation circulating testosterone levels in the two experimental groups (T and T&A) were increased from baseline approximately 238%. Estradiol increased an average of 81% in the testosterone-alone group and decreased by approximately 50% in the T&A group. Results showed a significant improvement in spatial memory for both the T and T&A groups, however only the group with elevated estradiol showed improvements in verbal memory. This suggested to these authors that in healthy older males, improved verbal memory appears to be mediated by an indirect action of estradiol (aromatized from testosterone) on estrogen receptors, however improved spatial performance occurred in the absence of increases in estradiol and was therefore directly related to testosterone supplementation alone; this latter effect being mediated by the direct action of testosterone on androgen receptors (Cherrier et al,

2005). As Anastrazole has its effects in the periphery and its ability to cross the blood brain barrier is currently unknown (Wiseman & Adkins, 1998), the specific location of the anti-aromatase effects still remains unclear however. That being said, this result is consistent with research addressing cognitive function in women, where higher estradiol levels is associated with better verbal memory scores and higher androgens related to better spatial scores (Gouchie & Kimura, 1991; Hampson & Kimura, 1988; Kampen & Sherwin, 1994; Sherwin, 1988).

Additional support for androgenic effects on cognitive function comes from studies with female-to-male (F2M) and male-to-female (M2F) transsexuals who were treated with cross-sex hormone therapy in preparation for sex-reassignment surgery. Among the female-to-male transsexuals who received 250mg biweekly injections of testosterone, performance on spatial tasks improved while verbal fluency deteriorated. Among the male-to-female transsexuals cross-sex hormone therapy (anti-androgen and estrogen) resulted in decrements in spatial ability, along with a concomitant improvement in verbal fluency (Van Goozen, Cohen-Kettenis, Gooren, & Frijda, 1995). Moreover, subsequent research has shown this effect of an inverse relationship between spatial skills and verbal fluency has not changed with time (Slabbekoorn, van Goozen, Megens, Gooren, & Cohen-Kettenis 1999).

Comparative Animal Studies

In order to test spatial performance in non-human species, researchers have developed specific types of mazes that are designed to evaluate acquisition and performance of navigational and spatial skills. When placed in these structures animals

are encouraged using motivational factors such as food rewards or negative reinforcement strategies, to solve the maze. The three most used are the Morris water maze, the radial arm maze and the T-maze (Wenk, 1997). Tasks using mazes that encourage exploration behaviour by using food as a reward are generally known as appetitive tasks. Mazes in this group include the radial arm maze and T-maze. Tasks in which correctly solving the maze results in escape from an unpleasant environment are generally referred to as aversive. As many rodent species do not like water, any maze where an animal must swim to escape the watery environment is generally considered to be an aversive task (Morris, 1984). The Morris water maze is a well-used example of such a maze.

Sex differences in spatial tasks, as measured by these mazes are evident in non-human species. Although some exceptions are present (Bucci, Chiba & Gallagher, 1995), male rats solve both appetitive (Luine & Rodrigues, 1994; Williams, Barnett & Meck, 1990); and aversive (Beatty, 1979; Frye, 1995; Roof & Havens, 1992; Warren & Nadel, 1993) spatial navigation tasks faster and with fewer errors than female conspecifics. As in humans, this male advantage is believed to be due in part to organizational effects of the prenatal hormonal environment, where circulating androgens permanently masculinize and defeminize the fetal nervous system (Nelson, 2000). This effect was demonstrated when researchers prenatally androgenized female rat pups by injecting pregnant females with testosterone (Roof & Havens, 1992). The spatial performance of female pups was then evaluated during adulthood. The female rats that had received the prenatal treatments performed significantly better than control females, and as well as the males on the spatial navigation task.

Like humans, male and female rats appear to use different information when solving spatial navigational tasks. In the radial arm maze, male rats seem to use geometric cues such as shapes and angles in the room when locating the food rewards. If these geometric cues are removed by encircling the maze with a plain curtain, the male rats make more errors than when the curtain was not there. Conversely, female rats appear to use landmark cues. As long as items such as pictures or doors are visible, performance of female rats are not affected when the geometry of the room is altered. If the landmarks are moved, the error rates for the females increase significantly (Williams, Barnett & Meck, 1990). To investigate the relative contribution of early exposure to sex hormones to these different navigational strategies these authors manipulated steroid hormone exposure. Male rat pups were castrated at birth to remove endogenous sources of androgens, while female rat pups received an injection of estrogen. In rodents it is aromatized estrogen, rather than androgens *per se* that masculinizes the developing nervous system (Nelson, 2000). When tested on the radial arm maze as adults, the castrated males used a female-like pattern to solve the maze. That is, they used landmark cues to locate the food rewards. Conversely, the estrogen-treated females displayed male-like strategies to locate the food rewards using primarily geometric cues (Williams, Barnett & Meck, 1990).

Tasks of spatial performance vary across the rat ovarian cycle. Normally cycling adult female rats demonstrate cyclic shifts in levels of performance on specific spatial tasks. During proestrus, when ovarian steroids are high, spatial performance as measured by the Morris water maze is impaired, with these females taking significantly longer to solve and escape the maze. Conversely, during the low estrogen phase of diestrus, performance was markedly improved (Warren & Juraska, 1997). Additionally,

ovariectomized females performed better on the Morris water maze, with both shorter escape latencies and path lengths than ovariectomized adult females who received an estrogen supplement (Frye, 1995). Both studies suggest in adult female rats, low estrogen is beneficial to spatial performance on the Morris water maze.

Rodent species other than rats also reveal a sex difference in spatial performance. The strength of the effect however, appears to be related to the ecology of the species. For example, although closely related, pine *(Microtus ochrogaster)* and meadow *(M. pennsylvanicus)* voles show different reproductive tactics (Dewsbury, 1981). The monogamous pine voles live in social groups with adult males and females maintaining similar sized territories. Within this species sex differences on laboratory tasks of spatial navigation are absent. Conversely, polygynous meadow voles, with male ranges much larger than female conspecifics, reveal a significant sex difference, with males outperforming females on laboratory tests of spatial ability (Gaulin & Fitzgerald, 1986). These authors note that as natural selection would favour spatial ability in proportion to the amount of spatial data an animal must process; male voles will evolve superior spatial abilities when their home range size is larger than females. This suggests the sex difference in spatial abilities has evolved as a result of both a differential mating system, and as a consequence of ranging patterns.

Meadow Voles *(M. pennsylvanicus)* are induced ovulators, requiring male copulatory stimuli in order for females to ovulate. Females of reproductive age housed either alone or with other females' exhibit low levels of estrogen and as a consequence remain in permanent diestrus (Sawrey & Dewsbury, 1985). Pairing an adult male with a mature female triggers an estrogen surge within approximately 48 hours, inducing a state of constant behavioural estrus in the female (Cohen-Parsons & Carter, 1987).

When tested, diestrus females outperformed estrus females on the Morris water maze task, lending additional support to the existing evidence that similar to humans, other mammalian species show an inverse relationship between spatial performance and circulating ovarian steroid levels (Galea, Kavaliers, Ossenkopp & Hampson, 1995).

Evaluating Steroid Hormone Concentrations in Human Populations

Quantifying levels of sex steroid hormone for clinical applications has traditionally been done using serum testing where the aqueous fraction of blood is extracted and then analyzed for a specific steroid. Testing of serum typically yields a measurement that equals the total level of that steroid present in the blood (Bachmann et al, 2002; Speroff, Glass & Kase, 1999). However, due to the lipophilic nature of steroids, they must be bound to a water-soluble protein to facilitate transportation in blood. Different steroids preferentially bind to different types of transport proteins, for example testosterone binds to Sex Hormone Binding Gobulin (SHBG), but also can be found bound more weakly to albumin (Dunn, Nisula & Rodbard, 1981). Bound steroids are generally not biologically available as they are unable to readily diffuse from blood and are therefore unable to effect change at the cellular level. Some 90-99% of all steroids are present in this way, and are therefore unavailable to the cells of the body. In light of this, any measure of total steroid value, could not provide a direct indication of the unbound bio-available fraction, which is by far the smaller but highly potent portion. Some researchers and clinicians do however use a formula to convert a total steroid serum value to the free fraction using obtained values of the steroid binding factors (Goldstat, Briganti, Tran, Wolfe & Davis, 2003). It has also been shown that in some

cases total steroid serum values can accurately predict the free fraction (Bachmann et al, 2002). This correlation has limited applications however, especially in women, where these algorithms have not been extensively tested, and therefore lack reliability for use in clinical settings (Davison & Davis, 2003; Padero, Bhasin & Friedman, 2002).

Unbound, biologically active steroids can easily pass from the blood into the salivary glands and into saliva; therefore any assay derived from saliva will show a much lower absolute concentration of steroids, however this value will reflect the more potent bio-available fraction (Shirtcliffe et al, 2000). Salivary measures have needed to be highly sensitive in order to detect and quantify the miniscule quantities of steroids present.

Generally salivary measures of sex steroids are currently only used in experimental settings. It seems clinicians do not view this procedure to be sufficiently accurate or reliable as a diagnostic tool and currently do not recommend them (Bachmann et al, 2002). This belief persists despite a body of research suggesting a strong relationship between serum and salivary measures of the steroid hormones.

Serum and Saliva Correlations of Sex Steroid Profiles

A number of studies have been conducted to evaluate the degree to which salivary measures of steroids correlate to serum measures. The consistent finding suggests a correlation of approximately .70 -.80. Variability seems to exist based on the type of hormone assayed and inter-lab differences. Table 1 provides a summary of these results.

Table 1: Serum vs. Saliva Correlations

Steroid	r Value	Study
Androstenedione	.70	Wellen et al, 1983
Androstenedione	.92	Lac, Lac & Robert, 1993
DHEAs	.51	Lac, Lac & Robert, 1993
DHEA	.73	Lac, Lac & Robert, 1993
Estradiol	.77	Belkien, et al, 1985
Estradiol	.68	Shirtcliff et al, 2000
Estradiol	.79	Wang et al, 1986
Estriol	.90	Lachelin & McGarrigle, 1984
Estrone	.79	Folan, Gosling, Finn & Fottrell, 1989
Progesterone	.60	Delfs et al, 1994
Progesterone	.75	Lu, Chatterton, Vogelsong & May, 1997
Progesterone	.90	Meulenberg & Hofman, 1989
Testosterone	.71	Khan-Dawood, et al, 1984
Testosterone	.80	Vittek et al, 1985
Testosterone	.77	Lac, Lac & Robert, 1993
Cortisol	.74	Lac, Lac & Robert, 1993

The Assay Technique

Radioimmunoassay (RIA) is a technique that allows for the accurate measurement of very small quantities of biologically relevant molecules. Due to the minute quantities of sex steroids found in serum and saliva, this procedure has been extensively used in their analysis and quantification. Initially developed in 1960 by Solomon Berson and Rosalyn Yalow to evaluate plasma insulin levels, their work represented the first time hormone levels in the blood could be detected by an *in vitro* assay. This research led to the Nobel Prize in Medicine or Physiology for Yalow in 1977 (Kahn & Roth, 2004).

Radioimmunoassays are based on the specific binding reaction between an antibody and an antigen. A mixture is prepared of radioactively labelled antigen and known amounts of unlabeled or "cold" antigens are added to the samples of the mixture. A fixed amount of antibody is also added. The cold antigens then compete with the radioactively labelled antigens for binding sites on the antibody. As more unlabeled antigen is added it displaces the radioactive antigens from the antibody molecule. Thus, a high concentration of cold antigen will result in little radioactive "hot" antigen bound to the antibody and vice versa. After a set time, a second antibody directed against the first antibody is added which causes the formation of large molecular complexes. Centrifugation separates the sample into a solution of the large antigen-antibody complexes and supernatant. The large complexes containing both radioactive and cold bound antigens are separated from the supernatant that contains only the cold antigen. Both samples are then quantified and the relative radioactivity of each is measured. After determining the ratio of bound to free antigen in each sample, the antigen concentrations are then read directly from a standard curve. The concentration of the hormone in the serum is inversely proportional to the bound "hot" hormone at equilibrium. Identification of the radioactive counts from the centrifuged complexes coupled with this reference curve yields the unknown antigen concentration (Nelson, 2000).

Radioimmunoassays are extremely sensitive and are able to detect picomolar concentrations of molecules in some cases. They have provided considerable information about many different biochemical processes and are still widely used (Kahn & Roth, 2004). Because of the radioactive waste generated from the assays, techniques have been developed to assay molecules using non-radioactive procedures such as the

use of fluorescent enzyme labels. These enzyme immunoassays (EIA) are conceptually identical to RIAs, differing only in the use of a colorimetric enzyme in place of the radioactive label. Enzyme Immunoassay of specific salivary hormones is the way steroids have been evaluated in the current study.

Distal Explanations for Human Sex Differences in Cognition

> *"If psychologists want to understand the processes that shape the human mind, they must understand the process that shaped the human species"*
>
> Wright
> 1994, p. 319

The human brain is the product of millions of years of evolution, but remains largely unchanged in the last fifty thousand or more years (Falk, 1993; Futuyma, 1998). Therefore, the human nervous system of the 21st century evolved under considerably different life circumstances than any individual would encounter today (Strickberger, 1996). For example, generally survival today does not depend upon the ability to hunt or scavenge for meat, harvest berries and wild fruits or avoid large predators as it did for our hominid ancestors. It was under these circumstances however, that our present nervous system evolved. So, developing a full and thorough understanding of current human cognitive functions requires an understanding of both the physical environment and social structure in which these neural characteristics evolved. That being said, it must be acknowledged that ancestral cognitions and behaviours did not fossilize like teeth or bones. Therefore, there exists no clear and specific trail of evidence as to how ancient hominids interacted with the environment, making much of the current explanations in this area quite speculative.

One of the more prominent evolutionary explanations for cognitive sex differences assumes in ancestral environments different selective pressures were operating on men and women (Sherry & Hampson, 1997). It has been proposed that these selection pressures could well have been related to ancestral divisions of labour, where species success depended not only on differing reproductive roles, but also on the differential tasks performed by men and women (Eals & Silverman, 1994; Kolakowski & Malina, 1974; Lovejoy, 1981; Silverman & Eals, 1992). There was little overlap in these duties and in existing hunter-gatherer societies and they remain that way to this day (Tooby & DeVore, 1987). Men were active in tool manufacture, weapons and transport devices. They also hunted and/or scavenged both large and small game, a task that probably took the able-bodied males on trips of considerable distance from their home base. Men also took responsibility for defence of the group against larger predators and enemies (Silverman & Eals, 1992). Tasks managed by the women included the gathering of food such a seasonal fruits and berries from locations near the home base. Preparation of food and the manufacture of food-related utensils and clothing were also done by women, as was caring for the home and any dependent children (Silverman & Eals, 1992).

In existing hunter-gatherer societies, men are almost exclusively the sex involved in hunting, a finding that appears to be both universal (Daly & Wilson, 1983) and consistent with current theories of ancestral environments (Kolakowski & Malina, 1974). This would include such tasks as pursuit and killing of prey and/or scavenging carcass remains of earlier kills made by larger predators. In the case of hunting, the ability to accurately throw a rock or missile would have conferred a significant advantage. Great skill would have been needed to incorporate distance, accuracy, direction and speed of

the projectile at the target; a task made more difficult if the prey was both small and in motion at the time of the strike. This ability to spatially evaluate trajectory and timing may well account for the current superiority of men in targeting and accuracy in throwing (Watson & Kimura, 1991). Recall, this sex difference between men and women is one of the largest reported cognitive differences, on the order of one effect size (Kimura, 1999).

Hunting of larger prey may have required ancestral males to travel considerable distances either following migratory herds or tracking of faster moving more solitary animals. Either way, the ability to navigate in a changing environment and maintain their bearings when on long trips from the home base would have been a necessary skill for survival. Men were also the primary toolmakers both for manufacture of weapons and hunting implements such as stone axes and sharp projectiles (Daly & Wilson, 1983; Kolakowski & Malina, 1974). Both tasks of hunting and tool making would have put greater selective pressure on men to develop superior spatial skills for navigating in the external environment. In addition, the skills necessary for successful tool making might also have taxed spatial abilities as men would have needed to mentally rotate an object while symmetrically forming the tool or weapon. The current large male advantage of imaginal rotation may be a consequence of these ancestral selective pressures. Moreover, this spatial advantage seems to be practically universal, being reported in African peoples (Mayes & Jahoda, 1988), East Indians (Owen & Lynn, 1983), Asians (Mann, Sasanuma, Sakuma & Masaki, 1990) and Western cultures (Watson & Kimura, 1991), suggesting an evolutionarily old adaptation.

Ancestral women took care of the home and the infants (Silverman & Eals, 1992). These tasks required a different set of cognitive skills. It was the responsibility of women to gather much of the harvestable foods consumed by the group (Daly & Wilson,

1983; Eals & Silverman, 1994). Women foraged for wild fruits, seeds, nuts and berries closer to the home base. These short distance trips probably involved not only the women but also the mobile and non-mobile dependent children. This would have limited the distances travelled due to matters related to safety and convenience. Natural selection would have favoured the ability of women to be able to accurately remember the location of food sources, especially if it was a seasonal product or the local environment was patchy. It is also possible that, since these females did not travel long distances, the use of fixed landmarks (female advantage), rather than cardinal directions (male advantage) to guide and orient would have been the preferred strategy; a strategy very different to that of their male conspecifics. This difference between men and women in finding their way thorough the environment, and the kinds of cues they appear to use may account for much of the spatial sex differences we see today. As previously discussed women on average are superior to men at remembering the location of an object (Eals & Silverman, 1994; James & Kimura, 1997). Of the skills tested, this is the only spatial task at which women on average, outperform men (Kimura, 1999).

It has been suggested (Kimura, 1999) that if ancestral women used landmarks for navigating short distance trips, this may have put heavier demands on verbal memory than the male strategy of navigating by the use of cardinal points. As most landmarks can be labelled in some way, once a route has been learned, recalling landmarks by name would make it much easier to find them again and would also make it easier to communicate the location of the resources to others in the group.

The female advantage of fine motor coordination also could be a result of different selective pressures between ancestral men and women. Ancestral women predominantly engaged in domestic chores such as gathering of small foods like berries

and the construction of food-related utensils and clothing, such as basket weaving and the manufacture of fabrics and threads (Silverman & Eals, 1992). Tasks like this would have required good control of distal musculature and the ability to coordinate several fine finger movements into a unit of behaviour. Natural selection would have favoured those women who could perform these task quickly and accurately, resulting in the current strong sex difference favouring women in contemporary Western culture (Purdue Pegboard Examiners Manual, (1987), NCS: London House).

Cognition and Pregnancy I: Cognitive Function

Cognition is most generally defined as all the mental activities associated with thinking, knowing, communicating and memory (Myers, 2001; Weiten, 1998). The cognitive component of memory requires the attending to, storing, working with, and retrieval of information (Baddeley, 1993), reflecting the persistence of learning over time. In information processing models human memory involves the encoding, storage and retrieval of information. The components of memory storage are categorized by input, capacity and duration, beginning at the very brief and limited sensory memory to the largely infinite long-term memory store (Myers, 2001).

Information first enters the memory system through the senses. This initial trace is called *sensory memory* (Sperling, 1960) and it registers and briefly stores visual, auditory and tactile information. Among the vast amounts of information that registers in sensory memory only a tiny portion is attended to and meaningfully encoded into *short-term memory* (Peterson & Peterson, 1959). This second store is limited in both duration and capacity, and without active processing/rehearsal information fades quickly. As will

be discussed, the idea of short-term memory has recently been replaced with the more inclusive term of *"working memory"*. Information that is processed in short-term memory/working memory, by either rehearsal or encoding becomes part of *long-term memory* (Landauer, 1986). This largely limitless storage system can be divided into two major categories: Implicit and explicit memories. An *implicit memory* is when information retention has occurred in the absence of the conscious recollection. An example of this would be when a student uses a word, for example, "capitulate" instead of "surrender" unaware that their history teacher had recently used the word "capitulate".

When implicit learning involves physiological motor systems such as the coordination required to drive a standard transmission automobile or ride a two-wheeler bike, it is called *procedural memory* (Myers, 2001). *Priming* is a research method that has been used to measure both implicit and procedural memory, where prior exposure prepares or "primes" a specific memory association as in the "capitulate" example above. Similar to implicit memory, *incidental memory* is when learning has occurred without conscious effort, however in this type of memory the individual can usually recall where the learning occurred (Weiten, 1998). For example, accurately recalling a newspaper heading in which no previous effort had been made to memorize.

The opposite of implicit memory is *explicit memory*. This is the conscious recall of a studied fact or known event or experience (Myers, 2001). An example of explicit memory would be recalling the events of a previously heard or recited narrative piece, such as a written paragraph or recalling a conversation. Explicit memory is also called *declarative memory*, that is, a person can "declare" that they have the memory of an event or experience. Explicit memories often involve the encoding, storage and/or retrieval of words, word meanings or information that have been presented aurally. This

type of memory is known as verbal memory and it logically reflects the recall of words or material that can be readily mediated verbally (Myers, 2001). Verbal memory would therefore include all information that is processed in words (reading a book), or described and recalled by words (naming objects or people).

It is generally agreed (Myers, 2001) that implicit memories and explicit memories are stored in different regions of the brain, as damage to the hippocampus disrupts explicit memories while leaving implicit memories largely intact (Squire, 1992). Classic experiments have shown that amnesic patients can successfully learn to perform new tasks such as a mirror tracing test and show improvement on subsequent trials, all the time having no conscious awareness of having initially learned them (Corkin, 1984; Schacter, 1992).

Research using conditioned eye-blink responses in rabbits has shown some implicit memories to be linked to the cerebellum (Krupa, Thompson & Thompson, 1993; Steinmetz, 1999). Severing connections or lesions to this hindbrain structure permanently abolishes the ability to for these animals to learn to associate a tone with an impending puff of air. Human patients with cerebellar damage are also incapable of this type of eye-blink conditioning (Daum & Schugens, 1996).

Perhaps one of the most studied components of memory involves the ability to temporarily store information while concurrently processing another piece of information; this type of "working with" memory, has been the focus of considerable research (Myers, 2001).

Working Memory: The Ability to Process Concurrent Information

The idea of *working memory* appears to have a number of different meanings in the cognitive sciences (Baddeley, 2000). In Psychology it is generally refers to a limited capacity memory system that allows for the temporary storage and manipulation of information that is needed to execute some complex task such as learning or comprehension (Baddeley & Hitch, 1974). The notion of working memory grew out of the earlier concept of short-term memory, which was believed to comprise a single temporary global storage system. Under this system, with active attention, short-term memory would harvest information from the sensory stores, process and discard it, or process and rehearse it into long-term memory (Atkinson & Shiffrin, 1968). This idea was eventually abandoned when it was shown that short-term memory was much more than a simple rehearsal buffer shuttling information from the sensory to the long-term store. Moreover, the existing model could not account for other processes inextricably linked to the "middle memory". For example, under the existing model there was no way to account for the cognitive skill of concurrent task management, where an individual can hold one piece of information in consciousness while simultaneously processing another (Baddeley & Hitch, 1974).

In a now famous paper, in 1974 Baddeley and Hitch proposed a three-component model in an attempt to reconcile the earlier deficiencies. Under this new *working memory* model a master regulator controlled two subsidiary slave systems. Baddeley and Hitch (1974) named the slave systems the "phonological loop" and the "visuospatial sketchpad". The master regulator, which governed attention, was called the "central executive". The phonological loop comprised a temporary phonological

store in which auditory memory traces decay over a period of a few seconds, unless revived by rehearsal. This component represents all of short-term memory under the original model. The visuospatial sketchpad held visual and spatial and possibly kinesthetic components (Baddeley & Hitch, 1974), and would be taxed when one manipulated an object in cognitive space, such as imagining a rotating object, or what a room would look like when the furniture was rearranged.

Recently the working memory framework was revised to include a new component (Baddeley, 2000). The "episodic buffer" was incorporated to formally link the three working memory systems (phonological loop, visuospatial sketch pad and the central executive) to both conscious awareness and to long-term memory. These two connections had been unaccounted for under the initial working memory model. Baddeley (2000) contends that the episodic buffer is also controlled by the central executive and functions to bind sequences of events and information from differing sources into cohesive episodes, such as linking current actions to old information (Baddeley, 2000). He argues this was an important and necessary addition considering one of the key features of memory requires the active integration of new information to existing knowledge; knowledge that must be retrieved from the long-term store. An example of the episodic buffer at work would be the ability to admire and enjoy looking at a famous painting while recognizing it as the work of Renoir, the Impressionist painter. Failures of working memory have been formally linked to the everyday process of forgetting, or absentmindedness (Reason, 1982). In both humans and nonhuman primates, activation of the prefrontal cortex has been linked to the performance of tasks with a working memory component (see Goldman-Rakic, 1987 for a review).

Cognition and Pregnancy II: Pregnancy

The Major Hormones of Pregnancy: Steroid Hormones

Fetal steroidogenesis does not follow the conventional mechanisms of hormone production within a single organ system. Rather, the final products result from critical interactions between fetal organs and the placenta, structures that individually do not possess the necessary steroidogenic enzyme capabilities. Together, these two units are complementary and form a complete system that utilizes maternal resources as a source of precursors and a mechanism for steroid clearance (Speroff, Glass & Kase, 1999).

Progesterone

The placenta obtains cholesterol from the maternal bloodstream for progesterone synthesis. Prior to placenta formation however, this steroid is produced by the maternal corpus luteum, which sustains the early pregnancy until about ten weeks gestation (Csapo, Pulkkinen & Wiest, 1973). The rescue of the pregnant corpus luteum from post-ovulatory demise is attributable to human chorionic gonadotropin (hCG) (Bonduelle, Dodd, Liebaers, Steirteghem, Williamson & Akhurst, 1988). This proluteotropic factor is produced by the rudimentary conceptus and signals the ovary to continue progesterone secretion. Successful pregnancy maintenance by the corpus luteum is associated with circulating levels of maternal progesterone of approximately 10ng/mL (Schneider, Davies & Honour, 1993). After a transition period of shared progesterone synthesis between the seventh to tenth week of pregnancy, the placenta emerges as the dominant source and maternal circulating levels progressively increase (Schneider, Davies &

Honour, 1993). At term, progesterone levels range from 100ng/mL to 200ng/mL, and the placenta is producing about 250mg per day. Most of the progesterone produced in the placenta enters maternal circulation (Speroff, Glass & Kase, 1999).

Progesterone maintenance of uterine quiescence and its withdrawal resulting in myometrial excitability are clearly established as a parturition mechanism in non-primates (Garfield, Saade & Chwalisz, 1998). In primates, however the role of progesterone at parturition is less clear, primarily because clinical research has failed to identify a definitive pre-parturition decline in peripheral blood levels of progesterone (Garfield, Saade & Chwalisz, 1998; Walsh, Stanczyk & Novy, 1984). Nevertheless, treatment with either progesterone or a synthetic analogue has been shown to have some effect in preventing premature labour, although not labour in term pregnancies (Erny et al, 1986; Femini et al, 1985). Furthermore, interruption of progesterone exposure by antagonists leads to uterine contractions (Haluska, Stanczyk, Cook & Novy, 1987). This suggests the parturition trigger in primates may be considerably more complex. Perhaps related to interactions between local progesterone synthesis, estrogen and their combined effects on prostaglandin production/secretion rather than a critical drop in progesterone *per se* (Speroff, Glass & Kase, 1999).

Estrogen

Production of the estrogens in pregnancy is under the control of the fetus and is a fundamental signalling method by which important physiologic processes are directed, such as uteroplacental blood flow, mammary gland development, and fetal adrenal gland function (Pepe & Albrecht, 1995). As mentioned earlier, the obligate precursors of the

estrogens are androgens, however the placenta is unable to directly form androgens. Androgens are derived from maternal and fetal adrenal precursors, which are then aromatized into estrone and estradiol within the placental unit. Estriol is also synthesized in the placenta, however its precursor is derived from the fetal liver (Speroff, Glass & Kase, 1999). Normally, placental aromatization is so efficient that little androgen presented to the placenta escapes (MacDonald & Siiteri, 1965), preventing masculinization of fetal neural or peripheral tissues. As fetal tissues lacks the necessary enzymes responsible for estrogen synthesis, it is dependent on the placenta for steroidogenesis of these hormones (Speroff, Glass & Kase, 1999).

All three estrogens increase significantly across pregnancy. Serum levels of estradiol increase from 0.5 to 1ng/mL in the first weeks of pregnancy to an overall mean of approximately 16ng/mL near parturition. A rise in estrone begins at six to ten weeks from approximately 2ng/mL to an average of 7.5ng/mL near term. During pregnancy the most significant estrogenic increases are seen with estriol, which is first detectable at around nine weeks. Concentrations plateau at 9ng/mL around 31-35 weeks, increasing again at 36 weeks (see Speroff, Glass & Kase, 1999, for a review). Although considered to be a weak estrogen, estriol increases by about 1000 fold over non-pregnant levels, making it capable of exerting a biologic effect equivalent to that of estradiol (Katzenellenbogen, 1984).

A sharp increase in estrogen levels in maternal blood begins at around 34-35 weeks of gestation, however, a late increase just before parturition has not been observed in human pregnancies as it has in other species (Garfield, Saade & Chwalisz, 1998). This suggests at least in human parturition there is not a triggering increase of estrogen necessary to initiate birth. It could be however; the estrogenic changes that

are taking place at the local uterine level simply may not be reflected as concomitant increases in maternal circulation (Davidson, Murray, Challis & Valenzuela, 1987).

Androgens

During pregnancy circulating testosterone levels also rise dramatically. Concentrations increase from an ovulatory level of approximately 30ng/dl plasma to approximately 200ng/dl (Boots, 1993). Despite this significant increase, there is a notable absence of virilization in pregnant women (Demisch, Grant & Black, 1968). This has been attributed to the concurrent increase in circulating sex-hormone binding globulin (SHBG), which reduces the bioavailability of testosterone (Speroff, Glass & Kase, 1999).

Sex-hormone binding globulin is produced in the liver and is differentially affected by the sex hormones. Both pregnancy and estrogen administration increase SHBG, while progesterone, corticoids and androgens all decrease SHBG. This protein carrier binds approximately 69% of available testosterone and estradiol. Another 10-30% is loosely bound to albumin, leaving only about 1% unbound or free to exert a biologic effect (Speroff, Glass & Kase, 1999). In fact, although testosterone levels increase throughout pregnancy, the free fraction of circulating testosterone remains unchanged until approximately week 28 (Buckwalter, Buckwalter, Bluestein & Stanczyk, 2001). Serum concentrations of testosterone remain at pregnancy levels immediately following delivery, but decrease by about a half between the fourth and sixth post partum day (Demisch, Grant & Black, 1968).

In contrast to estrogens, progesterone and testosterone, maternal serum levels of the weaker androgens dehydroepiandrosterone (DHEA) and its ester metabolite dehydroepiandrosterone sulfate (DHEAs) actually decrease in pregnancy to about 30%-50% of normal menstrual cycle values (Peter, Door & Sippell, 1994). It is believed the decline in these steroids, which are synthesised in the fetal adrenal glands, are directly related to their rapid metabolism by the placenta and fetal liver to produce estrogens. In addition, DHEA is bound primarily to albumin; as this is a very weak affinity, the majority of this androgen appears to be readily bioavailable for cellular processing and a source of estrogenic precursors (Speroff, Glass and Kase, 1999). This may also be the case for testosterone (Manni et al, 1985). Peter, Door & Sippell (1994) reported a decrease in DHEAs levels from 3.25(+/- 0.38) ug/ml in early gestation to a minimum of 1.50(+/- 0.16) ug/ml in week 38. In comparison to maternal production the fetal adrenals produce more than 200mg of DHEAs daily, about 10 times more than the mother (Speroff, Glass and Kase, 1999).

Glucocorticoids

Placenta-derived progesterone serves as the substrate for fetal adrenal gland production of glucocorticoids and mineralocorticoids; however, cortisol synthesis is also derived from cholesterol obtained from fetal circulation and synthesized in the fetal liver (Speroff, Glass & Kase, 1999). The maternal adrenal glands also synthesises cortisol, however it has been suggested it is unlikely that the increases in fetal increments represent changes in maternal adrenal activity in response to stress (Speroff, Glass & Kase, 1999). Although maternal cortisol readily crosses the placenta, it is mostly

metabolised to the biologically inactive cortisone in the process, and the fetal liver has a very limited capacity to convert this cortisone back to cortisol. Conversely, the fetal lung does possess the capacity to convert cortisone back to cortisol and this may be an important source of lung cortisol (Speroff, Glass & Kase, 1999).

Cortisol increases during pregnancy, although to a lesser extent than the increases seen in progesterone and estrogen. The most dramatic increases are seen beginning at 34-36 weeks gestation, which correlates with fetal pulmonary maturation (Mendelson & Boggaram, 1991). Once parturition has occurred cortisol levels fall, but do not attain prepregnancy levels until several weeks after delivery (Hooper & Young, 1998).

The Major Hormones of Pregnancy: Peptide Hormones

Human Chorionic Gonadotropin (hCG)

The local uterine signal of conception is the secretion of Human Chorionic Gonadotropin by the blastocyst. HCG takes over from the anterior pituitary luteotropic hormone; luteinizing hormone (LH) on about the eighth day after ovulation in maintaining the corpus luteum (Csapo, Pulkkinen & Wiest, 1973). HCG can be first detected in maternal blood just one day after implantation, and using sensitive molecular assays is evident as a secretory product at the eight cell embryonic stage (Bonduelle, Dodd, Liebaers, Steirteghem, Williamson & Akhurst, 1988). Continued survival of the corpus luteum is totally dependent on hCG until approximately seven weeks gestation (Csapo, Pulkkinen & Wiest, 1973). As previously discussed, from the seventh to the tenth week,

the placenta as the sole source of progesterone synthesis gradually replaces the corpus luteum. Maternal circulating hCG is approximately 100IU/L at the time of missed menses (Schneider, Davies & Honour, 1993). A maximal level of about 100,000IU/L in maternal circulation is reached at eight to ten weeks of gestation. The corpus luteum then involutes when hCG attain these high pregnancy levels (Nakajima, McAuliffe & Gibson, 1990). Reported pregnancy sickness also correlates with increasing levels of hCG. Human chorionic gonadotropin levels then decrease to about 10,000-20,000IU/L by 18-20 weeks and remain at that level until term (Speroff, Glass & Kase, 1999). It is not known why hCG levels decrease through the second half of pregnancy but it has been hypothesized that progesterone levels may have an inhibitory effect on hCG synthesis (Maruo, Matsuo, Ohtani, Hoshina & Mochizuchi, 1986).

HCG levels throughout pregnancy are higher in women bearing female fetuses (Meyer, Burton &, Scommegna, 1997; Obiekwe & Chard, 1982; Santolaya-Forgas, 1997; Yaron et al, 2002). This is true of serum levels, placental content, urinary levels, and amniotic fluid concentrations. The mechanism and function of this sex difference is currently not known.

Prolactin

A major function of prolactin is to initiate and maintain lactation and breast tissue development. The effect on the mammary gland by this hormone is minimal however without the prior presence and preparation of breast tissue by estrogen, progesterone, corticosteroids and insulin (Kletzky, Marrs, Howard, McCormick & Mishell Jr, 1980). In pregnancy, plasma prolactin secretion is limited to the fetal pituitary, the maternal

pituitary and the uterus (Barberia, Abu-Fadil, Kletzky & Nakamura, 1975). Neither the placenta nor the amniotic membrane (amnion and chorion) synthesise prolactin. During gestation prolactin levels rise from the normal level of 10-25 ng/mL to high concentrations, beginning about week eight, reaching a peak of 200-400 ng/mL at term (Tyson, Hwang, Guyda & Friesen, 1972). Nursing causes a further potentiation of prolactin secretion, which may be sustained indefinitely (Speroff, Glass & Kase, 1999). Neo-natal prolactin concentrations are high, but fall to adult levels by three months of age (Grattan, 2001).

Human Placental Lactogen (HPL)

The placenta produces human placental lactogen late in pregnancy (Speroff, Glass and Kase, 1999). It is very similar in structure to human growth hormone and appears to exert is physiologic effects via the human growth hormone receptor (Walker, Fitzpatrick, Barrera-Saldana, Resendes-Peres & Saunders, 1991). Little HPL reaches fetal circulation, and its primary function appears to be involved in the alteration of maternal carbohydrate and lipid metabolism to provide for fetal nutrient requirements (Felig, 1973). It also has been implicated as an important factor in stimulating mammary cell proliferation (Anthony, Limesand, Fanning & Liang, 1998). The levels of HPL in maternal circulation are correlated with fetal and placental weight, steadily increasing until it plateaus in the last four weeks of pregnancy (5-7mg/mL) (Speroff, Glass & Kase, 1999).

Pregnancy has been likened to a state of "accelerated starvation" in the mother (Felig, 1973). This expression is related to the superior skill of the placenta to obtain the

necessary resources to maintain the fetoplacental unit at the expense of maternal need. Glucose provides the major fuel requirement of the fetus, and the differential glucose gradient transfer favours the fetus. In a fasting state (i.e., between maternal meals), it is believed to be the effects of human placental lactogen that mediate maternal hypoglycemia (low blood sugar) (Felig & Lynch, 1970). In the second half of pregnancy when HPL levels rise approximately 10-fold, there is an attendant increase in the level of insulin along with a decreased cellular response, suggests HPL may be involved in the diabetogenic effects of pregnancy (Felig & Lynch, 1970). Moreover, in a fasting state, as glucose decreases HPL levels rise. This stimulates maternal lipolysis leading to an increase in circulating free fatty acids, thus providing a different fuel for maternal use so the glucose and, to a lesser extent, the amino acids can be conserved for the fetus (Speroff, Glass & Kase, 1999).

Relaxin

Relaxin is a peptide hormone produced by the pregnant corpus luteum and has been identified in the human placenta, decidua and chorion (Weiss, O'Byrne, Hochman, Steinetz, Godlsmith & Flitcraft, 1978). It is not detectable in men or non-pregnant women. The maternal serum concentration rises during the first trimester when the corpus luteum is dominant, then declines in the second trimester (Quagliarello, Steinetz & Weiss, 1979). This suggests a role for maintaining the early pregnancy, but its function is currently unknown (Speroff, Glass & Kase, 1999). To examine the contribution of the corpus luteum to relaxin production, normally pregnant women were compared with women pregnant with donated oocytes, and therefore without corpora

lutea. Relaxin was undetectable in the women without functioning ovaries (Emmi et al, 1991). The fact that the women pregnant with donated oocytes, and undetectable relaxin levels, did not differ in pregnancy outcomes from the normally pregnant women suggests it is not necessary for the maintenance of pregnancy, labour or delivery. In animals relaxin softens the cervix, inhibits uterine contractions and relaxes the pubic symphysis (MacLennan, Katz & Creasy, 1985).

Oxytocin

Oxytocin is a peptide hormone synthesised in the hypothalamus and secreted by the posterior pituitary (Nelson, 2000). During the very final stages of pregnancy oxytocin levels rise dramatically to facilitate birth and lactation (Bazer, 1998). Using sensitive assays, an increase in maternal levels of oxytocin can be detected prior to parturition, initially only at night however (Hirst, Chibbart & Mitchell, 1993). Once labour has begun, oxytocin levels rise dramatically, with the greatest increases seen during the second stage of labour, suggesting it may be necessary for development of the more intense uterine contractions (Speroff, Glass & Kase, 1999). Levels decline quickly following delivery, however suckling causes spurts of oxytocin release that results in brief, but varying increases in maternal plasma levels (Brett & Baxendale, 2001).

Cognitive Function During Pregnancy

"I'm not usually absentminded, but I am now [six months pregnant].

I'll be leaving a meeting and looking for my toddler.

I start to panic, only to find I already have him on my hip."

Parsons & Redman
1991, page 25

Maternal anecdotal reports of cognitive decrements during pregnancy are not uncommon (Baildam, 1991; Ellison, 2005; Moore, 1997; Parsons & Redman, 1991; Welsh, 1991). Terms such as 'dumb-mum syndrome" and "baby brain" are well-known lay descriptors for the phenomenon. Consistent with these subjective accounts, a small research literature supports the finding of cognitive decrements during pregnancy (Buckwalter et al, 1999; Keenan Yaldoo, Stress, Fuerst & Ginsburg, 1998; Sharp, Brindle, Brown & Turner, 1993; Woodfield, 1984). Researchers in this area have identified a cluster of cognitive traits that appear to be adversely affected by pregnancy, namely deficits in aspects of memory performance, lapses in concentration and attention, and decrements in spatial performance. These findings are not without contention: Other researchers in this area (Casey, 2000; Crawley, Dennison & Carter, 2003; McDowall and Moriarty, 2000; Schneider, 1989) contend that pregnancy does not appear to negatively affect maternal cognitive function and produce their own evidence to support this claim.

Memory

Impairments in verbal memory have been reported when pregnant women were compared to control women (Sharp et al, 1993). Using recall of word lists as the dependent measure, these authors found pregnant women to be significantly impaired when compared to non-pregnant women. This was particularly true when learning was incidental rather than explicit. In addition, using a priming task (word-stem completion), pregnant women were also demonstrated to be impaired on two measures of implicit memory. These authors noted deficits for both primiparous (first pregnancy) and multiparous (second or subsequent pregnancy) women across all trimesters of pregnancy.

Also using a word-stem completion task, other researchers have documented a decrement in implicit memory when primiparous women were compared to controls (Brindle, Brown, Brown, Griffith & Turner, 1991). However, in this study, researchers observed no significant group differences in explicit memory when experimental and control participants were tested on photograph recognition of faces, and object and word recall tasks. This result suggests that implicit memory, but not explicit memory, is selectively impaired during pregnancy. Other researchers have been less successful in identifying a pregnancy-related decline in memory, however. Janes et al (1999) compared performance between primiparous, multiparous and nulliparous (never pregnant) women. On tests of both explicit (questioned about a previously viewed video) and implicit (word stem completion) memory, no between group differences were identified.

McDowall and Moriarty (2000) have recently challenged the earlier findings of Brindle et al (1991). They proposed it is inconsistent with existing memory research for implicit memory, as tested by word stem completion to be impaired while explicit memory remained unchanged. They cite research from amnesic patients where explicit memory is the system that is generally severely impaired while performance on implicit priming tasks tend to be near normal levels (Cermak, Talbot, Chandler & Wolbarst, 1985; Cermak, Verfaellie & Chase, 1995; Graf & Mandler, 1984). Moreover, McDowall and Moriarty (2000) contend the tasks that were used by Brindle et al, (1991) to assess implicit and explicit memory probably tapped into different cognitive processing styles. Implicit tests such as word stem completion emphasize perceptual processing, which primarily relies on word form. Conversely, standard explicit memory tests such as recall and recognition tasks rely on conceptual processes such as word meaning (Weldon & Roediger, 1987). This resulted in a confound between the task and type of cognitive processing involved. McDowall and Moriarty (2000) replicated the earlier work completed by Brindle et al (1991), however this time they noted and controlled for the different types of cognitive styles used when completing implicit or explicit memory tasks. When this effect was experimentally removed, between group differences were non-significant.

When evaluating the effects of gestation on working memory using both a number and verbal span test, Janes, Casey, Huntsdale and Angus (1999) reported a significant difference in performance when primiparous women were compared to control women. This effect was only evident on the number span task however, as the verbal span task failed to reach significance. Trends in the data for the verbal span task suggest the small sample size (20 per group) may have precluded the possibility of

detecting an effect for this test however. Consistent with other research in this area, two within-group studies compared verbal memory function late in pregnancy with a postnatal test day. In comparison with performance one month after delivery, Buckwalter et al (1999) reported that women showed significantly more impairments in verbal memory during pregnancy. Although these women tended to report more negative mood states prenatally, the memory deficits were not explained by the mood disturbances. In contrast, although Jarrahi-Zadeh, Kane, Van De Castlf, Lachenbruch and Ewing (1969) identified a pregnancy-related memory decrement when compared to a postnatal test, they suggested this was probably caused by negative affect. They noted the observed poorer test performance during pregnancy seemed to be related to emotional disturbances in general, rather than specific effects of gestation on mental functioning.

Some researchers have looked specifically at effects that could be related to the peripartum. When evaluating cognitive function of recently parturient women, Eidelman, Hoffmann and Kaitz (1993) identified deficits in verbal memory scores when these women were compared to non-pregnant controls. This effect was evident from the first postnatal day but by day two scores between groups no longer differed. This suggested to these authors that the observed cognitive decline appears to be directly mediated by labour and delivery. The heterogeneity of the control group does call these results into question however. Half the comparison group were the husbands of the women who comprised the experimental group. Another fifteen controls were high-risk third trimester pregnant women and the remaining twenty controls were nulliparous women. While it is not always possible to obtain a control group that exactly matches the experimental group on all variables of interest, it is important to at least match groups based on

biological sex (Cozby, 2001). This is probably all the more important when possible mechanisms offered to account for the observed differences include endocrinological explanations (Eidelman, Hoffman & Kaitz, 1993).

Most researchers have used a cross-sectional design when evaluating the relative contribution of gestation to cognitive change. This is a methodological approach that in itself can introduce confounds and sometimes muddy results (Cozby, 2001). When pregnant women in differing stages of pregnancy are systematically grouped into the three respective trimesters of pregnancy, gestational dates within each group can vary widely. For example, Sharp et al, (1993) grouped women less than 14 weeks pregnant into "first trimester". Women fourteen to 27 weeks were placed in the "second trimester" group and women greater than 27 weeks were in the "third trimester" group. Test performance results were then generated based on this type of grouping. The problem with this system, as in any cohort study, is it is difficult to make discrete distinctions with variables, such as gestational length, that are inherently continuous by nature. Thus the system of grouping may not capture the richness of any potential effects. In addition, there are no controls for the very wide variations that occur within each trimester. For example women in the "second trimester" and "third trimester" groups ranged across thirteen weeks of gestation. Moreover, these types of designs lack the statistical power of a longitudinal design where a participant's performance can be compared to earlier and later test sessions (Cozby, 2001). Keenan et al (1998) attempted to control for this effect by testing and tracking the same set of pregnant women.

Keenan et al (1998) investigated memory in women over the course of a normal pregnancy and into the postpartum period. Closely matched non-pregnant controls were

similarly studied at equivalent intervals. Pregnant women were shown to be significantly impaired for both immediate and delayed recall of paragraph material, with the effect persisting independent of mood and anxiety scores. Unlike the study conducted by Sharp et al (1993), this effect was only evident in the third trimester of pregnancy.

Not all longitudinal studies have identified an effect of pregnancy on cognitive change however. Casey (2000) evaluated pregnant and control women six times at approximately three-month intervals beginning early in pregnancy and continuing until late in the postpartum. Among the cognitive battery, which included verbal and working memory tasks, Casey (2000) found no differences between groups on objective tests at any time phase. Finding similar to this were reported by Casey et al (1999), when women in differing stages of pregnancy were compared to non-pregnant control groups. Again, pregnant women performed no worse than control participants.

Concentration and Attention

Along with memory decrements, attention and concentration also appear to be affected by pregnancy. Harris, Deary, Harris, Lees and Wilson (1996) tested a sample of recently parturient women and reported significantly lower scores than controls on one of two measures of concentration and attention. This effect was not replicated prenatally or later in the postnatal period. It was found that self-rated depression scores were a significant covariate of the memory impairments, prompting the researchers to suggest the cognitive decline might well be secondary to depression. Unlike other researchers (Brindle et al, 1991; Eidelman et al, 1993), Harris et al (1996) failed to detect significant group differences on measures of memory or general cognitive function.

Other authors have also noted deficits in attentional tasks. Silber, Almkvist, Larsson and Uvnas-Mober (1990) investigated pregnant women at five different intervals beginning in the 36th week of pregnancy. Subsequent tests occurred around delivery and at three, six and twelve months postpartum. When late postnatal tests were compared with those from the end of pregnancy, participants in the experimental group showed significantly greater improvements in their performance on measures of attention.

Like the memory research in this area, published findings regarding attention and pregnancy are also somewhat ambiguous (Crawley, Dennison and Carter, 2003; Schneider, 1989; Silber et al, 1990). In a longitudinal study, pregnant women were tested on verbal memory as well as focused and divided attention at four occasions across pregnancy and up to one year postnatal. Comparing these women to controls Crawley, Dennison and Carter (2003) found no difference in performance. Schneider (1989) also did not detect pregnancy-related decrements in performance. In fact, without exception, performance by women in this study on the battery of cognitive tests administered prior to and during pregnancy actually improved over time. The absence of a control group and the repeated use of the same tests throughout the duration of the study (four exposures) suggest the reported improvements may be a practice artefact rather than the relative contribution of pregnancy *per se* (Schneider, 1989).

Spatial Performance

Using the embedded figures test, a measure of spatial function, one study has reported a pregnancy-related effect. Woodfield (1984) tested women at 38 and 40

weeks gestation. When this group was retested in the sixth postnatal week, there was a significant improvement in performance. This result persisted independent of practice effects suggesting gestation had a direct and detrimental effect on spatial performance.

Studies with Self Report Measures of Cognitive Decrements

A number of studies have included a self-report scale in an attempt to evaluate maternal perceptions of cognitive change (Brindle et al, 1991; Casey 2000; Casey, Huntsdale, Angus & Janes, 1999; Crawley, Dennison & Carter, 2003; Janes et al, 1999; McDowall & Moriarty, 2000; Parsons & Redman, 1991; Sharp et al, 1993). Perhaps the best in this group surveyed both subjective accounts and the content (type, range and salience) of the cognitive changes (Parsons & Redman, 1991). In this study, sixty-four percent of women reported subjective experiences of cognitive deficits during pregnancy. Educated, older, married women described the greatest degree of cognitive change. In a prospective follow–up study 82% of women who reported cognitive deficits during the perinatal period specifically noted concentration problems, increased absentmindedness and impairments in perceived memory skills.

Of the studies that have included self-report measures most but not all report pregnant women as either rating their memories as worse than normal (Brindle et al, 1991; McDowall & Moriarty, 2000), or significantly poorer than those ratings provided by control women (Casey 2000; Casey, Huntsdale, Angus & Janes, 1999; Crawley, Dennison & Carter, 2003; Janes et al, 1999; Sharp et al, 1993). In three other studies subjective ratings of cognitive change did not differ significantly between groups (Gross & Pattison, 1994; Keenan et al, 1998; Morris, Toms, Easthope & Biddulph 1998). In fact,

in one of these studies the scores obtained from the self reported Cognitive Failures Questionnaire provided a better predictor of mood in the pregnant participants than among the control women. This suggests that perhaps mood may be closely linked to cognitive competency perception during gestation (Morris, Toms, Easthope & Biddulph 1998).

Crawley (2002) has addressed the impact of subjective accounts of cognitive decline during pregnancy amongst the myriad of other changes that accompanies pregnancy. She suggests that although some women will report impairments when specifically questioned about cognitive changes, the changes may not be salient enough to impact everyday functioning. If this is the case in a research setting, pregnant women may not spontaneously report cognitive decrements. When tested by Crawley (2002), pregnant women were given the opportunity to provide a free report of any changes they have experienced during pregnancy; only 2% of women reported a cognitive decline. When questioned directly however, pregnant women disclosed more cognitive failures than control women, primarily in the areas of memory, concentration, clarity of thought and attention.

Some authors who have included self-report measures have obtained results that need further clarification. Research conducted by Christensen, Poyser, Pollitt and Cubis (1999) indicated that although pregnant women rated their memory as better before pregnancy, these evaluations did not differ from controls in their absolute rating of current memory performance. Considering the similarity between the group measures on subjective memory ratings, Christensen et al (1999) interpreted this finding as an *over-rating* by pregnant woman on pre-pregnancy cognitive function, rather than an *under-rating* of memory skills while pregnant. Consistent with the reports of the

pregnant women, their partners also rated their spouses memories while pregnant, as worse than normal. So, if the authors of this study are correct in their interpretation – that pregnant women over rated their pre-gestation memory performance, then it would be expected that the spouses of these women would have not noticed any cognitive change in pregnancy. This was not the case however. Spouses like the pregnant women, both believed her memory performance to be negatively affected by pregnancy.

Along with subjective memory complaints, Christensen et al (1999) also assessed objective performance on a variety of tests of attention and memory. Although women reported memory decrements during pregnancy, objective tests did not reveal a difference between pregnant women and controls. In an incidental memory task, third trimester pregnant women recognized more pregnancy-related words than neutral or anxious words. This result prompted the authors to conclude that although women may "falsely" perceive their memory to have deteriorated during pregnancy, performance may in fact be better than controls when material is pregnancy-related. It is possible however, that the negative memory findings reported here could be more related to a lack of sensitivity of the memory tasks used in this study, rather than errors in participant self-evaluation of their cognitive function.

Summary of Research Conducted to Date

As is evident from the studies summarized here, a general measurable trend of pregnancy-related cognitive decrements is present, yet the results are variable and inconsistent. Previous authors have attributed the discrepant findings to design limitations including inadequate test materials (Jarrahi-Zadeh, et al, 1969; McDowall &

Moriarty, 2000), poorly matched or lack of control groups, and the failure to correct for Type 1 errors (rejecting a true null hypothesis (Cozby, 2001) (Harris et al, 1996). In addition, some studies appear to have inadvertently alerted their participants to the research hypothesis preventing the possible control of demand characteristics (Christensen et al, 1999; Gross & Pattison, 1994). Many other sources of unexplained variation remain untested such as task difficulty, parity, age, fetal sex and the potential effects of placenta-derived diffusible factors. To date the most common explanation given for the cause of pregnancy-related cognitive change have implicated sex steroids and other hormones of pregnancy (see Brett & Baxendale, 2001 for a review).

Possible Mechanisms Contributing to Cognitive Change in Pregnancy

Steroid Hormones

Considering the existing literature linking steroid hormones to cognitive change in both animal and human models (Bachevalier, Hagger & Bercu, 1989; Beatty, 1984; Collins & Kimura, 1997; Gaulin & Fitzgerald, 1986; Hampson, 1990a; Hampson, 1990b; Hampson & Kimura, 1988; Kimura, 2002; Kimura, 2004; Maccoby & Jacklin, 1974; Michael & Zumpe, 1998; Roof & Haverns, 1992), it is indeed plausible that these same sex hormones may also be involved in the cognitive changes seen during pregnancy.

One study has attempted to link gestational hormones to pregnancy-related cognitive deficits (Buckwalter et al, 1999). Using serum radioimmunoassay techniques these authors evaluated potential relationships between cognitive profiles and estradiol, progesterone, testosterone, DHEA, and cortisol during the latter stages of pregnancy,

and again in the early postnatal period. None of the hormones assayed however were consistently related to cognitive performance during gestation (Buckwalter et al, 1999). Methodological issues may be able to explain this negative link however. As the study lacked both a control group and baseline data, it is difficult to determine if the observed postnatal performance improvements were related to practice effects or the effects of sex steroids *per se*. Moreover, as serum was the medium from which the steroid hormones were assayed, reported values were that of the total levels present in blood. This value, obtained for each of the assayed hormones, would include both the bound and unbound fractions. As salivary assays were not conducted, nor was an estimate of the unbound portion reported (which may have been estimated from the total serum levels if details regarding serum binding factors had been recorded), it remains unknown if cognitive test performance correlated with the bioavailable fraction of the hormones assayed.

The glucocorticoid cortisol has been implicated as a potential agent in cognitive function disturbances (Lupien, Lecours, Lussier & Schwartz, 1994; Miller et al, 1998; Ohl & Fuchs, 1998; Wolkowitz, 1994). In rats, performance on spatial memory tasks is inversely related to serum glucocorticoid levels (Bodnoff, Humphreys, Lehman, Diamond, Rose & Meaney, 1995). Consistent with these animal data, human studies have shown synthetic glucocorticoids can cause a specific reduction in verbal memory recall scores in both normal (Newcomber, Craft, Hershey, Askins & Bardgett, 1994) and clinical (Keenan, 1996) populations. Moreover, patients with Cushings Syndrome, who have an endogenous overproduction of cortisol, also show deficits in verbal memory. In these patients, when excess glucocorticoids were reduced, memory performance improved (Mauri et al, 1993).

As discussed earlier, cortisol levels rise during the last trimester of pregnancy (Bazer, 1998) and as such may underlie the reported cognitive changes seen in pregnancy. One study has attempted to find an association between maternal serum cortisol levels late in pregnancy and the concomitant cognitive profile. Buckwalter et al (1999) failed to find a relationship, but these authors noted; "Our protocol for blood collection was not designed to allow for analysis of diurnal variation, which questions the reliability of our findings" (Buckwalter et al, 1990, p. 80). This suggests perhaps these authors were unaware at the time of testing that cortisol secretion shows a reliable circadian rhythm (Richardson & Martin, 1988). Indeed, this papers' method section identifies no participant testing time of day. To date, no other studies have evaluated relationships between maternal cognitive function and cortisol secretion while also controlling for its circadian cycle.

Oxytocin

Oxytocin has also been implicated in the cognitive decrements related to gestation (Silber et al, 1990). This peptide hormone has been demonstrated to inhibit learning and memory in animal models (Fehm-Wolfsdorf, Born, Voigt & Fehm, 1984; Ostrowski, 1998), however the links to cognitive change in humans in less clear. Some evidence suggests it may be involved in verbal memory (Kennett Devlin & Ferrier, 1982), although this finding has not been consistently reported (Fehm-Wolfsdorf, Bacholz, Born, Voigt, & Fehm, 1988). One attempt has been made to link cognitive performance during pregnancy to plasma oxytocin concentrations. Silber et al, (1990) tested 20 pregnant women at five different points beginning late in pregnancy continuing until twelve months

postpartum. At each test session performance on cognitive tests of alertness, implicit and explicit memory was evaluated and serum oxytocin levels were simultaneously assayed. As discussed earlier, when late postnatal tests were compared with those from the end of pregnancy, participants in the experimental group showed significantly greater improvements in their performance on measures of attention. Although pregnant women had significantly higher oxytocin concentrations than controls for the first three test sessions, no correlation was found between any cognitive tests and maternal serum oxytocin levels (Silber et al, 1990).

Sleep Deprivation and Circadian Rhythms

When asked, almost any pregnant woman in the latter stages of gestation, or any new parent, will generally concede pregnancy and the postnatal period is a time of chronic sleep deprivation (Douglas, 2000; Lee, Zaffke & McEnany, 2000). This statement is so commonly known and accepted (Ellison, 2005), it barely needs the support of a citation. A number of explanations have been proposed for the reported sleep loss (Kryger, Roth & Dement, 2000). These include; the increasing girth of impending motherhood along with the nocturnal activities of a squirming fetus makes it difficult to fall and remain asleep. Increased occurrences of night-time awakenings have also been linked to frequent bathroom visits as the expanding uterus begins to put downward pressure on the bladder; resulting in urinary urge in the presence of only a partially full bladder. And finally, in the early postpartum normal parental sleep patterns are regularly disturbed by infant cries signalling the need for feeding, diapering or comfort (Kryger, Roth & Dement, 2000; Lee, Zaffke & McEnany, 2000; Smith, 2004).

Sleep deprivation has been consistently and systematically linked to cognitive decrements and has been reported in most of the cognitive domains studied (Blagrove, Alexander & Horne, 1995; Harrison & Horne, 2000; Pilcher & Huffcutt, 1996). A recent review paper on this topic provides a rather exhaustive summary of the cognitive faculties believed to be affected (Durmer & Dinges, 2005). Included are deficits in working memory, impairments in learning novel tasks, cognitive slowing, and when under a time pressure to complete a task, increases in error rates. Performance of sleep-deprived individuals deteriorates as task duration increases and response times increase. Attention also suffers as a consequence of sleep deprivation, as does higher order cognitive processing such as lateral thinking, insight, innovation, risk assessment and response inhibition (see Durmer & Dinges, 2005 for a review).

Although the effects of total sleep deprivation on cognitive function has been the subject of considerable research, it is, in reality a much less common form of sleep loss than partial sleep restriction. In a real world setting, partial sleep deprivation more closely parallels sleep loss in society, being caused by a wide range of factors such as shift work, medical conditions, work and social commitments as well as family responsibilities. Perhaps the most extensive investigation of chronic sleep restriction conducted to date evaluated the effects of sleep loss when sleep was limited to 4, 6 or 8 hours time in bed (Van Dongen, Maislin, Mullington & Dinges, 2003). A total sleep deprivation condition for 1, 2 and 3 nights was also included. Participants were given cognitive tests every two hours from 7:30am until 11:30pm each day for the 14 days of the study. Subjective sleepiness and fatigue were also evaluated. Participants limited to 8 hours in bed showed no cognitive deficits, however, for those restricted to four or six hours of sleep, decrements in attention, working memory and cognitive "throughput"

tasks (cognitive processing time) were observed. Subjects limited to just four hours sleep per night showed decrements in performance equivalent to those seen after two nights total sleep deprivation. Similarly, performance after six hours sleep per night for two weeks paralleled cognitive deficits seen after one night of total sleep deprivation. The cumulative cognitive deficits increased in an almost linear fashion over the four and six hour groups. Subjective ratings of sleepiness and fatigue showed much smaller increases however. This difference suggested an increasing dissociation between subjective perceptions of sleepiness and actual cognitive performance. Or put more simply, the more sleep deprived an individual became, the poorer their ability to self evaluate how tired they in fact were when subjective ratings were compared to actual performance. This finding is consistent with other research in this area where subjective ratings of tiredness when chronically sleep restricted can be dissociated from actual cognitive task performance (Van Dongen, Baynard, Maislin & Dinges, 2004).

Although disorders affecting mood can also concurrently affect quality of sleep (for example; depression), sleep deprivation in and of itself can alter mood (Pilcher & Huffcutt, 1996). This is true with either total sleep deprivation or partial sleep deprivation, with both types resulting in generally negative mood states in normal populations (e.g. non-depressed individuals). This is especially evident in the areas of fatigue, loss of vigour, sleepiness and confusion (Durmer & Dinges, 2005). Feelings of irritability, anxiety and depression can also result from inadequate sleep however, experimental models designed to evaluate this link have been restricted to a limited type of environmental setting (i.e. research is lacking where sleep deprived mood states are evaluated in a comfortable environment) (Durmer & Dinges, 2005).

Considering the relationship between gestation/sleep deprivation, and

gestation/cognitive impairment, research addressing the effects of pregnancy on maternal cognitive change needs to evaluate and control for the possible effects of sleepiness on task performance. Although in the past pregnancy researchers have questioned women about their sleep habits during gestation (Casey et al, 1999; Crawley, 2002; Gross & Pattison, 1994), a thorough investigation of sleepiness and sleep habits during and after pregnancy has currently not been completed. Current work in the area of cognitive changes in pregnancy has also not considered the impact of individual participant circadian rhythms when scheduling test sessions (for example: Buckwalter et al, 1999; Keenan et al, 1998; Sharp et al 1993; Woodfield, 1984). It has been shown that people tend to perform best when cognitive testing coincides with the daily peak in circadian arousal (Smith, Reilly & Midkiff, 1989).

Across the 24-hour circadian rhythm many common biological processes have been shown to fluctuate. This includes such factors as body temperature, blood pressure and hormone levels (Nelson 2000). Psychological factors such as mood, alertness and task performance also show the same circadian effects (Freeman & Hovland, 1934). The implications for this variation are significant; for example industrial accidents often occur during the early morning hours when many cognitive variables are at their lowest levels in the circadian cycle (Dinges, 1995). Although these psychological rhythms tend to be consistent across individuals, differences do exist. In some cases this is a consequence of aging, while in other situations, it appears to be simply due to individual variations in circadian periodicity (Kerkhof, 1985; Kerkhof, 1998).

Some people consistently prefer daytime activity, and perform best earlier in the day. Individuals in this group are often called "morning types" or "larks". Others prefer night activities and show best performance much later in the day. These are "evening

types" or "owls" (Kerkhof, 1985; Kerkhof, 1998). Generally, with age individuals move from "owls" to "larks", i.e. adolescents tend to be much more evening active, while retirees are more morning active (May, Hasher & Stoltzfus, 1993). However, within each age range, individual variation is present (Kerkhof, 1985). In light of this, research addressing potential links between sleep deprivation and the cognitive changes seen in pregnancy should consider individual circadian periodicity variation. This would ensure all participants were being tested at times that isn't out of phase with their circadian peak performance. For example, testing a pregnant woman identified as a "lark" late in the afternoon, probably would not be sampling her performance at an optimal circadian time of the day.

Mood

Like lack of sleep, depressed mood has also been shown to directly affect cognitive performance (Gallassi, Morreale & Pagni, 2001). These effects are most commonly seen as impairments in tasks that tax attention, psychomotor speed and memory systems. When performing tests requiring focused attention, depressed patients tend to show the most impairment when the greatest attentive effort is demanded (Golinkoff & Sweneey, 1989). In cases such as this, successful task performance requires a mental strategy for successful completion. Depressed patients appear to approach these tasks with less cognitive effort than non-depressed individuals (Widlocher, 1983). When performing attentional tasks depressed patients also show motor slowing. This reduced psychomotor activity affects not only cognitive processes but also decreases the rapidity of motor output (Widlocher, 1983).

Research addressing the effects of depression on memory suggests long-term memory may be more affected than short-term/working memory (Gallassi, Morreale & Pagni, 2001). Although some authors have reported deficits in short-term/working memory (Ilsey, Moffoot & O'Carroll, 1995), others have attributed the decline to attentive dysfunction caused by the increased distractibility seen in depressed patients, rather than failure of a memory system *per se* (Sackeim, Freeman, McElhiney, Coleman, Prudic & Devanand, 1992). Long-term memory tasks that require patients to either recall or recognize earlier presented material appear to also be sensitive to depressive changes. It is unclear if the effect is due to defective encoding (Weingartner, Cohen, Murphy, Martello & Gerdt, 1981) or failures of information retrieval (Gorlinkoff & Sweeney, 1989), but what does seem clear however, is once again performance is related to the cognitive effort required in inputting or outputting the material. The greater the effort required, the more difficult the task is for the depressed person.

Autobiographical memories are sensitive to changes in mood (Gallassi, Morreale & Pagni, 2001). The mood congruent hypothesis argues that memory is better when there is a congruence between the mood of the person and the affective tone of the event to be remembered (Myers, 2001). According to this theory depressed subjects (negative mood) will recall positive events with more difficulty than negative events. They will however, more readily remember negative events, as these events are the most congruent with their current affect. This hypothesis is not without challenge (Ilsey et al, 1995), nevertheless, depressed patients do tend to supply poorly detailed autobiographical memories, especially if the response is to positive stimuli. When the stimulus is negative, their richness of recall is similar to that of controls (Kuyken & Dalgleish, 1995).

Pregnancy and the postpartum is a time when women are very vulnerable to disturbances in mood (Pritchard & Harris, 1996). Although this effect has been addressed primarily in relation to postnatal depression, changes in affective states are also common during pregnancy (Cox, Connor & Kendell, 1982; O'Hara, Schlecte, Lewis & Wright, 1991). Mood changes in the postnatal period range from mild forms of dysphoria, typically referred to as "baby blues" to clinical depression and in more rare cases; puerperal psychosis (Cox, Connor & Kendell, 1982; Pritchard & Harris, 1996). Mild postnatal depression illness is generally short lived and along with mild negative affect women often report anxiety and tearfulness. Depending on the study, prevalence rates for this type of illness range from 30% to 70% (Pritchard & Harris, 1996). More serious types of illness can occur. Postnatal clinical depression tends to be longer lasting, with a more severe and debilitating depressed mood (Saks, Frank, Lowe, Berman, Naftolin & Cohen, 1985). The most extreme form of postnatal mental illness is puerperal psychosis. In this state women can oscillate between bouts of mania and depression. In some cases psychotic episodes result, where delusions can put the woman at great risk for self harm or harm to that of her baby or other children in the home (Harris, 1994). The exact cause of postnatal illness is unknown, however it has been suggested that the post-parturition drop in steroid hormones might trigger it. Both progesterone and estradiol have been implicated (Harris, Lovett, Newcomb, Read, Walker & Riad-Fahmy, 1994; O'Hara, Schlecte, Lewis & Wright, 1991), however, other researchers have identified no such link (Heidrich et al, 1994). Nonetheless, estrogen has been successfully used in the treatment of women with recurrent postnatal depression (Gregoire, Kumar, Everitt, Henderson & Studd, 1996).

Analysis 1:
Longitudinal Study of the Relationship Between Gestational Hormones and Cognition

In an effort to better understand and empirically quantify the effects of pregnancy on maternal cognition and evaluate the relative contribution of gestational steroid hormones, this study tested women across pregnancy and into the postnatal phase. The presence of an age and education matched control group addressed practice effects and other confounding variables. Women in both groups were tested on a variety of cognitive tasks designed to evaluate changes in concentration and attention, verbal memory, working memory, spatial performance and general cognitive function. Using saliva samples, steroid hormone profiles were generated for each test session for all women in the study.

The use of a longitudinal design, although more costly and time consuming than a cross-sectional study was selected for two reasons: Firstly, it provides considerably greater statistical power than a standard between-subjects study. Secondly, the primary tenant of this research is to measure cognitive *change across* pregnancy, and as time is inseparable from the measurement of change, the longitudinal design was deemed the most appropriate. This decision was made despite the inherent risks associated with participant attrition as the study progressed.

Analysis 1: Formal Hypotheses

The expected research outcomes were specified in advance of the study. It was predicted there would be an interaction effect between group and time. This assumed

performance of women in the experimental group would be affected by pregnancy and this effect would change in the postnatal phase. It was also predicted there would be a main effect of group on the dependent measures, with women in the experimental group performing differently to that of women in the control group.

Discussion of Analysis 1 Hypotheses

Early in the study the differences between the experimental and control group on the dependent measures would be very small, but as pregnancy progressed experimental women would fail to show the practice-related improvements in performance seen by the control women. The size of the difference between the two groups would increase until parturition. Once parturition had occurred, women in the experimental group would recover some of their cognitive function during the postnatal phase, however this recovery would not attain the levels of the control participants due to such factors as sleepiness. At the final test session, control women would still be out performing women in the experimental group *(session x group interaction)*. It was also predicted that control women would outperform pregnant woman on the cognitive tasks, with pregnant women showing a gestation-related impairment. This would result in control women consistently outperforming pregnant women on the cognitive test battery *(group main effect)*.

As some of the tests included in the cognitive battery have been demonstrated to show a positive relationship (i.e. estrogen) or a negative relationship (i.e. progesterone) to the hormones present during gestation, the exact nature of the effects of these hormones on cognitive function as they gradually increase over the term of a human

pregnancy was unknown. If pregnancy itself was causing a global impairment in function, any beneficial effects of steroids on cognition may be washed out. Alternatively, as the hormones of pregnancy differ in type, amount and kind to other reproductive profiles, it is unclear how they might affect maternal cognition in this situation. In light of this, no formal *apriori* hypotheses were made as to the effects of the sex hormone milieu during pregnancy on the specific cognitive tests administered.

ANALYSIS 1: METHOD

Participants

Informed written consent was obtained from all participants at the outset of the study, and all procedures had received prior approval from the Simon Fraser University Research Ethics Board. The experimental group comprised of 49 participants who were recruited during the early stages of pregnancy through midwifery practices within the Greater Vancouver Regional District. Of these, four women miscarried early in pregnancy and their data was excluded. Forty-five women completed the study and delivered singleton pregnancies; thirty-one were delivered vaginally and fourteen were delivered by Caesarean section. Twenty-nine women gave birth to boys and 16 delivered girls. An additional 45 non-pregnant control women were recruited via print ads in local community newspapers (Appendix A). All 90 subjects spoke English fluently although for a few women this was not their first language (4 – exptal group/6 – control group). The average age of all women in the study was 33.37 years (s.d. = 5.056). Generally participants had some postsecondary education, with the average years of education being 14.80 years (s.d = 1.837).

Testing Schedule

Using a longitudinal experimental design, each woman was assessed at five different time points. At the time of their first visit, when women in the experimental group were approximately nine to twelve weeks from the date of their last menstrual

period (LMP) they received an A-4-size paper entitled "Does Pregnancy Change the Way you Think?" (Appendix B). This provided information about the study along with contact information. This sheet was included in a folder of information that is routinely given to all newly pregnant clients seeking the licensed midwifery care. Interested women contacted a confidential pager and the first test session was scheduled. Four subsequent test sessions occurred as the women moved through their pregnancies and into the postnatal phase. Test sessions were three months apart, occurring approximately 12 weeks, 24 weeks and 37 weeks since LMP. A fourth test session occurred six weeks post natal and one final session was scheduled once menstruation had resumed. The interval between the fourth and fifth test session ranged from three to eighteen months for both groups. On average, the first test session took approximately one and a half hours to complete and the subsequent four test sessions were usually completed within an hour.

Women in the control group were also tested approximately every three months with the exception of test session five. For this last session, control women were temporally yoked to women in the experimental group to ensure a similar gap between sessions four and five for the two groups. For women in the control group and for test session five of the experimental group, testing occurred during the menstrual phase of the ovarian cycle (days 2-8). All testing occurred in the homes of the participants between 3pm and 8pm.

Procedure

On the first test day, along with informed consent documentation, all women in the study completed a brief questionnaire outlining contact and demographic information. Reports regarding medical, reproductive and personal history were also completed, as were questionnaires related to mood and sleep habits. During this first test session fluid intelligence and crystallized intelligence were evaluated using short-form I.Q tests. The eight-test cognitive battery was then administered (Table 2). Each test session ended with participants providing a sample of saliva for later steroid hormone analyses. Test sessions two to five followed a standard repeated measures procedure with mood scales being administered first, then sleep scales, then the test battery and finally the saliva sample was collected. The order of administration of tests in the cognitive battery was counterbalanced across the five sessions.

Many factors other than issues related to pregnancy and the post partum have the potential to interfere with a woman's' cognitive clarity. In light of these possible confounds, an attempt was made to identify as these variables prior to beginning the study to allow for later statistical control. These variables included any factors that would compete at a specific test session, or across all the test sessions for a participant's attention, availability and/or cognitive clarity. Table 3 outlines this list of control variables identified prior to the inception of the study.

Table 2: Summary of Cognitive Tests

Test Name	Participant's Task	Cognitive Function Sampled
WAIS III Symbol Search	Identify instances where target objects appeared within a short series of stimuli.	Perceptual speed & accuracy
WAIS III Digit Symbol - Coding	Rapidly identify simple symbols encoded by numbers.	Visual-motor coordination
Purdue Peg Board Dominant and Non-Dominant Hand	Rapidly select small metal components from a cup and assemble them in a row of holes in a board.	Fine motor skills
California Verbal Learning Task (CVLT)	Memorize and recall a list of 16 common shopping items	List Memorization
Silverman-Eals Object Location Memory Task	Scan a two-dimensional array of objects, and then identify on a probe array whether or not the items have been moved to a new location.	Object location memory
Listening-Span (L-Span)	Answer a simple question about a sentence while at the same time remembering the final word of the sentence. The number of sentences presented is increased over trials to a maximum of seven.	Verbal working memory
Computation-Span (C-Span)	Solve a simple mathematical equation, while at the same time remembering the final number of the equation. The number of equations presented is increased over trials to a maximum of seven	Arithmetic working memory
Shepard-Metzler Mental Rotation (MRT)	Identify, from a set of choices, the new orientation of a complex figure that has been rotated three-dimensionally	Spatial visualization / spatial working memory

Table 3: Variables Included in Study to Address Potential Confounds

First language spoken	Paid employment outside the home vs. stay-at-home Mom
Parity (number of children previously borne)	Age at first test session
Sex of any sibling children in the home	Total number of years of education
Single parent or cohabiting	Employment status just prior to parturition
Subjective rating of pregnancy sickness	Employment status at the final test session
Handedness	

The Mood Measure

As mood (Gallassi, Morreale & Pagni, 2001) has been shown to interfere with cognitive function, one measure was included in the study. The Profile of Mood States (POMS) (EdiTs, San Diego, California) is a 65-item, five-point adjective rating scale designed to evaluate current mood. Participants were required to identify how well each of the 65 feeling descriptors (such as; bushed, tense, helpless, full of pep, guilty) fit their current mood. Choices from which they rate their current feelings ranged from "0= Not at all" to "4= Extremely". The POMS loads on six different mood factors, these are Tension-Anxiety, Depression-Dejection, Anger-Hostility, Vigour-Activity, Fatigue-Inertia and Confusion-Bewilderment. A separate score can be generated for each of the six factors simply by summing the scores of each of feelings that comprise that particular factor. A total mood disturbance score can also be obtained by summing the scores across all six factors, with Vigour-Activity weighed negatively (EdITS, San Diego, California, U.S.A.). For simplicity, the total mood disturbance score was used in this study (one for each of the five test sessions/woman) as it provided a single global estimate of current affective state, and it has been shown to reliably correlate with the six primary factors (McNair, Lorr & Droppleman, 1992).

The Sleep Measures

Due to the clear and distinct possibility that women in the experimental group would experience some form of sleep deprivation during the study, detailed questionnaires requesting information about sleep behaviours were included. The sleep scales comprised six measures. Using a Morning/Eveningness Composite Scale

(Smith, Reilly & Midkiff, 1989), the approximate circadian peak for each of the women in the study could be identified simply by summing obtained scores for each of the thirteen items in the test. Higher scores suggest a more "morning type" person (or "lark", i.e. scores over 44). Particular interest was paid to women who scored higher, as test sessions for these women needed to occur earlier in the four-hour test session window. Although these women were most certainly past their circadian peak, the testing did not occur during the evening hours, when they would have been considerably more tired. Women with scores lower than 44 tended to be more "owl-like" and as a consequence, were being tested at a time of the day that did not conflict with their circadian peak.

Women were also asked to provide information regarding current sleep behaviours. This question was divided into four subordinate questions. Firstly, women were asked to identify how many hours of night-time sleep they had the night before the test session. They then answered yes or no if this amount was considered to be enough sleep for them. As a single night of sleep may not accurately reflect recent trends in sleep behaviours, women were then asked to report on the average amount of sleep they had had over the last week. They then reported if they considered this amount to be adequate for their needs.

The last item included in the sleep battery was the Karolinska Sleepiness Scale (KSS). This single-item, nine-point Likert scale required participants to rate how alert or sleepy they were currently feeling. Ratings ranged from "1=very alert to "5= neither alert nor sleepy" to "9=very sleepy (fighting sleep). Verbal descriptors occurred at every second point of the scale (Akerstedt & Gillberg, 1990). Although recent research has shown subjective ratings of sleepiness can be dissociated from task performance (Van Dongen, Baynard, Maislin & Dinges, 2004), this scale was included in the battery for two

reasons (other than its practical use in field research). Firstly, regardless of performance, subjective feelings of tiredness *are* an indicator to a person that they *do* in fact feel tired. In a real world setting, this subjective signal is probably an early sleepiness clue that a person is feeling the need for sleep, and is therefore sleep deprived. Moreover, in some natural settings (such as performing domestic chores), quality of task performance may not provide adequate feedback to allow for self-evaluations of sleepiness (Gillberg, Kecklund & Akerstedt, 1994). Secondly, this measure has been strongly correlated with both performance tasks (vigilance and reaction time)(Gillberg, Kecklund & Akerstedt, 1994) and electroencephalogram signals of sleepiness (Akerstedt & Gillberg, 1990) and has been reliably used in sleep labs around the world (Mistlberger, personal communication, 2000).

The Cognitive Test Battery

I.Q Measures

The cognitive tests included in the study were chosen based on either their known sensitivity to changes in sex steroids profiles, or their ability to selectively access specific aspects of cognition (e.g. working memory, concentration). The first measure of interest was general intelligence. As it was necessary to ensure both groups of women were equal on measures of I.Q at the beginning of the study, both fluid and crystallized intelligence tests were included. Fluid intelligence has been defined as the ability to reason in an abstract way (Myers, 2001). For this measure the Cattell "Culture Fair test of "g" (Scale 2, Form A) was used. This is a standard and well-used measure of fluid

intelligence (Cattell, 1963). The test of crystallized intelligence, i.e. information and verbal skill that accumulates over time (Myers, 2001) was evaluated by a vocabulary test. Participants were required to match a target word (18 in total) to its closest synonym presented in a multiple (5)-choice format.

Working Memory

As earlier research in this area had consistently revealed pregnancy-related memory deficits (see Brett & Baxendale, 2001 for a review), it was important to include in the study some measures that evaluated this construct. The Computation Span (C-Span) and The Listening Span (L-Span) tasks have both been identified as sensitive measures of working memory and concentration (Salthouse, 1991). Both require a subject to mentally store information while concurrently processing other information. The C-Span uses simple arithmetic problems and the L-Span uses short sentences. Both tests are presented aurally, and require the ability to concentrate on answering either a question (L-Span) or solving a mathematical problem (C-Span) while simultaneously storing and recalling related, but new information. Although well used in other populations (Salthouse, 1991; Salthouse & Babcock, 1990), to date neither of these tasks have been used to evaluate working memory in a sample of pregnant women.

Verbal Memory

Like working memory, earlier research suggests verbal memory is also affected by pregnancy (Sharp et al, 1993). The California Verbal Learning Task (CVLT) requires

participants to recall a list of aurally presented shopping items, and readily taps into verbal memory (Elwood, 1995). Three trials were completed, for each trial subjects were instructed to recall as many items as they could from the 16-item list they had just heard.

Perceptual Speed and Visual Motor Co-ordination

Progesterone has been shown to impair motor co-ordination and processing speed (Freeman, Purdy, Coutifaris, Rickels, & Paul, 1993). As this steroid increases dramatically across a pregnancy (Speroff, Glass & Kase, 1999), measures to evaluate potential effects on cognition were included in this study. To evaluate visual motor co-ordination and perceptual speed the WAIS III Digit Symbol Coding test and the WAIS III Symbol Search were included. These two scales are part of the Wechsler Adult Intelligence Scale, version three (WAIS III). Digit symbol coding requires participants to rapidly match symbols to numbers, and taxes motor co-ordination and processing speed. The Symbol Search task requires speeded matching of a target object to its identicate which must be selected from an array of adjacent symbols (WAIS III Manual, 1997. The Psychological Corporation, Toronto, Ont.).

Tests Sensitive to Sex Steroid Profiles

Three additional tests were included in the battery simply because they have been shown to be sensitive to either fluctuations in sex steroids, or to show reliable sex differences (see Kimura 1999 for a review). None however, appear to have been used to evaluate the cognitive changes seen in pregnancy.

Silverman Eals Object Location Memory Task

This task requires a participant to recall the location of a previously viewed object when its location has been moved around in a large array. As discussed earlier, this task is the only spatial measure reported to favour women (Eals & Silverman, 1994) and as such may well be dependent on estrogenic effects.

Shepard Metzler Mental Rotation Task

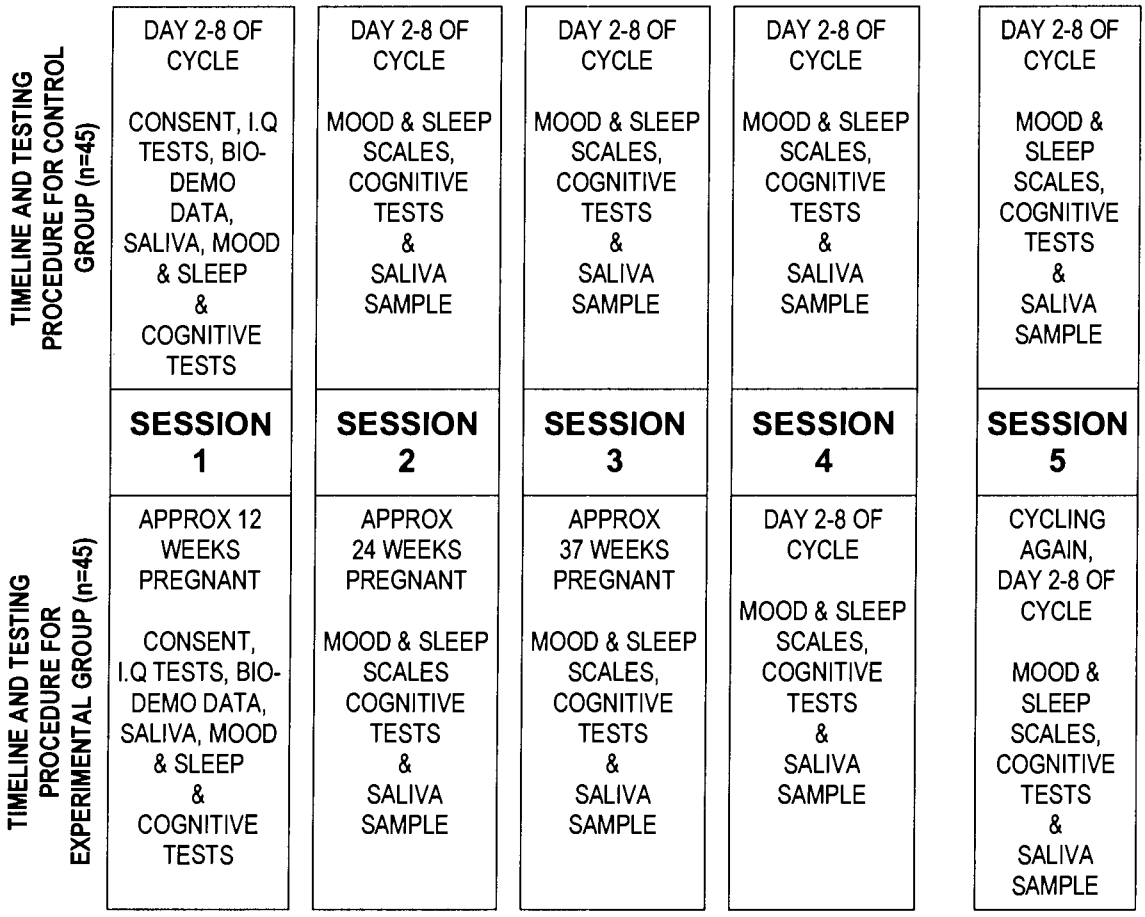
This paper-and-pencil test shows a strong male advantage (Vandenberg & Kuse, 1978) and therefore may be androgen dependent. In addition, as it requires the ability to mentally rotate a target object and then correctly identify the new orientation chosen from a set of four possible objects, it readily taps into working memory and spatial abilities. Finally, it is reported to be a difficult task by researchers who have used it extensively (Kimura, personal communication, 2000). This makes it very suitable for use in repeated measure designs, where ceiling effects can result with recurring exposures to the same test.

Purdue Pegboard

The Purdue Pegboard has previously been used to evaluate steroid hormone effects both within and between the sexes. Women generally outperform men on this task (Purdue Pegboard Examiners Manual, (1987), NCS: London House), while among women performance fluctuates across the menstrual cycle, with better performance being related to higher levels of estrogen (Hampson & Kimura, 1988). This test of fine motor skill requires subjects to rapidly select and place pegs in predrilled holes in a large wooden board (Purdue Pegboard Examiners Manual, (1987), NCS: London House). For

this study a measure for both the dominant and the non-dominant hand was obtained. Figure 1 provides a graphical representation of the experimental design of the study.

Figure 1: Repeated Measures, Longitudinal Research Design



Saliva Samples

General Procedure

At the end of each test session a saliva sample was collected for all women in the study. Participants had not drank or eaten for one hour prior to expectorating. To facilitate salivary flow women were provided with a cherry-flavoured sugarless gum (Trident cherry flavour). Saliva was collected directly into a screw-capped polypropylene

10 ml specimen tube previously been treated with 122ul of the preservative sodium azide dissolved in distilled water (1gm/20ml). Specimens were stored at room temperature for approximately 20 hours to allow the salivary mucins to settle (Mead & Hampson, 1997). All samples were then frozen at -20C awaiting shipment. Once a significant quantity of samples had accumulated they were shipped on dry ice to ZRT Laboratory (Beaverton, Oregon) for enzyme immunoassay where hormone assays were performed as described below. This occurred three times over the course of the study.

Stability of Salivary Steroids Specimens

Unpublished research has shown saliva specimens stored without sodium azide are stable at room temperature for up to 21 days (D. Zava, personal communication, ZRT Laboratory, Beaverton, Oregon, USA, December 2004). Saliva stored at room temperature with this preservative extends the shelf life to one year. Freezing sodium azide-treated samples at - 20 °C or lower preserves the hormone status of the saliva indefinitely (Methods Manual, ZRT, 2001).

Preparation and Extraction

Upon arrival at ZRT Laboratory saliva samples were thawed at room temperature and treated with a solution of dithiothreitol (common name: Clelands reagent). This treatment breaks the disulfide bonds and renders the saliva less viscous which is essential for the steroid extraction process. Collection tubes were then centrifuged to separate the larger particles and contaminants. Samples are transferred to the deck of a laboratory liquid handling machine (Tecan, Genesis, Clontech Laboratories, Palo Alto, California), which orchestrates a set of serial dilutions and transfers to a deep multi-well

plate. Saliva is then extracted by C18 chromatography, which collects and concentrates the steroid hormones and other lipophilic small-molecule substances. Extensive washing removes any proteinacious materials. Finally, samples are then eluted with an alcohol solvent and dried over nitrogen.

Procedural Controls

Inter-assay and intra-assay Biorad Liphocheck controls were run in parallel with each enzyme extraction and immunoassay. Control samples were diluted to steroid hormone concentrations commonly found in saliva for low, medium and high salivary values. Assay grid results for Biorad controls were then compared to a table of acceptable ranges for each of the steroid hormones. Analytical sensitivity for each steroid was evaluated by interpolating the mean minus two standard deviations for ten sets of assay duplicates. Intraassay variations were determined from the means of twelve replicates each at lower, midrange and higher values. Control samples were checked to ensure assays were within these ranges for each immunoassay run.

Enzyme Immunoassay

Similar to RIA, EIA uses competitive binding of salivary-extracted steroids with enzyme (perioxidase) -linked steroid conjugates for a highly specific antibody tethered to a multiwell microliter plate (Methods Manual, ZRT, 2001). Samples were reconstituted in sonicated phosphate buffered saline solution prior to assay. Alioquots of reconstituted steroids were then assayed for the specific steroid hormones: Estradiol, Estrone, Estriol, DHEAs, Testosterone, Progesterone and Cortisol. As the manufacturer's kits were designed specifically to handle a serum medium, both the enzyme assay procedure and

the standard curve were modified for use with saliva. Completed assays were read by a scanning spectrophotometer, which generates the factored steroid concentration. As discussed earlier, the unknown steroid fraction is determined from a standard curve of known steroid concentrations. Colour development from the enzyme conjugate is inversely proportional to salivary steroid content.

ANALYSIS 1: RESULTS

Initial Statistical Considerations

All analyses were conducted on SPSS standard version (release 11.0.1) using the general linear model function for ANOVA, ANCOVA and t-tests for mean comparisons. Bi-variate relationships were analyzed using Pearson's product moment correlations. Because multiple measures were used, a Bonferroni correction was made to control the familywise error rate. Generally, this resulted in the significance level being set at .005.

All graphs generated from this study show both group means and standard error bars for each of the five test sessions. Approximations of confidence intervals may be obtained by simply doubling the error bar length (Howell, 1992).

Occasionally women in both groups did not complete all of the five test sessions. This was due to such factors as schedule conflicts, travel, premature delivery, illness or relocation. In these cases the missing values in the data set were reconstructed using regression linear trend at point analyses for repeated measures designs. Table 4 details the number of missing values replaced for each test session. Over the course of the study there was approximately 11% (or 50 of a total of 450) values estimated. Twenty-two were from women in the experimental group and 28 values were replaced from women in the control group. Other than two premature deliveries, there is no other reason to suspect any type of systematic differences between groups for this attrition. Because the data set now includes approximately 10% estimated values for the nine cognitive tests, statistical manipulations will be shown for both the raw non-estimated

data and the data set where the missing values have been included. These will be referred to as Raw Data and Replaced Data respectively.

Table 4: ***Missing Values Replaced Using Linear Trend at Point Regression Analysis***

Test Session	**# of replaced values (missing cases/Analysis 1 n)**	**% replaced**
One	4/90	4%
Two	7/90	7%
Three	11/90	12%
Four	14/90	15%
Five	14/90	15%
Total	50/450	11% attrition

Demographics and I.Q. Measures

Women who comprised the *Experimental Group* were pregnant for the first three test sessions. These women were in the early and late postpartum period for test session four and five. The women who comprised the *Control Group* were tested during the menstrual phase of the ovarian cycle for all five of the test sessions. Testing occurred between day two and day eight, with day one being menses onset. Table 5 outlines the demographic descriptive statistics by group.

Table 5: Summary Demographic Descriptive Statistics by Group

Demographic Variable		Experimental Group	Control Group
N		45	45
Age at first test session (years):	Mean	31.3	35.3
	s.d.	4.4	4.9
Years of education:	Mean	14.9	14.6
	s.d.	1.7	1.9
First Language:	English:	41	39
	Other:	4	6
Children resident in the home:	0	18	9
	1	18	13
	2	8	20
	3	1	3
Sex of resident children:	0 (n/a)	18	9
	Girls	8	11
	Boys	14	16
	Both	5	9
Marital Status:	Cohabiting	45	40
	Single Parent	0	5
Handedness:	Right	40	44
	Left	5	1
Stay at home Mom?	Yes	12	10
	No	33	35
Working at the 3rd test session?	Yes	16	34
	No	24	5
	Missing cases	5	6
Working at the final session?	Full-time	7	21
	Part-time	13	10
	Not working	21	4
	Missing cases	4	10

When control women were compared to experimental women on demographic and general intelligence variables between group differences were evident. *Post hoc* t-tests revealed control women were more likely to already have children at the time of first test session ($t(88) = 3.111$, $p = .003$). Women in this group were also more likely to be a single parent ($t(88) = 3.084$, $p = .004$) and be older ($t(88) = 4.041$, $p < .001$).

Although control women performed worse on the Cattell test of "g", fluid intelligence test (t(88) = 2.026, p=.046), and completed the crystallized intelligence (vocab) task faster (t(88) = 2.328, p= .02), these results did not achieve significance at the corrected alpha. Unlike the vocab test where participants could take all the time they needed to finish the task, the Cattell Culture Fair test was time-limited, for this reason there exists no Cattell "time to complete" variable. Table 6 summaries the one-time tests of fluid and crystallized intelligence. Recall these tests were conducted during the first test session only.

As would be expected, pregnant women were significantly less likely to be working at the third test session (t(77) = 4.947, p< .001). Recall these women were within a few short weeks of parturition. Women in the experimental group were also less likely to be working at the final test session (t(74) 4.923, p< .001); also an expected result as many women in the experimental group were still on maternity leave.

Table 6: Summary Fluid and Crystallized Intelligence Measures by Group

Test		Exptal Grp	Control Grp
Fluid Intelligence	Mean	34.5	32.6
Cattell Culture Fair Scale 2, Form A	*s.d.*	4.5	4.4
Crystallized Intelligence	Mean	9.5	10.4
18-item vocab test	*s.d.*	3.3	2.8
Time to complete vocab test (seconds)	Mean	192.0	162.0
	s.d.	69.5	51.1

Dependent Variables (Cognitive Tests)

Covariates

As a number of extraneous variables (previously identified in Table 3) could possibly be related to the dependent measures, ANCOVAs were initially calculated for each of the nine tests incorporating these fourteen variables. Table 7 lists the variables included as the covariates.

Table 7: ***Covariates Included in Each ANCOVA***

First Language
Number of older siblings
Sex of older siblings
Mother at first test session?
Single Parent?
Handedness
Stay at home Mom?
Age at first test session
Education level attained
Working at 3rd test session?
Working at 5th test session?
Cattell score
Vocab score
Vocab completion time

Of the fourteen covariates identified and tested within an ANCOVA model for each of the nine dependent variables, only two significant relationships emerged. For the Mental Rotation Task, the Cattell test of fluid intelligence was a significant covariate. For the Listening Span Task, the vocab test of crystallized intelligence was a significant

covariate. When the proportion of variance in these dependent variables explained by the covariates was calculated, the covariates accounted for only 4% and 2% respectively. Given the minor contribution of these covariates, Analysis of Variance (Repeated Measures) was subsequently run without consideration of these two variables. Appendix C provides a summary of the ANCOVAs for each of the nine dependent variables. Significant effects have been bolded.

Analysis of Variance

Each of the nine dependent measures was administered once per test session to both experimental and control women. Appendix D lists the means and standard deviations for each of the dependent measures for the raw and replaced data sets across the five test sessions.

Group by Session Interaction

No group by session interaction was observed. Women in the experimental group did not show a gestation-related decrement in performance on any of the nine dependent measures.

Main Effect of Session

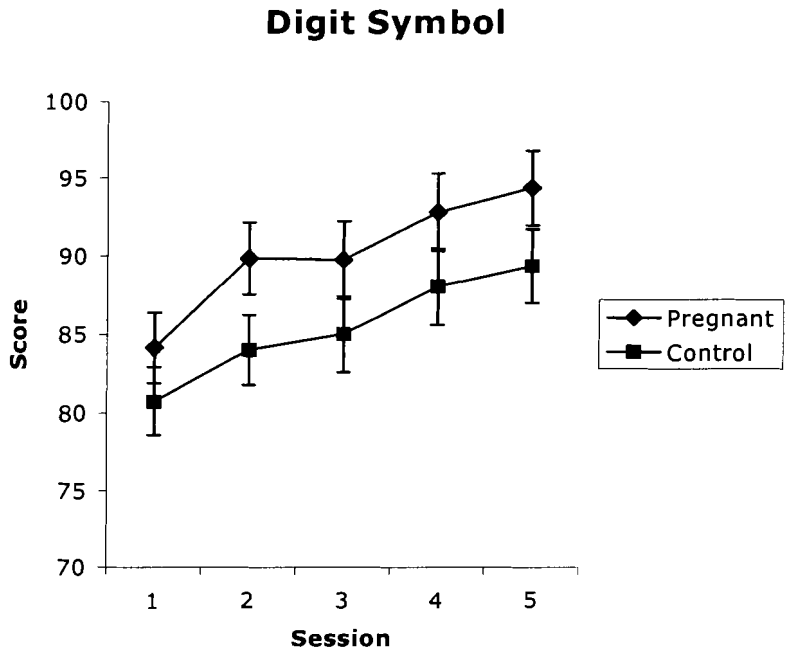
A main effect of session was evident. In all tests except the Silverman Eals Object location Task, both the experimental and control group performed better with subsequent exposures to the tests, suggesting practice effects were evident for the two groups.

Main Effect of Group

In eight of the nine cognitive tests there was no main effect for group. Performance of women in the experimental group did not differ significantly from performance of the control women for these tasks. When considering the raw data alone, performance of women in the experimental group was significantly different from that of women in the control group on one test. Across the five test sessions, pregnant women outperformed control women on the California Verbal Memory Test. This result did not persist when analyses included the replaced missing values, with the p value becoming non-significant.

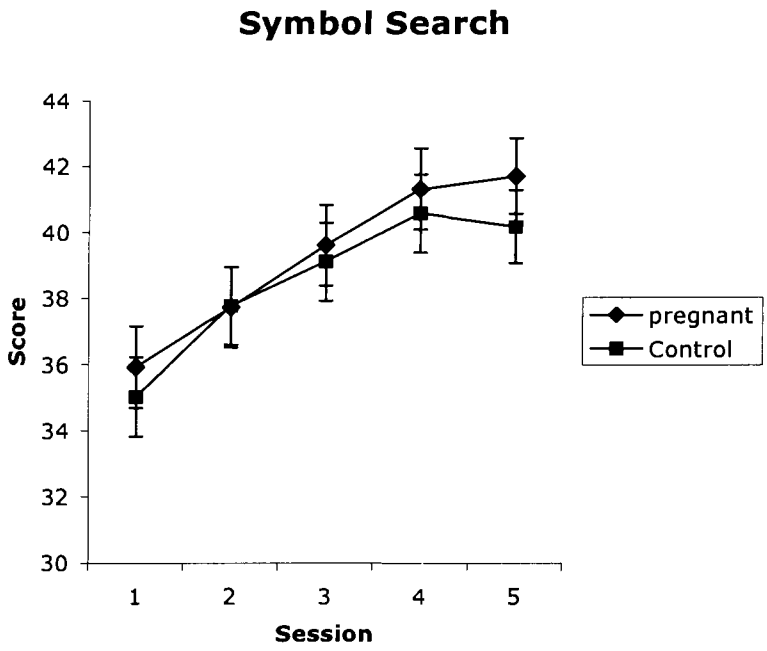
Figures 2 to 10 illustrates the ANOVA raw data results for each of the cognitive tests. Under each graph are the ANOVA main and interaction results for both the raw and replaced data sets. All significant effects have been bolded.

Figure 2: Experimental vs. Control Group – Digit Symbol Coding (Raw Data)



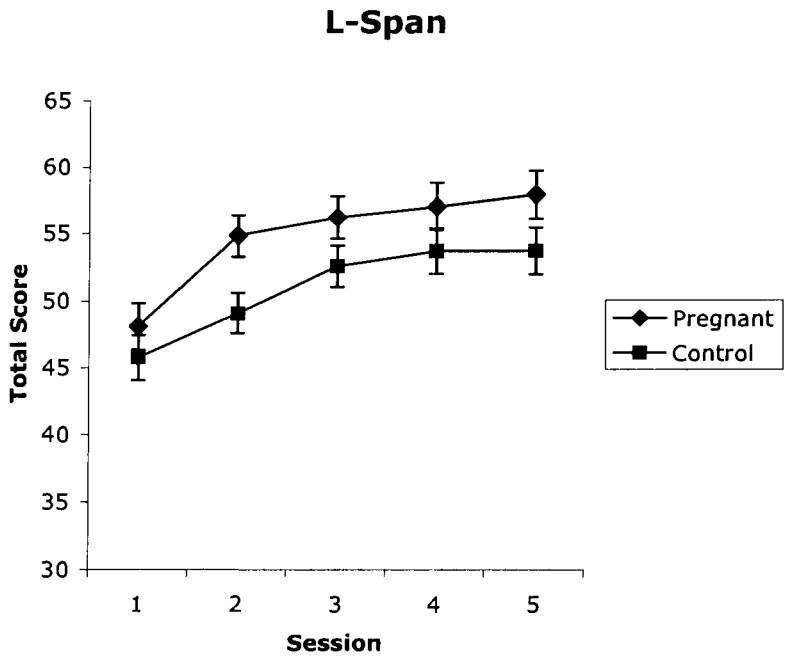
Test	Raw Data (33 exptal, 35 control)	Replaced Data (45 exptal, 45 control)
Digit Symbol Coding	Main Effect: Group F(1,66) = 2.344, p= .131 Main Effect: Session **F(4, 66) = 27.731, p< .001*** Interaction Effect: Group x Session F(4, 66) = .406, p= .775	Main Effect: Group F(1,88) = 1.207, p= .275 Main Effect: Session **F(4, 88) = 20.049, p< .001*** Interaction Effect: Group x Session F(4, 88) = .488, p= .700

Figure 3: Experimental vs. Control Group – Symbol Search (Raw Data)



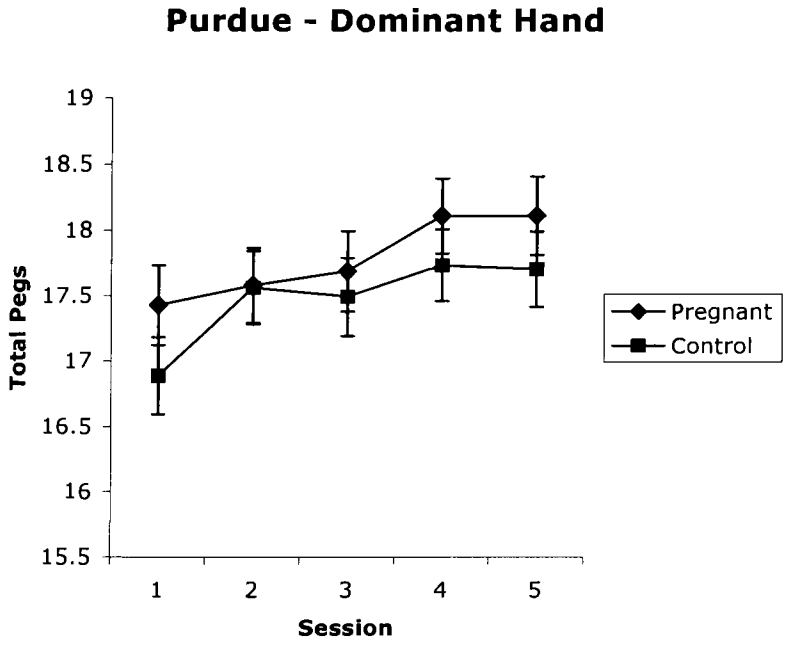
Test	Raw Data (33 exptal, 35 control)	Replaced Data (45 exptal, 45 control)
Symbol Search	Main Effect: Group F(1,66) = .264, p= .609 Main Effect: Session **F(4, 66) = 20.453, p< .001*** Interaction Effect: Group x Session F(4, 66) = .311, p= .870	Main Effect: Group F(1,88) = .024, p= .877 Main Effect: Session **F(4, 88) = 17.758, p< .001*** Interaction Effect: Group x Session F(4, 88) = .688, p= .597

Figure 4: Experimental vs. Control Group – Listening Span (Raw Data)



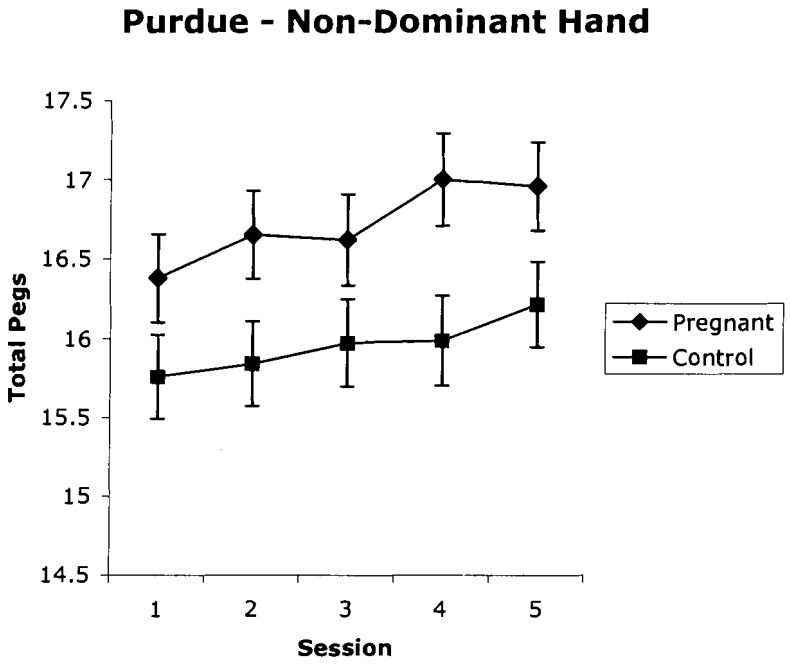
Test	Raw Data (33 exptal, 35 control)	Replaced Data (45 exptal, 45 control)
Listening Span	Main Effect: Group F(1,66) = 3.231, p= .077 Main Effect: Session **F(4, 66) = 42.767, p< .001*** Interaction Effect: Group x Session F(4, 66) = 1.289, p =.260	Main Effect: Group F(1,88) = 2.073, p=.153 Main Effect: Session **F(4,88) = 39.839, p< .001*** Interaction Effect: Group x Session F(4, 88) = 1.440, p= .233

Figure 5: Experimental vs. Control Group – Purdue Pegboard (Raw Data)



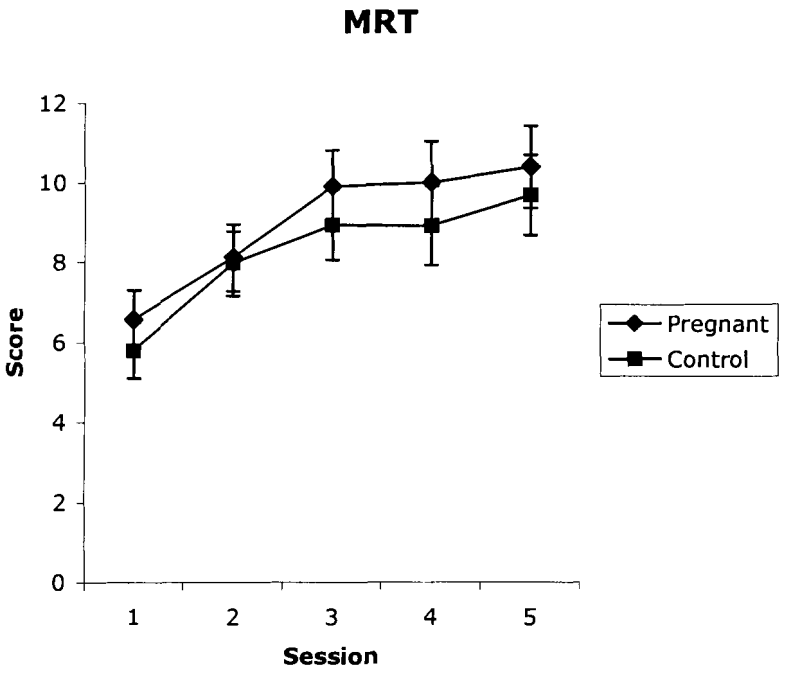
Test	Raw Data (33 exptal, 35 control)	Replaced Data(45 exptal, 45 control)
Purdue (Dominant Hand)	Main Effect: Group F(1,66) = .721, p= .399 Main Effect: Session **F(4, 66) = 7.811, p< .001*** Interaction Effect: Group x Session F(4, 66) = .823, p= .512	Main Effect: Group F(1,88) = .578, p= .449 Main Effect: Session **F(4, 88) = 10.233, p< .001*** Interaction Effect: Group x Session F(4, 88) = 1.323, p= .261

Figure 6: Experimental vs. Control Group – Purdue Pegboard (Raw Data)



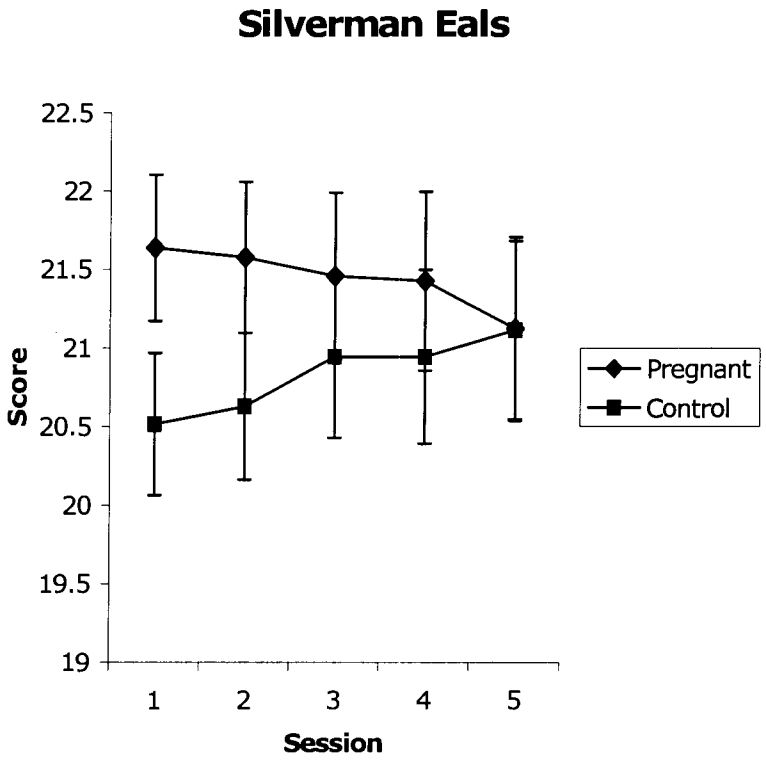
Test	Raw Data (33 exptal, 35 control)	Replaced Data (45 exptal, 45 control)
Purdue (Non-Dominant Hand)	Main Effect: Group F(1,66) = 5.082, p= .027 Main Effect: Session F(4, 66) = 3.551, p= .008 Interaction Effect: Group x Session F(4, 66) = .522, p= .473	Main Effect: Group F(1,88) = 3.920, p=.051 Main Effect: Session **F(4, 88) = 5.796, p< .001*** Interaction Effect: Group x Session F(4, 88) = .781, p= .379

Figure 7: Experimental vs. Control Group – Mental Rotation Task (Raw Data)



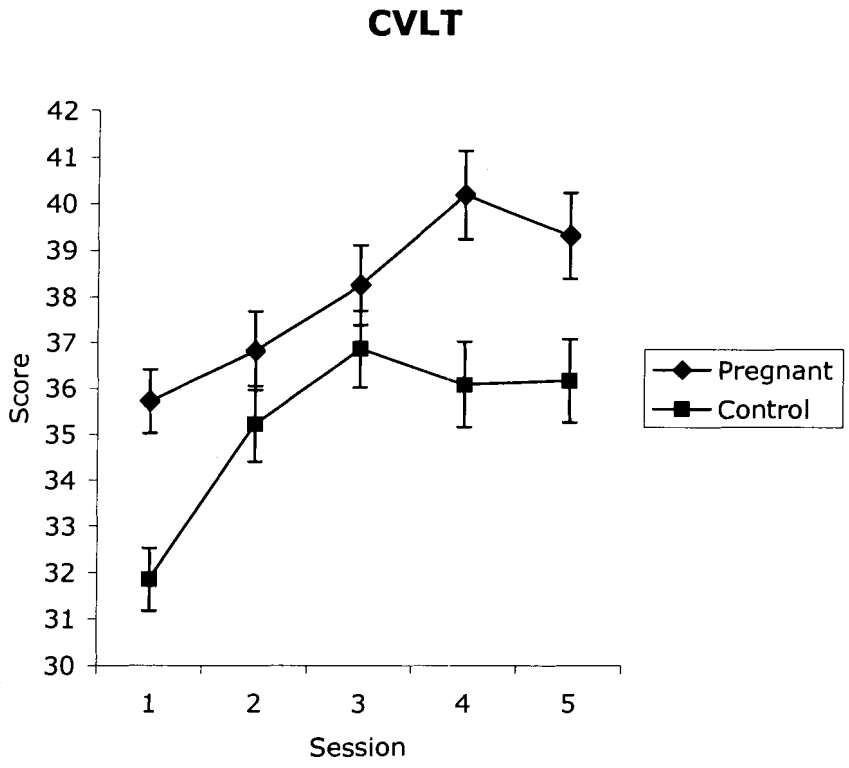
Test	Raw Data (33 exptal, 35 control)	Replaced Data (45 exptal, 45 control)
Mental Rotation Task	Main Effect: Group F(1,66) = .419, p= .520 Main Effect: Session **F(4, 66) = 22.357, p< 001*** Interaction Effect: Group x Session F(4, 66) = .308, p= .873	Main Effect: Group F(1,88) = .104, p= .748 Main Effect: Session **F(4, 88) = 22.273, p< .001*** Interaction Effect: Group x Session F(4, 88) = .563, p= .455

Figure 8: ***Experimental vs. Control Group – Silverman Eals Object Location (Raw Data)***



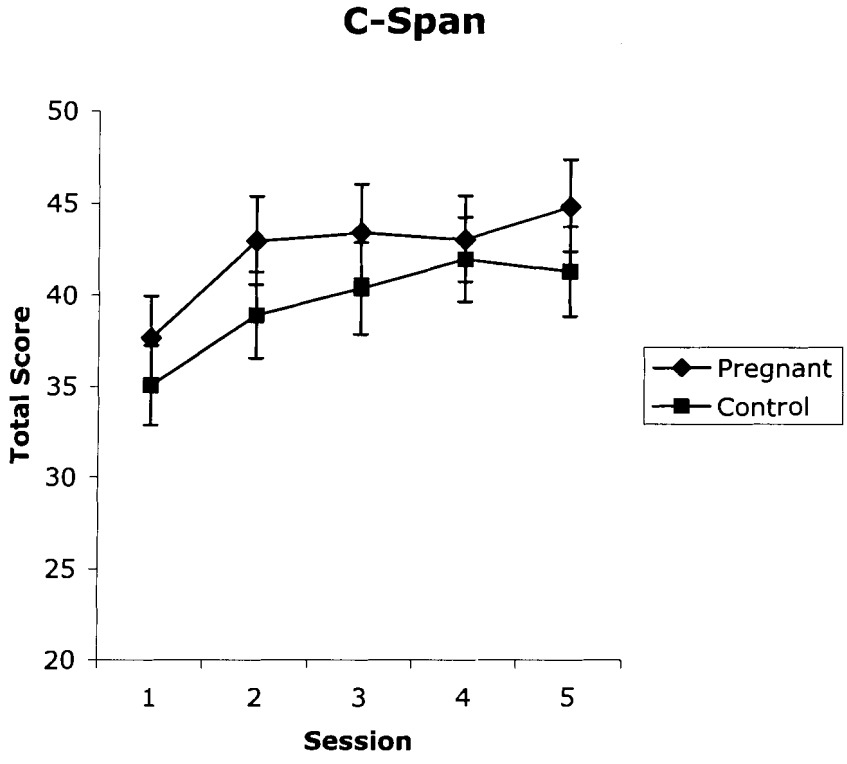
Test	Raw Data (33 exptal, 35 control)	Replaced Data (45 exptal, 45 control)
Silverman Eals Object Location	Main Effect: Group F(1,66) = 1.225, p=.272 Main Effect: Session F(4, 66) = .039, p= .997 Interaction Effect: Group x Session F(4, 66) = .654, p= .622	Main Effect: Group F(1,88) = .909, p= .343 Main Effect: Session F(4, 88) .400, p= .807 Interaction Effect: Group x Session F(4, 88) = .671, p= .611

Figure 9: ***Experimental vs. Control Group – California Verbal Memory Test (Raw Data)***



Test	Raw Data (33 exptal, 35 control)	Replaced Data (45 exptal, 45 control)
CVLT	Main Effect: Group **F(1,66) = 8.704, p= .004*** Main Effect: Session **F(4, 66) = 18.957, p< .001*** Interaction Effect: Group x Session F(4, 66) 2.379, p= .128	Main Effect: Group F(1,88) = 3.519, p= .064 Main Effect: Session **F(4, 88) = 23.048, p< .001*** Interaction Effect: Group x Session F(4, 88) = 2.432, .p =.058

Figure 10: Experimental vs. Control Group – Computation Span (Raw Data)



Test	Raw Data (33 exptal, 35 control)	Replaced Data (45 exptal, 45 control)
Computation Span	Main Effect: Group F(1,65) = .764, p= .385 Main Effect: Session **F(4, 65) = 22.835, p< .001*** Interaction Effect: Group x Session F(4, 65) = 1.000, p= .407	Main Effect: Group F(1,88) = .413, p= .522 Main Effect: Session **F(1,88) = 16.374, p< .001*** Interaction Effect: Group x Session F(4, 88) = .874, p= .476

Salivary Analyses

Salivary analyses are based entirely on raw data. This resulted in the experimental group n being reduced from 45 to 34 women, and the control group n fell from 45 to 33 women.

Analysis of Variance

As previously stated, saliva was collected at each test session from both experimental and control women. All samples were analysed for seven steroid hormones: Testosterone, DHEAs, cortisol, estradiol, estrone, estriol and progesterone. Appendix E lists the group means and standard deviations for each of the sex hormones across the five test sessions. Analysis of Variance results are reported along with the respective graphs for each hormone. All significant effects are bolded.

Group by Session Interactions

Interaction effects were observed on four of the seven salivary measures. Progesterone and the three estrogens all showed a session by group interaction. This suggested a clear effect of pregnancy, with gestation and the postpartum resulting in a very different hormonal profile for the experimental women. Generally this followed a trend of low early pregnancy levels, which rose to a peak just prior to parturition and dropped precipitously during the postnatal period. Hormone profiles of women in the control group showed almost no variability across the duration of the study (Figures 11 to 14).

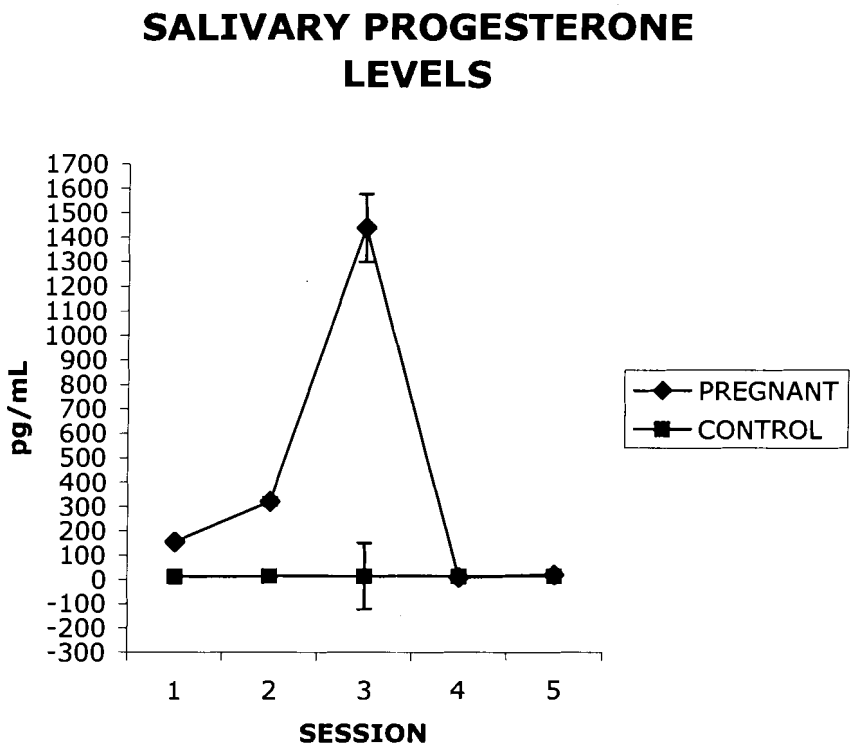
Main Effect of Session

Although no interaction effect was evident for DHEAs at the corrected alpha, a clear trend was present. Gestation resulted in a decline in this hormone with levels increasing again after parturition. The significant main effect of session along with the significant main effect of group also supports this result (Figure 15).

Main Effect of Group

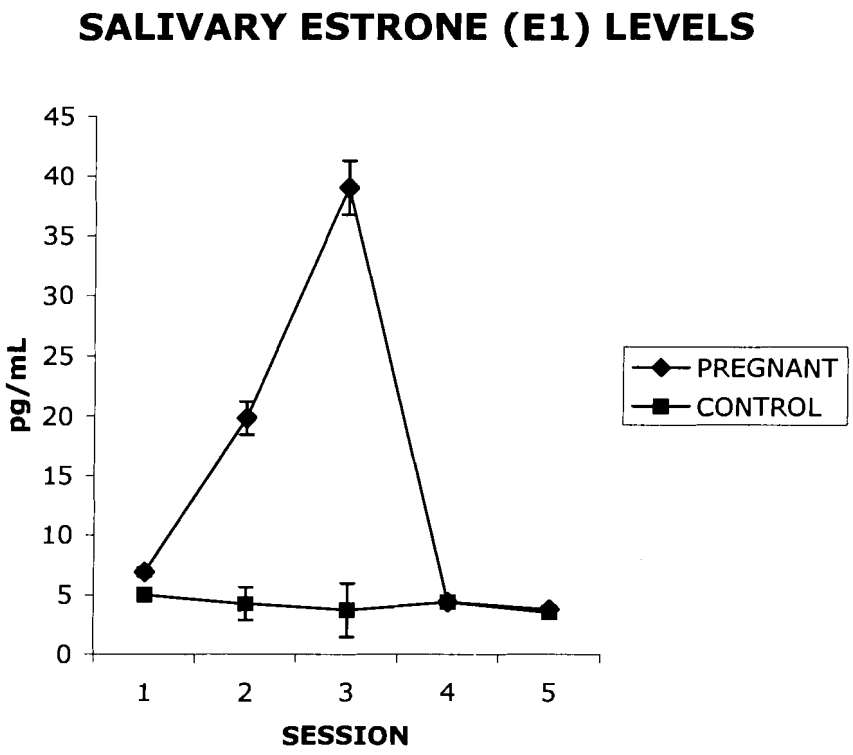
As previously stated a main effect of group was evident for DHEAs, with women in the experimental group having consistently lower levels of this sex hormone than women in the control group. Neither cortisol nor testosterone differed between the two groups across the five test sessions, however trends in the data suggest a main effect of group for testosterone (Figures 16 and 17 respectively).

Figure 11: Progesterone Profile: Experimental Group vs. Control Group



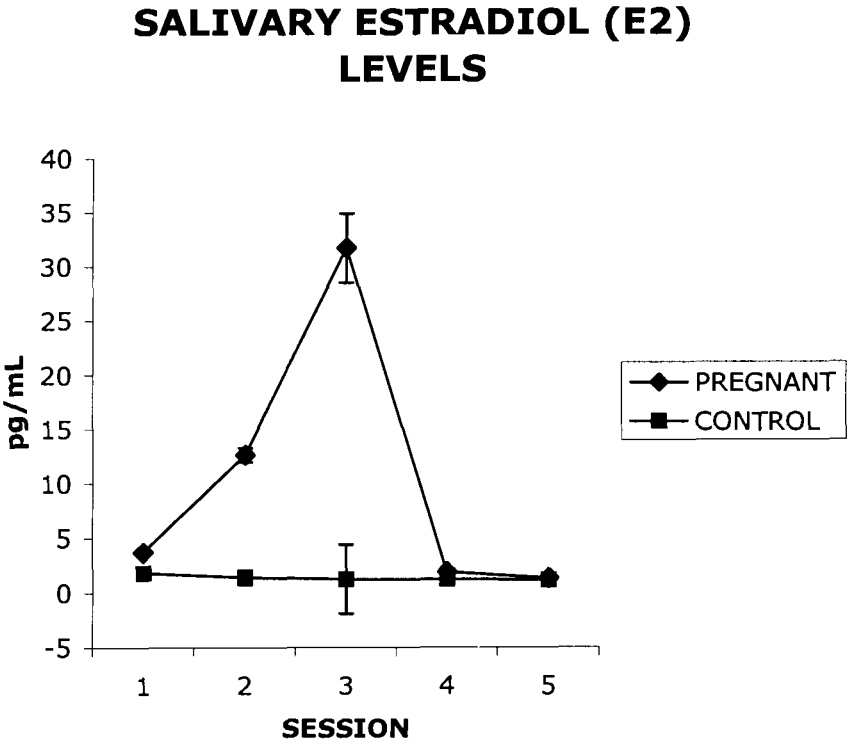
Salivary Hormone	Raw Data (34 exptal, 33 control)
Progesterone	Main Effect: Group **F(1, 65) = 78.858, p< .001*** Main Effect: Session **F(4, 65) = 48.324, p< .001*** Interaction Effect: Group x Session **F(4, 65) = 48.163, p< .001***

Figure 12: Estrone Profile: Experimental Group vs. Control Group



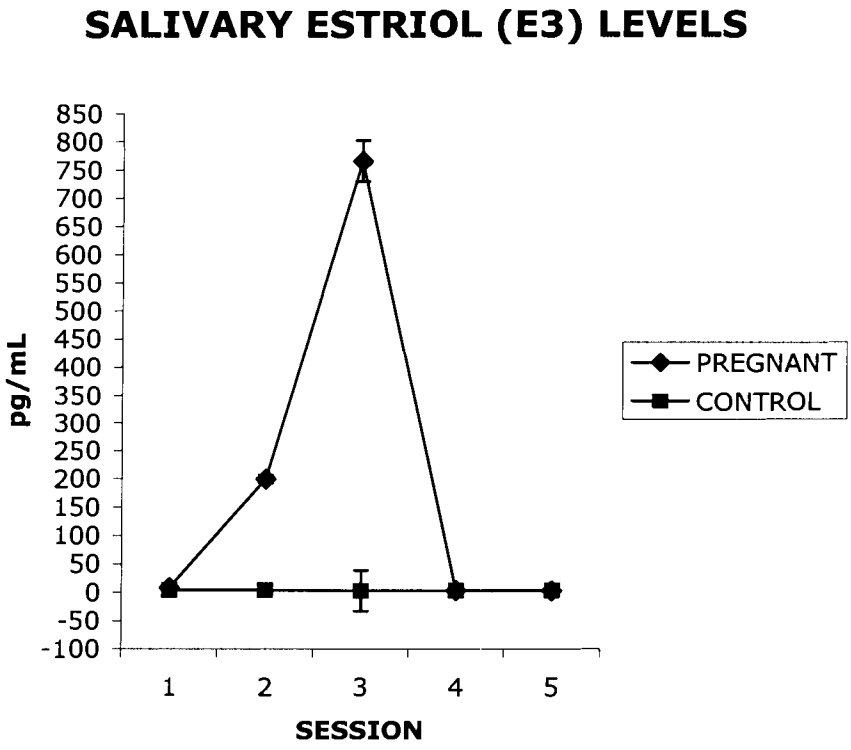
Salivary Hormone	Raw Data (34 exptal, 33 control)
Estrone (E1)	Main Effect: Group **F(1, 65) = 102.66, p< .001*** Main Effect: Session **F(4, 65) = 91.469, p< .001*** Interaction Effect: Group x Session **F(4, 65) = 96.808, p< .001***

Figure 13: Estradiol Profile: Experimental Group vs. Control Group



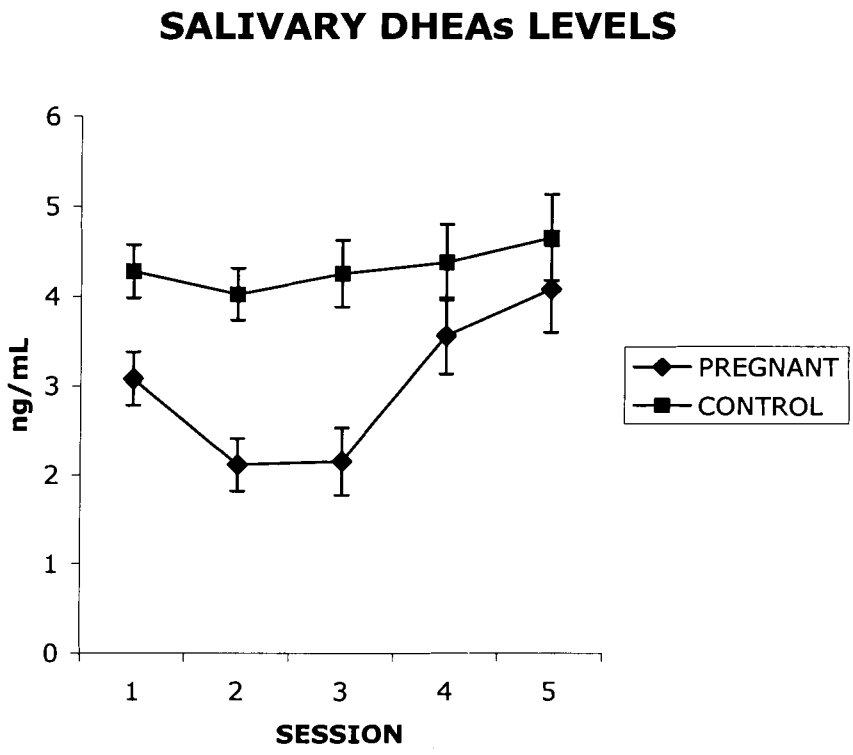
Salivary Hormone	Raw Data (34 exptal, 33 control)
Estradiol (E2)	Main Effect: Group **F(1, 65) = 66.651, p< .001*** Main Effect: Session **F(4, 65) = 43.400, p< .001*** Interaction Effect: Group x Session **F(4, 65) = 44.131, p< .001***

Figure 14: Estriol Profile: Experimental Group vs. Control Group



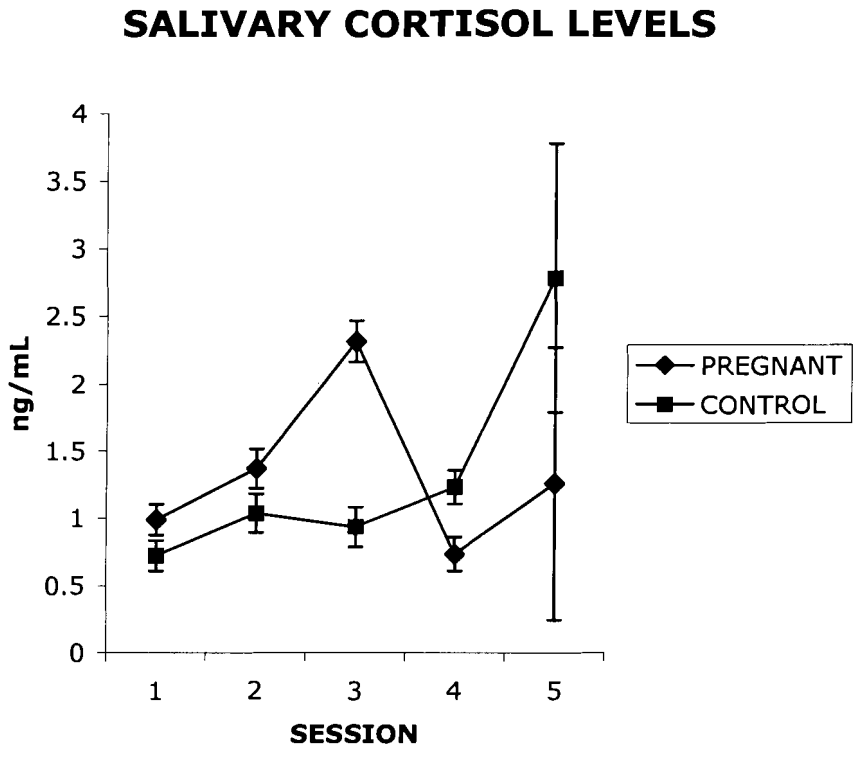
Salivary Hormone	Raw Data (34 exptal, 33 control)
Estriol (E3)	Main Effect: Group **F(1, 65) = 291.05, p< .001*** Main Effect: Session **F(4, 65) = 208.24, p< .001*** Interaction Effect: Group x Session **F(4, 65) = 209.25, p< .001***

Figure 15: DHEAs Profile: Experimental Group vs. Control Group



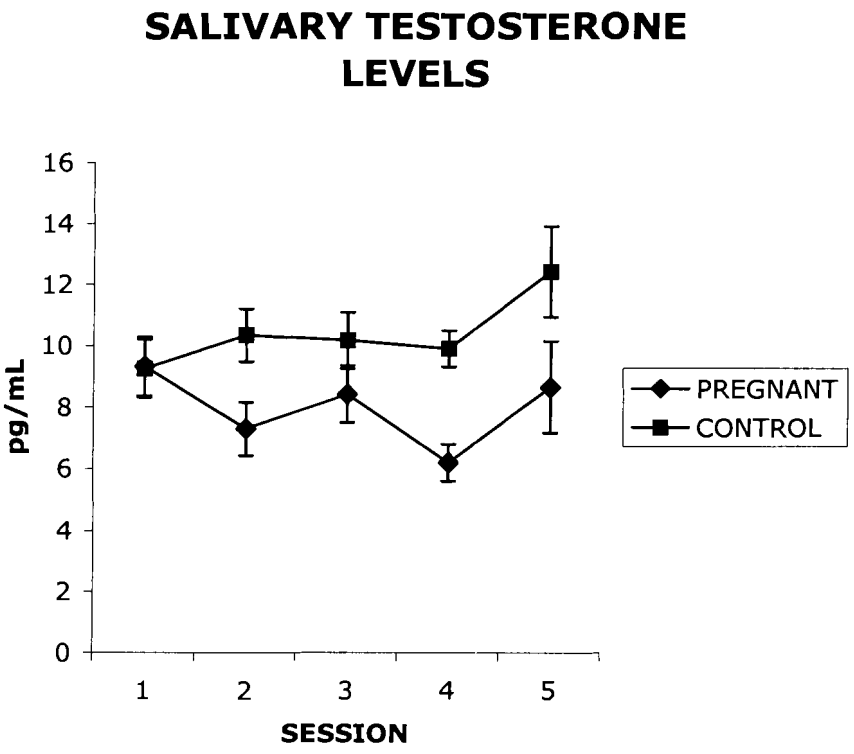
Salivary Hormone	Raw Data (34 exptal, 33 control)
DHEAs	Main Effect: Group **F(1, 65) = 9.236, p= .003*** Main Effect: Session **F(4, 65) = 9.276, p< .001*** Interaction Effect: Group x Session F(4, 65) = 3.586, p= .012

Figure 16: Cortisol Profile: Experimental Group vs. Control Group



Salivary Hormone	Raw Data (34 exptal, 33 control)
Cortisol	Main Effect: Group F(1, 65) = .001, p= .976 Main Effect: Session F(4, 65) = 2.223, p= .138 Interaction Effect: Group x Session F(4, 65) = 2.800, p= .09

Figure 17: Testosterone Profile: Experimental Group vs. Control Group



Salivary Hormone	Raw Data (34 exptal, 33 control)
Testosterone	Main Effect: Group F(1, 65) = 7. 735, p= .007 Main Effect: Session F(4, 65) = 2.084, p= .114 Interaction Effect: Group x Session F(4, 65) = 1.685, p= .180

Relationships Between Dependent Measures and Salivary Hormone Profiles

When analyzed, specific steroid hormones did not reliably or consistently correlate with any of the dependent measures across the five test sessions. This was true for the overall correlations and also true when separate analyses were conducted for both the experimental group and the control group. In addition, scatterplots (9 x 7 = 63 graphs) of the dependent measures by the specific salivary hormones also revealed no obvious visual trends in the direction or strength of any potential relationships.

Possible Relationships Between Age and Salivary Hormone Profiles

Among women in the experimental group, their age at the first test session consistently correlated with two of the seven steroids. In pregnant women, but not women in the control group, DHEAs showed a persistent negative correlation with maternal age; with older women having lower DHEAs levels during gestation. This effect was evident from the first test session and remained until the third test session. By the fourth test session, which occurred during the postnatal phase, the relationship was fading. At the final test session, which occurred during the menstrual phase of the ovarian cycle, the effect was no longer evident. Similarly, Estradiol also showed a strong negative correlation with maternal age for pregnant women, but not control women, for the second and third test sessions. The relationship was lost once parturition had occurred. Of the seven hormones assayed in the experimental group, only these two were significantly correlated to maternal age. Table 8 outlines these

results. Women in the control group showed no age related decline in steroid hormones for any of the seven tested.

Table 8: Relationship between DHEAs and Estradiol to Maternal Age

Session	DHEAs	Estradiol
One	r= - .474, p= .002	r= - .221, p= .165
Two	r= - .613, p< .001	r= - .407, p=.008
Three	r= - .391, p= .013	r= - .471, p=.002
PARTURITION	**PARTURITION**	**PARTURITION**
Four	r= - .337, p= .036	r= - .293, p= .070
Five	r= - .260, p= .101	r= .009, p= .955

Note. Experimental Group only, Control Group was non significant for all hormones assayed.

Sleep and Mood

As with the salivary hormone results, raw data only was used in the analyses of both the sleep and mood scores.

Mood Measure

When the Profile of Mood States scores were analysed no group by session interaction ($F(4, 66) = 1.442$, $p = .234$) or main effect of session ($F(4, 66) = 3.080$, $p = .017$) was observed. In addition, experimental group mood scores did not significantly differ from control group scores across the five test sessions ($F(1, 66) = 5.208$, $p = .026$). Further, Analysis of covariance revealed no significant effects of any of the mood scores on the nine dependent measures across the five test sessions. In light of these findings,

no further consideration will be given to this variable in the overall results. Appendix F lists the descriptive statistics for the mood scores across the five test sessions.

Sleep Measures

Recall, six sleep measures were obtained from all women in the study at every test session. Descriptors used in the following tables identify each sleep measure. The word SLEEP appears first, this is followed by a number and a letter, for example "SLEEP1A". The number corresponds to the test session, and range from one to five. The letter is a reference to the actual question or sleep questionnaire item. Letters range from A to F. Table 9 explains in full each of the letter descriptors for the various sleep measures.

Table 9: Descriptors Used For Each of the Six Sleep Items

Title	Full Description
SLEEP1A	Morningness/eveningness questionnaire. Evaluates circadian preference for morning or evening activities. Scores above 44 = morning type, scores below 22 = evening type
SLEEP1B	How many hours of night-time sleep did you get last night?
SLEEP1C	Do you consider this to be enough night-time sleep for you? Yes = 0, No = 1
SLEEP1D	On average, approximately how many hours of night-time sleep have you been getting per night over the last week?
SLEEP1E	Do you consider this to be enough sleep for you? Yes = 0, No = 1
SLEEP1F	Rating of current alertness. 1=very alert, 5= neither alert nor sleepy, 9=very sleepy (fighting sleep)

Covariates

Analysis of covariance indicated some sleep measures were occasionally related to the dependent variables. During test session one, SLEEP1D was a covariate for digit symbol coding and SLEEP1E was a covariate for performance of the non-dominant hand on the Purdue pegboard. For test session two SLEEP2F was a covariate for performance of the non-dominant hand on the Purdue pegboard, and for test session three SLEEP3C was a covariate of the Listening Span task. Other than these four, there were no other significant sleep covariates for any other dependent variables across the five test sessions. Based on the reported R^2 in Table 10, the proportion of variance in the dependent measures explained by these covariates is miniscule. Given this minor contribution, Analysis of Variance was subsequently run without consideration of these extraneous variables.

Table 10: ANCOVA Results for Significant Sleep Covariates

Sleep Measure	DV	SS/TSS	F	sig.	R^2
SLEEP1D	digit symbol	1763/616423	9.650	.003	.002
SLEEP1E	Purdue (non dom)	20/22040	9.631	.003	.0009
SLEEP2F	Purdue (non dom)	24/22208	10.650	.002	.001
SLEEP3C	L-span	705/233274	9.057	.004	.003

Analysis of Variance

Group by Session Interactions

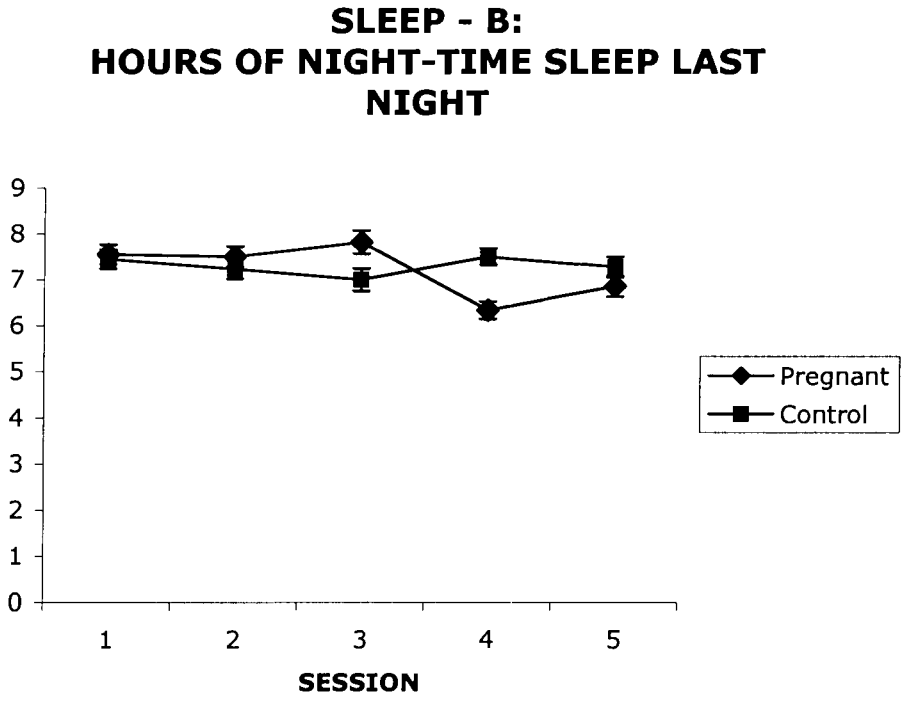
Analysis of variance results indicate session by group interactions for sleep measures B (*hours of sleep last night*), C (*is this amount of sleep enough for you?)* and D (*average hours of night-time sleep over the last week*). As Figure 18 and 19 reveal, this effect is caused by women in the experimental group getting considerably less night-time sleep during the early postnatal phase (test sessions four). There is evidence of some recovery at the final test session when infant children are older however.

Main Effect of Session

Main effects for session are present for sleep measures E (*is the sleep you have been getting over the last week enough for you?)* and F (*Current alertness rating*). The main effect of session for sleep measure F is evident in Figure 20, with both groups showing trends for increasing subjective ratings of sleepiness. However, no main effect of group was present here, or on any of the six sleeps measures.

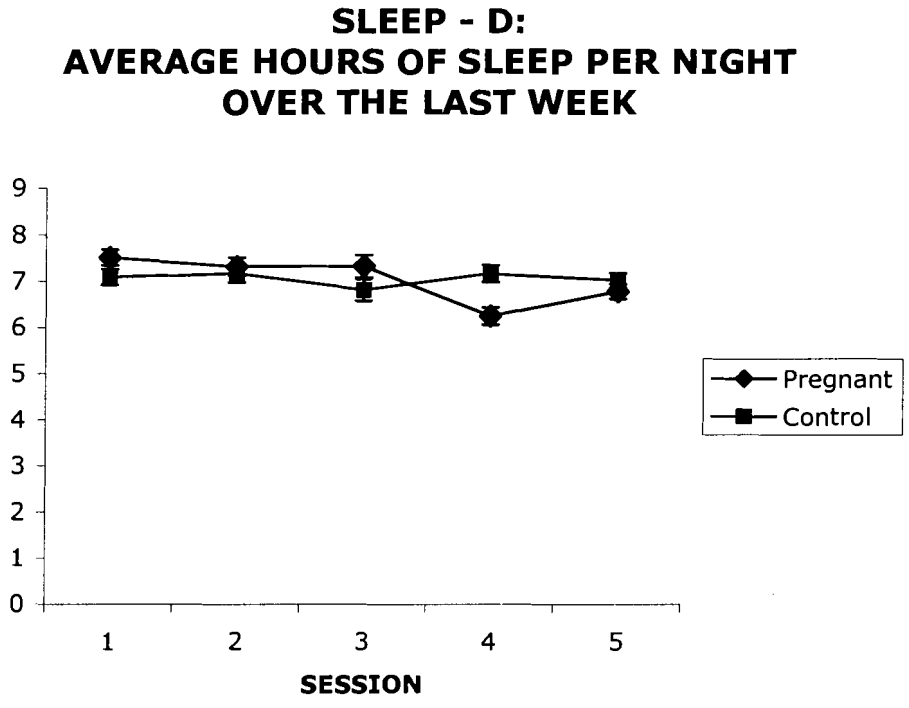
No interaction ($F(4, 66) = .418$, $p = .796$), session ($F(4, 66) = 1.699$, $p = .151$) or group ($F(1, 66) = .442$, $p = .509$) main effects were detected for sleep measure A *(morningingness/eveningness score)*.

Figure 18: Night-time Sleep: Experimental to Controls



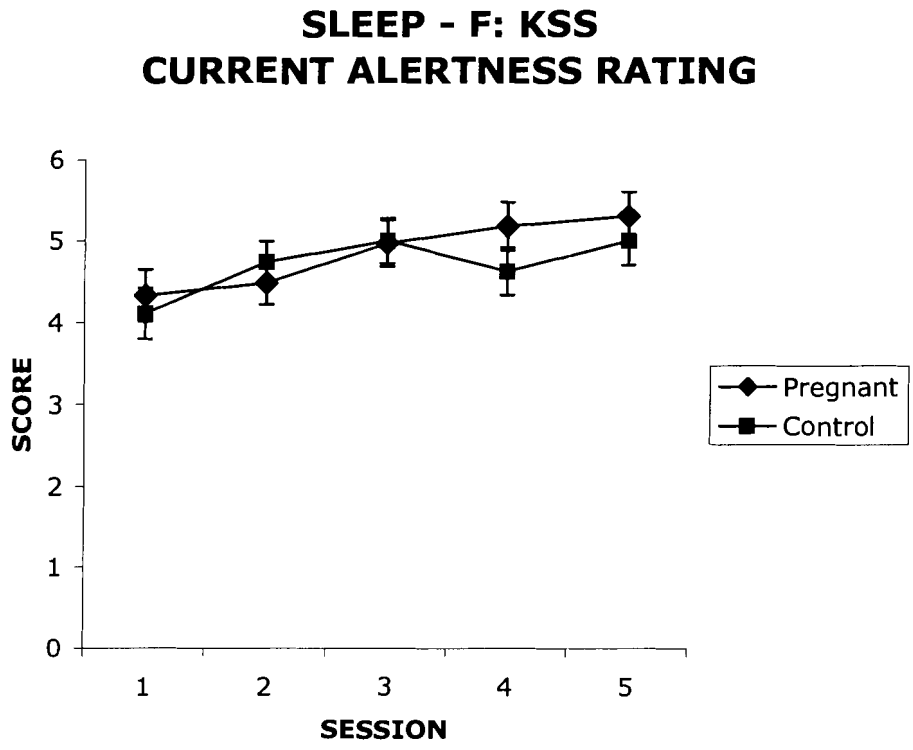
SLEEP – B Hours of sleep last night Raw Data (33 exptal, 35 control)	Main Effect: Group F(1, 66) = .160, p= .691 Main Effect: Session F(4, 66) = 3.522, p= .008 Interaction Effect: Group x Session F(4, 66) = 8.123, p< .001*
SLEEP – C Was this enough night-time sleep for you?	Main Effect: Group F(1, 66) = 3.025, p= .087 Main Effect: Session F(4, 66) = 2.570, p= .039 Interaction Effect: Group x Session F(4, 66) = 8.448, p< .001*

Figure 19: ***Average Hours of Night-time Sleep in Last Week: Experimentals to Controls***



SLEEP – D Average nightly sleep over the last week Raw Data (33 exptal, 35 control)	Main Effect: Group F(1, 66) = .009, p= .925 Main Effect: Session F(4, 66) = 5.704, p< .001* Interaction Effect: Group x Session F(4, 66) = 8.033, p< .001*
SLEEP – E Is this enough night-time sleep for you?	Main Effect: Group F(1, 66) = 3.430, p= .068 Main Effect: Session F(4, 66) = 4.123, p= .003* Interaction Effect: Group x Session F(4, 66) = 2.798, p= .028

Figure 20: Karolinska Sleepiness Scale: Experimentals to Controls



SLEEP – F Current alertness rating 1 = very alert 9 = very sleepy Raw Data (33 exptal, 35 control)	Main Effect: Group F(1, 66) = .361, p= .550 Main Effect: Session F(4, 66) = 4.356, p= .002* Interaction Effect: Group x Session F(4, 66) = .797, p= .375

Post Hoc Comparisons of Sleep Measures

Post hoc T-tests reveal women in the experimental group did not differ from women in the control group on any of the six sleep measures for test sessions one, two three and five. Sleep measures did differ significantly during test session four however. Recently parturient women reported having less sleep the night before the test session ($t(74) = 4.072$, $p < .001$) and on average, less night time sleep over the last week ($t(74) = 2.880$, $p = .001$). These women also rated themselves as not getting enough sleep over the last week ($t(74) = 3.426$, $p < .001$) or the night before the test session ($t(74) = 4.621$, $p < 0.01$). Interestingly, their subjective ratings of current alertness did not differ significantly to that of the ratings of the control women ($t(74) = 1.685$, $p = .10$). This suggests that although experimental women had had less sleep, and had rated themselves as more sleepy, it did not affect with their current subjective alertness score. Appendix G lists results of the *post hoc* t-tests.

ANALYSIS 1: DISCUSSION

Dependent Measures

As outlined in the results section, on eight of the nine cognitive tasks administered pregnant/recently parturient women did not differ significantly from control women after applying a Bonferroni error rate correction. This negative result is consistent with several studies in this area where other authors have also failed to detect pregnancy-related cognitive effect on similar tasks (Brindle et.al, 1991; Casey, 2000; Janes et al, 1999; Schneider, 1989). One of the nine dependent measures did reveal an effect of pregnancy on maternal cognitive function. When considering the raw data alone, performance on the California Verbal Memory Test was significantly different between the two groups, with experimental women performing better overall than control women. This positive effect appears to be mediated by the results from the first, fourth and fifth test sessions (see Figure 9). Groups did not differ however, during test sessions two and three (corresponding to pregnancy trimesters two and three). This is when placenta-derived estrogen and progesterone levels are increasing significantly (Speroff, Glass & Kase, 1999).

During other reproductive events (menopause, ovarian cycle) these steroids have been shown to affect cognition (Hampson, 1988; Hampson & Kimura, 1988; Freeman, Purdy, Coutifaris, Rickels, & Paul, 1993; Miles, Green, Sanders & Hines, 1988; Phillips & Sherwin, 1992). Estradiol especially has been linked to improved performance on verbal tasks like the CVLT (Hampson, 1988; Hampson & Kimura, 1988; Miles, Green, Sanders & Hines, 1988; Phillips & Sherwin, 1992, but see Owens

Matthews and Everson, 2002). It might well be however, that pregnancy *per se*, via perhaps a non-steroidal mechanism, may be causing a global decrement in cognitive function; and any beneficial effects of higher estrogen could therefore be washed out by this larger effect. Two results temper this suggestion however. Firstly, trends in the data suggest the test scores of the pregnant group were slightly better than those of women in the control group. Although in many cases not a significant difference, the line graph for the experimental group was always generally above that of the control group, arguing against a general trend of gestation-related cognitive decline. Secondly, other tasks included in the test battery, such as the Purdue Pegboard, which have also been shown to be positively correlated with salivary estrogen levels (Hampson, 1990; Hampson & Kimura, 1988), failed to show a significant between-group difference. It is important to note however, that although both tests have been demonstrated to be sensitive to fluctuations in gonadal steroid levels, they may be different enough in kind to not be identically affected by the high levels of estrogen seen during pregnancy. It would follow then that perhaps there exists an optimal steroid range necessary for maximal cognitive performance on some tasks, and this range might differ across tasks. The idea of a relationship between good cognitive performance and optimal steroid titres has already been identified with other steroid hormones (Gouchie & Kimura, 1991).

With few exceptions, performance of both groups improved on the dependent measures. Recall, one of the *apriori* predictions was for improvement for the experimental group to only occur once parturition had taken place. This was not supported in the results. Pregnant women, like the control women tended to get better with repeated exposure to the tasks. This was generally true both while pregnant and into early maternity.

The improving performance of both groups of women on the dependent measures across the test sessions certainly suggests a practice effect. It is possible these effects could be restricted in the upper ranges as women improved on the tasks with subsequent exposures. However, this does not appear to be the case, as the dependent measures show no evidence of a plateau effect in the latter test sessions.

An alternative explanation to the view the experimental group were somehow cognitively advantaged, is the possibility that control women were significantly different from the experimental women right from the outset of the study. Perhaps this difference contributed in some way to dependent measure outcomes? Control women *did* differ on a number of measures; they were older, they were more likely to have children in the home and they generally did poorer on the fluid intelligence task. In addition, although error rate did not differ from experimental women, they did complete the crystallized intelligence test more quickly, suggesting faster processing time on this task. However, when the set of covariates were analysed, no extraneous variables contributed significantly to any of the dependent measures. Therefore, despite the differences between the groups from the outset of the study these factors were not contributory to the respective test scores.

Salivary Assays

The individual hormone profiles are consistent with known levels for serum hormone titres during pregnancy (Speroff, Glass & Kase, 1999). Currently very few studies have evaluated salivary profiles of sex hormone levels throughout pregnancy and into the postnatal phase. Results reported here differ in some cases with those

obtained from other labs, however this difference may be due to small sample sizes of some studies (e.g. Berg & Wynne-Edwards, 2002) and differing collection techniques (Rondo, Vaz, Moraes & Tomkins, 2004). None of the assayed hormones reliably correlated with any of the dependent measures, for each of the five test sessions. This was true for the overall correlations and also true when separate analyses where conducted for both the experimental group and the control group.

Maternal age was significantly and consistently related to lower androgenic and estrogenic profiles during pregnancy. Among women in the experimental group, age at first test session consistently correlated with two of the seven steroids. In pregnant women, but not women in the control group, DHEAs showed a persistent negative correlation with maternal age. This effect was evident from the first test session and continued until the fourth test session. At the final test session, which occurred during the menstrual phase of the ovarian cycle, the relationship was no longer evident. Similarly, estradiol also showed a strong negative correlation to maternal age for pregnant women, but not control women, for the second and third test session. The relationship was lost once parturition had occurred. This finding is consistent with perimenopausal research in this area. Among non-pregnant women, published data shows a significant age related decline in DHEA and DHEAS (Zumoff, Rosenfeld, Strain, Levin & Fukushima, 1980). In women, testosterone has also been shown to drop by as much as 50% between ages of 21 and 40 (Zumoff, Strain, Miller & Rosner, 1995). Both estradiol and progesterone also decline after about age 25, which ultimately, at menopause reflects the cessation of folliculogenesis and ovulation (Judd & Fournet, 1994). Age related declines in steroidogenesis during pregnancy have not garnered the same degree of research however.

Although sufficient levels of both estradiol and progesterone are necessary for ovulation and the development of the normal endometrial architecture needed to sustain a normal pregnancy, age related profiles of minimal values seem to be lacking from the literature. A possible explanation for the apparent absence of this clinical information may be related to the known fact that in pregnancy sex steroids are generally placental rather than maternally-derived (Speroff, Glass & Kase, 1999) and thus would not be expected to change across age cohorts. Based on the findings reported here however, there is some indication that maternal age *is* related to gestational steroidogenesis, suggesting a new avenue of potentially fertile future research. This is a direction that may be particularly important considering the recent trend in women for increasing age at first pregnancy (Speroff, Glass & Kase, 1999).

Sleep and Mood Scores

Despite the research evidence reporting that pregnancy and the post partum are times of mood instability for women (Pritchard & Harris, 1996), this effect was not seen in this study. Pregnant women did not differ from control women on global measures of mood evaluated by the Profile of Mood States questionnaire. This was true throughout the study from the early prenatal period until the final test session. It is possible the total mood score used in this study may not have been sensitive enough to detect subtle affective changes in a sample of normal (i.e. not depressed) pregnant women. This is unlikely however considering adult normative samples show a similar range of means and standard deviations as those reported here for both groups of women (Appendix F) (McNair, Lorr & Droppleman, 1992).

Sleep measures only differed significantly between groups during the early postnatal test session. Pregnant women acknowledged chronically insufficient sleep in the recent past. Subjective measures of alertness did not differ between the two groups, suggesting although these women were more sleep deprived than control women, this did not affect their perceived state of alertness. As discussed earlier, recent research has shown individuals do tend to be poor self-evaluators of their current levels of sleepiness (Van Dongen, Baynard, Maislin & Dinges, 2004). An effect that can be dissociated from actual task performance, with increasing sleep deprivation being related to poorer task execution. This result was not evident in this study however, as performance did not differ between groups on the cognitive test battery; sleep deprived experimental women performed similarly to control women. This could be due to two reasons. Firstly, the tests used in the battery were not sensitive enough to detect the sleep-restricted state of the recently parturient women, suggesting perhaps the need for more difficult or longer tasks to reveal the effect. Alternatively, the Karolinska Sleepiness Scale as a one-item Likert scale, may be too coarse a measure to accurately assess current levels of alertness in new mothers. This is indeed plausible considering it has generally been used in work or laboratory settings (Akerstedt & Gillberg, 1990; Gillberg, Kecklund & Akerstedt, 1994) and not in domestic situations, where responsibilities are unique to the home environment.

Analysis 1: Summary

In general, pregnant and recently parturient women did not differ from control women on the dependent measures tested here. In addition, performance of both

groups improved with repeated task exposure. Although steroid profiles did differ between the two groups, this was a predictable consequence of the hormonal state associated with pregnancy and the postpartum. No steroid hormone was systematically related to performance on any of the dependent measures, however DHEAs negatively correlated with maternal age in the experimental group. Mood and sleep scores also did not correlate with any dependent measure. Among this cluster of negative findings however was an unexpected ratio of male to female births, with the delivery of sons disproportionately represented in the study. This observation became the impetus for the second analysis.

ANALYSIS 2: INTRODUCTION

Longitudinal Study of the Relationship Between Fetal Sex and Maternal Cognition

The ratio of male to female births in analysis one provided the impetus for analysis two. Recall, of the 45 women who ultimately delivered singleton pregnancies, 29 were male and 16 were female. Although this deviation from the expected 50:50 ratio was not significantly different ($\chi^2 = .007$, $p = .932$), it was the motivator for the reanalysis of the data. The sex ratio deviation was not attributable to a selective dropout of pregnant participants. Only four of the enrolled women dropped out of the study, in all cases as a consequence of miscarriage.

While it is widely recognized that maternally derived factors are readily taken up and utilized by the conceptus, it is also true that significant quantities of fetal-derived products make their way into the maternal blood supply (Speroff, Glass & Kase, 1999). Indeed, throughout pregnancy a bidirectional relationship exists between the conceptus and the maternal periphery and nervous system. This starts at conception with the rescue of the pregnant corpus luteum by hCG secreted by the germinal conceptus (Csapo, Pulkkinen & Wiest, 1973). Throughout pregnancy other hormones and diffusible factors also directly affect and modify the maternal system for the benefit of the conceptus. As discussed in Analysis 1, HPL is synthesized by the conceptus but little reaches fetal circulation. Instead, this product diffuses into the maternal system and alters carbohydrate and lipid metabolism to provide for fetal nutritional requirements (Felig, 1973). It also exerts a direct effect on breast tissue by stimulating the mammary

cell proliferation necessary for lactation (Anthony et al, 1998). Placental-derived relaxin similarly exerts control over maternal physiology. Based on animal research, it has been shown this peptide is necessary for normal labour and parturition (MacLennan, Katz & Creasy, 1985) however its function is less clear in women (Emmi et al, 1991). Nevertheless, it readily passes into the maternal system and is capable of exerting a significant biologic effect.

Steroid hormones are fat-soluble and readily cross lipid membranes; as a consequence, a signal to synthesize is also the signal to release. These secretory products have receptors both in the periphery and in the nervous system, and can readily influence behaviour via input sensory systems, output motor systems or the nervous system itself (Nelson, 2000). As discussed in Analysis 1, during pregnancy steroids are derived from a variety of maternal and feto-placental sources. An untested possibility is the nature and consequences of fetal-derived steroids may differentially affect the mother based primarily on the dissimilar steroidal milieu present in the development of a male versus a female fetus. Given that sex hormones are responsible for physiological and neural sexual differentiation and later activational effects, it is plausible that these same secretory products can also affect maternal physiology. Moreover, the wealth of literature demonstrating that sex steroids can affect cognitive functions in adults (Kimura, 2002; Kimura, 1999) suggest the possibility that any diffusible factor differing in type and kind between male and female fetuses could cross the placenta and differentially affect the maternal nervous system. This may result in dissimilar effects on maternal cognitive processes.

In an effort to better understand and empirically quantify the effects of fetal sex on maternal cognition and evaluate the relative contribution of gestational steroid

hormones, Analysis 2 tested women across pregnancy and into the postnatal phase. Fetal sex was identified and recorded at test session four for later analysis. The presence of an age and education matched control group addressed practice effects and other confounding variables. Women in the three groups (Boy-Moms, Girl-Moms, non-pregnant controls) were tested on a variety of cognitive tasks designed to evaluate changes in concentration and attention, verbal memory, working memory, spatial performance and general cognitive function. Using salivary samples, steroid hormone levels were measured for each test session for all women in the study.

ANALYSIS 2: METHOD

Participants, procedures, dependent measures, sleep questionnaires and the mood scale used in Analysis 2 did not differ from those used in Analysis 1.

Sex of the fetus was unknown to either the pregnant woman or the experimenters for test session one. Sex of the fetus may well have been known to the parents at test session two as this session occurred after the eighteen-week regularly scheduled ultrasound. Almost all the women advised they had elected to not pursue this information however. Regardless of the decisions of the parents in this situation, in no case was the experimenter advised as to the sex of the baby prior to parturition. Fetal sex was revealed to the experimenter during the post-parturition follow-up phone call. This generally occurred approximately two weeks after delivery. Forty-five women comprised the sample, all ultimately delivered singleton pregnancies, 29 were male and 16 were female.

ANALYSIS 2: RESULTS

Initial Statistical Considerations

All analyses were conducted on SPSS standard version (release 11.0.1) using the general linear model function for ANOVA, ANCOVA and t-tests for mean comparisons. Bi-variate relationships were analyzed using Pearson's product moment correlations. Because multiple measures were used, a Bonferroni correction was made to control the familywise error rate. Generally, this resulted in the significance level being set at .005.

Occasionally women in the study did not complete all of the five test sessions. This was due to such factors as schedule conflicts, travel, premature delivery, illness or relocation. As with Analysis 1, in these cases data sets were reconstructed. Table 11 details the number of missing values replaced for each test session. Over the course of the study there was approximately 10% or 22 (of a total of 225) values replaced. Sixteen were from women who ultimately delivered sons and six values were replaced from women delivering girls. There is no reason to suspect any type of systematic differences between the two groups for this attrition. Because the data set now includes approximately 10% estimated values for the nine cognitive tests, statistical manipulations are shown for both the raw non-estimated data and the data set where the missing values have been included. These will be referred to as Raw Data and Replaced Data respectively.

Table 11: ***Missing Values Replaced Using Linear Trend at Point Regression Analysis***

Test Session	# of replaced values (missing cases/Analysis 2 n)	% replaced
One	4/45	8%
Two	3/45	6%
Three	5/45	11%
Four	6/45	13%
Five	4/45	8%
Total	22/225	10% attrition

Demographics and I.Q. Measures

Women pregnant with and ultimately delivering boys are referred to as *"Boy-Moms"*. Women pregnant and ultimately delivering girls are referred to as *"Girl-Moms"*. Women in both groups were pregnant for the first three test sessions. These women were in the early and late postpartum period for test sessions four and five. The women who comprised the control group were tested during the menstrual phase of the ovarian cycle for all five of the test sessions. Table 12 outlines the demographic descriptive statistics for the Boy-Moms and the Girl-Moms.

Table 12: Summary Demographic Descriptive Statistics by Group

Demographic Variable		Boy-Moms	Girl-Moms
N		29	16
Age at first test session (years):	Mean	31.2	31.6
	s.d.	4.6	4.5
Years of education:	Mean	14.9	15.0
	s.d.	1.7	1.7
First Language:	English:	28 (96%)	13 (81%)
	Other:	1 (4%)	3 (19%)
Children resident in the home:	0	13 (45%)	5 (32%)
	1	12 (41%)	6 (37%)
	2	4 (14%)	4 (25%)
	3	0	1 (6%)
Sex of resident children:	0 (n/a)	13 (45%)	5 (31%)
	Girls	4 (14%)	4 (25%)
	Boys	11(38%)	3 (19%)
	Both	1 (3%)	4 (25%)
Handedness:	Right	25 (86%)	15 (94%)
	Left	4 (14%)	1 (6%)
Stay at home Mom?	Yes	8 (27%)	4 (25%)
	No	21 (73%)	12 (75%)
Subjective preg. sickness rating	Nil	10 (35%)	5 (31%)
	Mild	8 (27%)	7 (44%)
	Moderate	11 (38%)	4 (25%)
	Severe	0	0
Weeks pregnant at 3rd test session	Mean	36.9	36.8
	s.d.	1.1	.77
Working at the 3rd test session?	Yes	10 (35%)	6 (37%)
	No	15 (51%)	9 (57%)
	Missing cases	4 (14%)	1 (6%)
Route of delivery	Caesarean	9 (31%)	5 (31%)
	Vaginal	20 (69%)	11 (69%)
Working at the final test session?	Full-time	5 (17%)	2 (13%)
	Part-time	7 (24%)	6 (37%)
	Not working	14 (48%)	7 (44%)
	Missing cases	3 (11%)	1 (6%)

When Boy-Moms were compared to Girl-Moms on demographic and I.Q. variables using *post hoc* t-tests, no significant differences were detected. Women

pregnant with girls did not differ significantly from women pregnant with boys with regard to level of education (t= .064, p= .950), high school graduating grades (t= 1.21, p=.227), crystallized intelligence (as approximated by vocabulary testing; t= .372, p=.712) or fluid intelligence (Cattell test of "g"; t= 1.966, p= .060). Furthermore, the effect could not be attributed to group differences in the number of previous births (t= 1.395, p=.175), the sex of any older siblings (t=.452, .655), multiparous vs. primiparous pregnancy (t=.892, p=.379), first language (t= 1.747, p=.089), handedness (t= .835, p=.408), or severity of pregnancy sickness (t= .386, p= .702). On average, women carrying boys and women carrying girls were equivalent in employment status both throughout pregnancy (t= .185, p= .855), and just prior to parturition (t= .010, p= .992). The number of weeks pregnant at the third test session also did not differ between groups (t= .599, p= .553). Finally, there were no significant differences related to maternal age at first test session (t= .357, p=.723), route of delivery (vaginal or caesarean; t=.015, p=.988) and date of postnatal return to work (t= .053, p=.958). Table 13 summaries the one-time tests of fluid and crystallized intelligence.

Table 13: Summary Fluid and Crystallized Intelligence Measures by Group

Test		Boy-Moms	Girl-Moms
Fluid Intelligence	Mean	35.5	32.7
Cattell Culture Fair Scale 2, Form A	*s.d.*	4.1	4.8
Crystallized Intelligence	Mean	9.6	9.3
18-item vocab test	*s.d.*	3.7	2.6
Time to complete vocab test (seconds)	Mean	189.2	197.0
	s.d.	78.5	51.1

Dependent Variables (Cognitive Tests) Covariates

As a number of extraneous variables could possibly be related to the dependent measures, ANCOVAs were initially calculated for each of the nine tests incorporating these fifteen variables. Marital status, as defined by either being a single parent or cohabiting with a spouse, was not included as a covariate in Analysis 2 as all 45 participants were currently living with the birth father of their child. Table 14 lists the variables included as covariates in this initial analysis. Variables specific to Analysis 2 are italicized.

Table 14: Covariates included in each ANCOVA

First Language	*Subjective rating of pregnancy sickness at the first test session*
Parity	*Route of Delivery*
Sex of older siblings	Working at 3rd test session?
Mother at first test session?	Working at 5th test session?
Handedness	Cattell score
Stay at home Mom?	Vocab score
Age at first test session	Vocab completion time
Education level attained	

Of the fifteen covariates identified and tested within an ANCOVA model for each of the nine dependent variables, only one measure showed a significant effect. For the

Mental Rotation Task, the Cattell test of fluid intelligence was significant. When the proportion of variance in the dependent variable explained by this covariate was calculated, it accounted for only 4.4%. Given its minor contribution, ANOVAs (Repeated Measures) were subsequently run without any further consideration of the Cattell. Appendix H provides a summary of the ANCOVAs for each of the nine dependent variables. Significant effects have been bolded.

Analysis of Variance

Each of the nine dependent measures was administered once per test session to both the Boy-Moms and the Girl-Moms. Appendix I lists the means and standard deviations for the cognitive tests for both the raw and replaced data sets across the five test sessions.

Group by Session Interactions

No group by session interaction was observed on any of the nine dependent measures.

Main Effect of Session

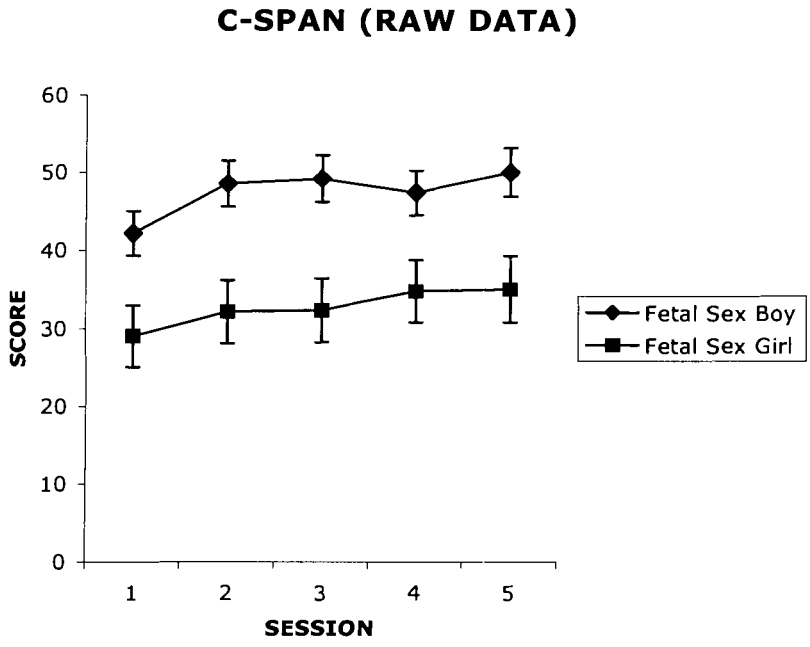
For seven of the nine tasks a main effect for session was evident, reflecting a probable practice effect. Generally women in both groups improved their performance over the duration of the study.

Main Effect of Group

A main effect of group was observed for the Computation Span, Listening Span and Shepard-Metzler Mental Rotation Task[1]. Women pregnant will male fetuses selectively and consistently outperformed women carrying female fetuses on these three cognitive tests. This clear and consistent effect was evident at the first test session and persisted throughout the duration of the study, up to and including the final postnatal evaluation. Figures 21 to 26 graphically represent these significant findings for both the raw and replaced data sets. Graphs of the six non-significant results follow this (raw data only) (Figures 27 to 32). Under each of the graphs are the ANOVA main and interaction results for both the raw and replaced data sets. All significant effects have been bolded.

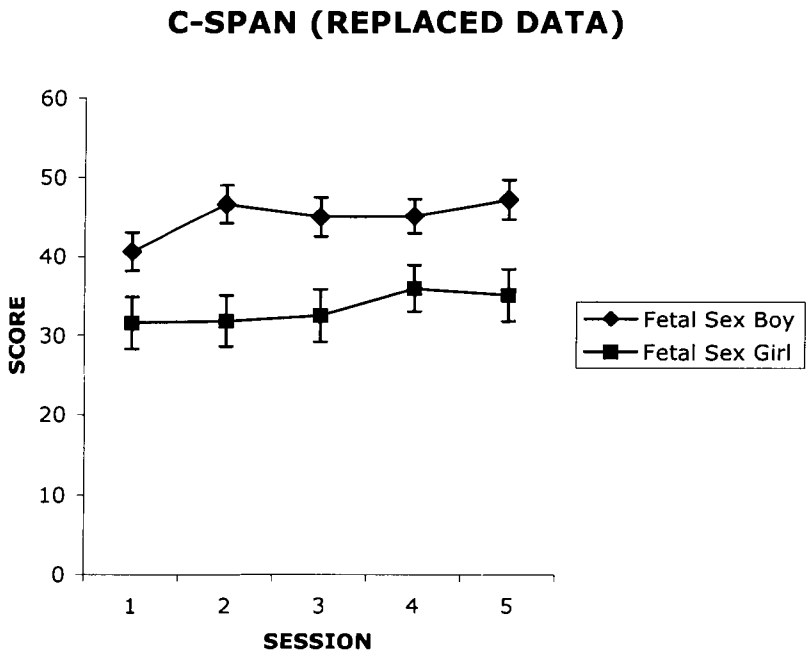
[1] Although not quite meeting the most conservative Bonferroni-adjusted alpha of .005, the overall main effect of group was .009, and absolutely consistent for all five test sessions. In light of this, discarding this result as non-significant incurs considerably greater risk of making a Type II error over a Type I error.

Figure 21: Boy-Moms to Girl-Moms: C-Span (Raw)



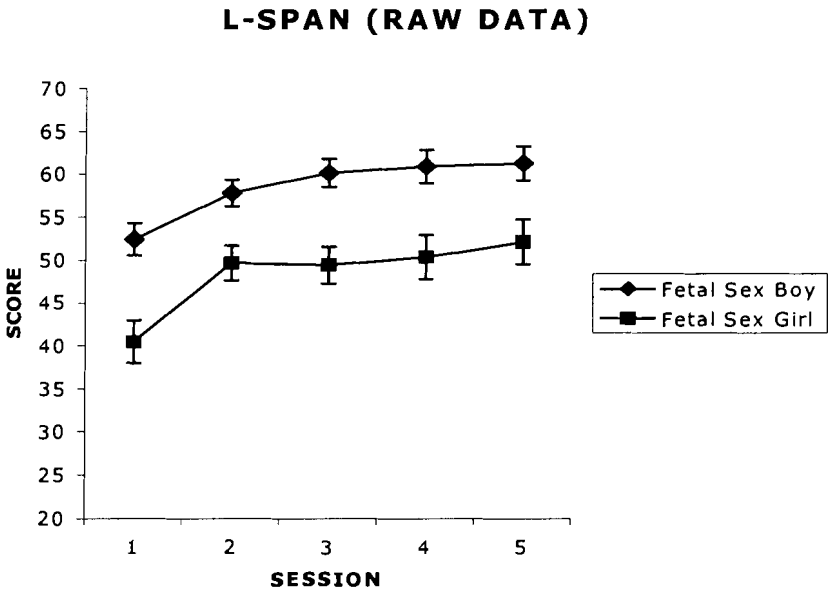
Computation Span Raw Data (21 Boy-Moms/12 Girl-Moms)	Main Effect: Group F(1, 30) = 9.592, p= .004* Main Effect: Session F(4, 30) = 8.950, p< .001* Interaction Effect: Group x Session F(4, 30) = 1.133, p= .345

Figure 22: Boy-Moms to Girl-Moms: C-Span (Replaced)



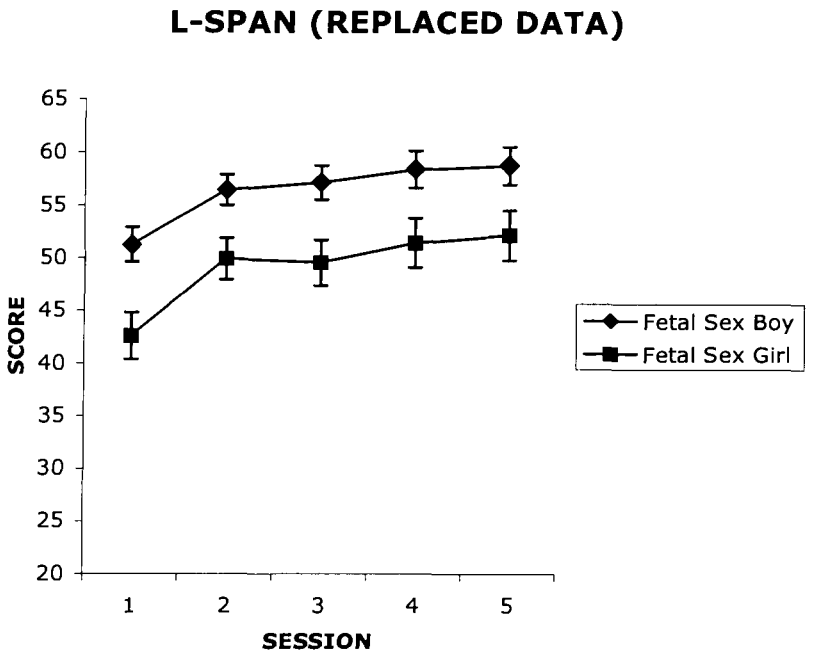
Computation Span Replaced Data (29 Boy-Moms/16 Girl-Moms)	Main Effect: Group $F(1,43) = 9.730$, $p = .003$* Main Effect: Session $F(4, 43) = 5.085$, $p = .001$* Interaction Effect: Group x Session $F(4, 43) = 1.943$, $p = .105$

Figure 23: Boy-Moms to Girl-Mom: L-Span (Raw)



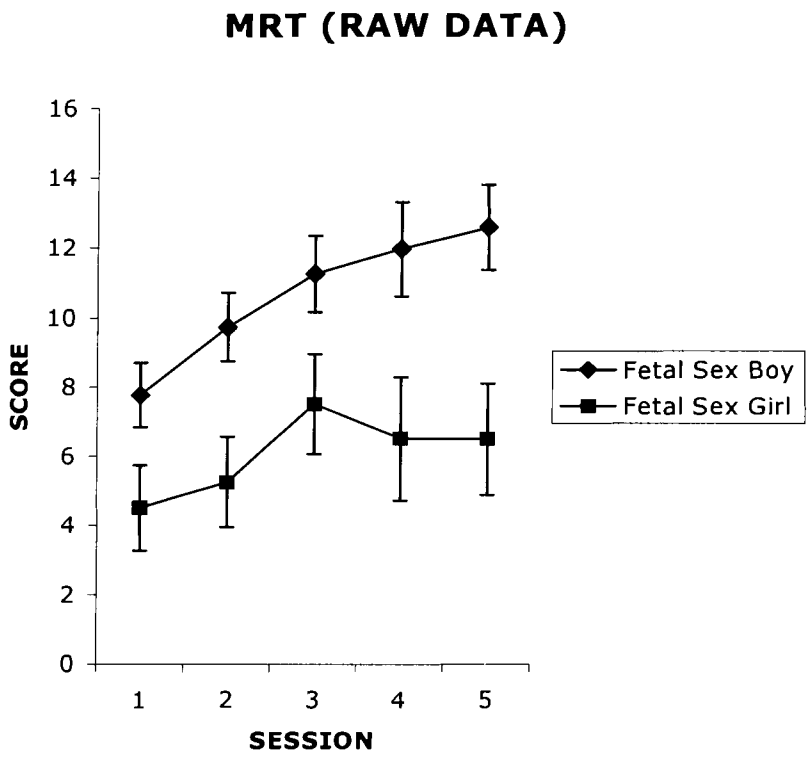
Listening Span Raw Data (21 Boy-Moms/12 Girl-Moms)	Main Effect: Group F(1,31) = 14.709, p= .001* Main Effect: Session F(4, 31) = 27.259, p< .001* Interaction Effect: Group x Session F(4, 31) = .893, p= .467

Figure 24: Boy-Moms to Girl-Moms: L-Span (Replaced)



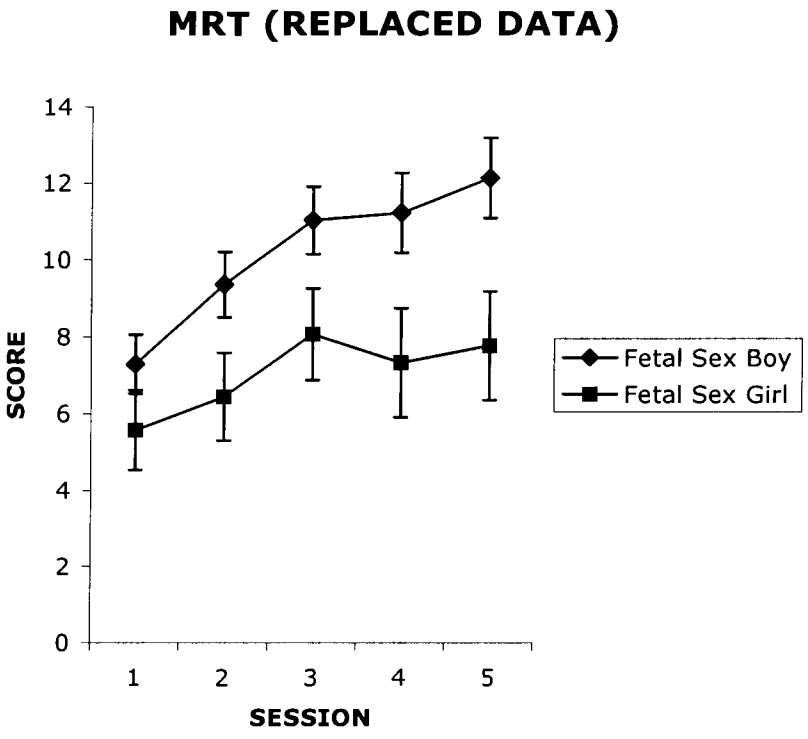
Listening Span Replaced Data (29 Boy-Moms/16 Girl-Moms)	Main Effect: Group F(1,43) = 9.027, p= .004* Main Effect: Session F(4, 43) = 21.297, p< .001* Interaction Effect: Group x Session F(4, 43) = .347, p= .821

Figure 25: Boy-Moms to Girl Moms: MRT (Raw)



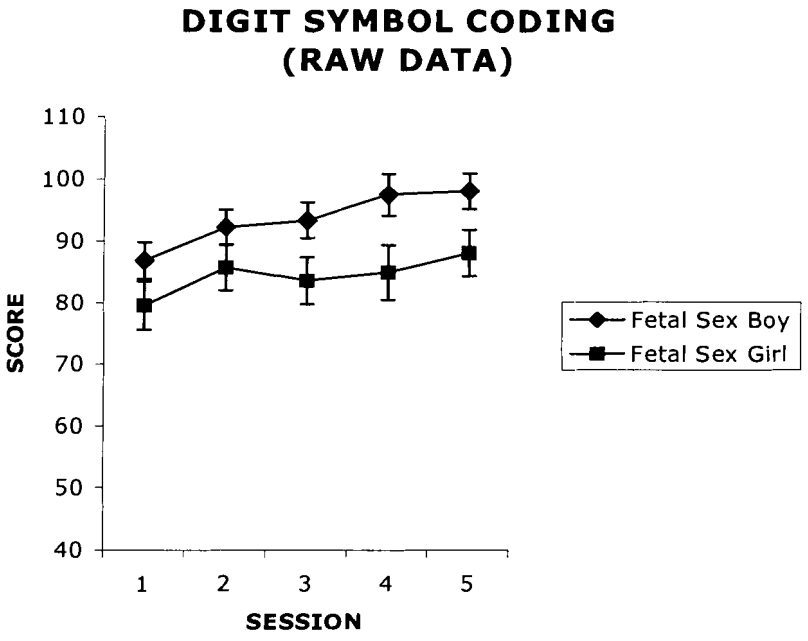
Mental Rotation Task Raw Data (21 Boy-Moms/12 Girl-Moms)	Main Effect: Group F(1, 31) = 7.681, p= .009 Main Effect: Session F(4, 31) = 9.731, p< .001* Interaction Effect: Group x Session F(4, 31) = 1.490, p= .212

Figure 26: Boy-Moms to Girl-Moms: MRT (Replaced)



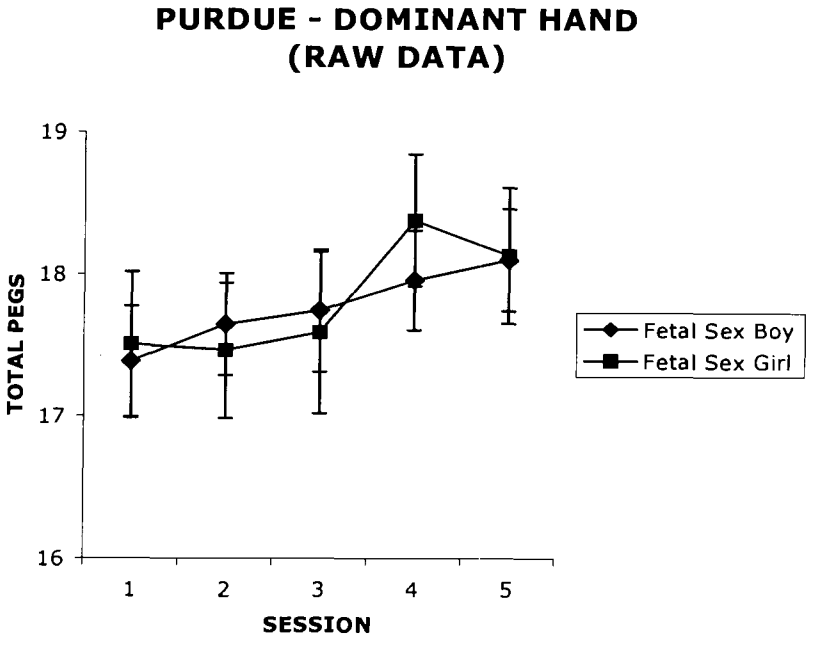
Mental Rotation Task Replaced Data (29 Boy-Moms/16 Girl-Moms)	Main Effect: Group $F(1,43) = 1.996$, $p = .165$ Main Effect: Session $F(4, 43) = 10.698$, $p < .001$* Interaction Effect: Group x Session $F(4, 43) = 1.343$, $p = .022$

Figure 27: Boy-Moms to Girl-Moms: Digit Symbol (Raw)



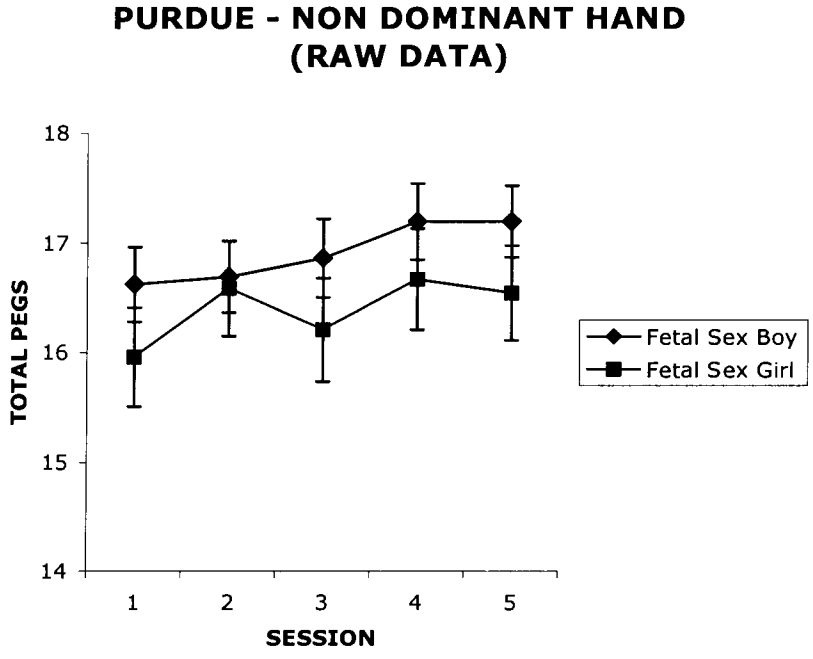
Test	Raw Data (21boys, 12 girls)	Replaced Data (29 boys, 16 girls)
Digit Symbol Coding	Main Effect: Group F(1,31) = 4.039, p=.053 Main Effect: Session F(4, 31) = 14.169, p< .001* Interaction Effect: Group x Session F(4, 31) = 1.465, p= .223	Main Effect: Group F(1,43) = 5.010, p=.030 Main Effect: Session F(4, 43) = 10.387, p< .001* Interaction Effect: Group x Session F(4, 43) = .275, p= .835

Figure 28: Boy-Moms to Girl-Moms: Purdue, Dom (Raw)



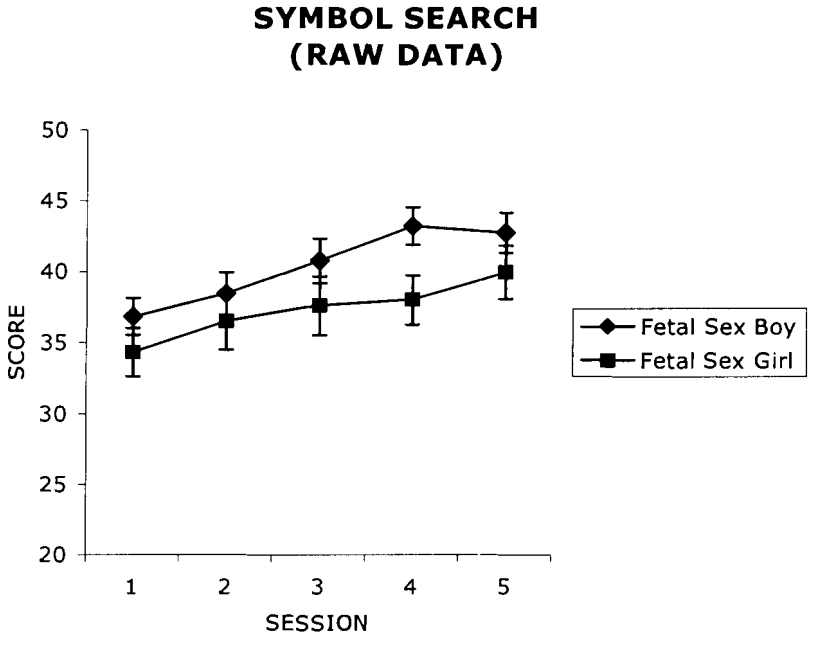
Test	Raw Data (21boys, 12 girls)	Replaced Data (29 boys, 16 girls)
Purdue Pegboard (Dominant Hand)	Main Effect: Group F(1,31) = .007, p=.933 Main Effect: Session F(4, 31) = 3.787, p= .006 Interaction Effect: Group x Session F(4, 31) = .520 p= .721	Main Effect: Group F(1,43) = .002, p= .964 Main Effect: Session F(4, 43) = 4.447, p= .002* Interaction Effect: Group x Session F(4, 43) = .813, p= .518

Figure 29: Boy-Moms to Girl-Moms: Purdue, Non Dom (Raw)



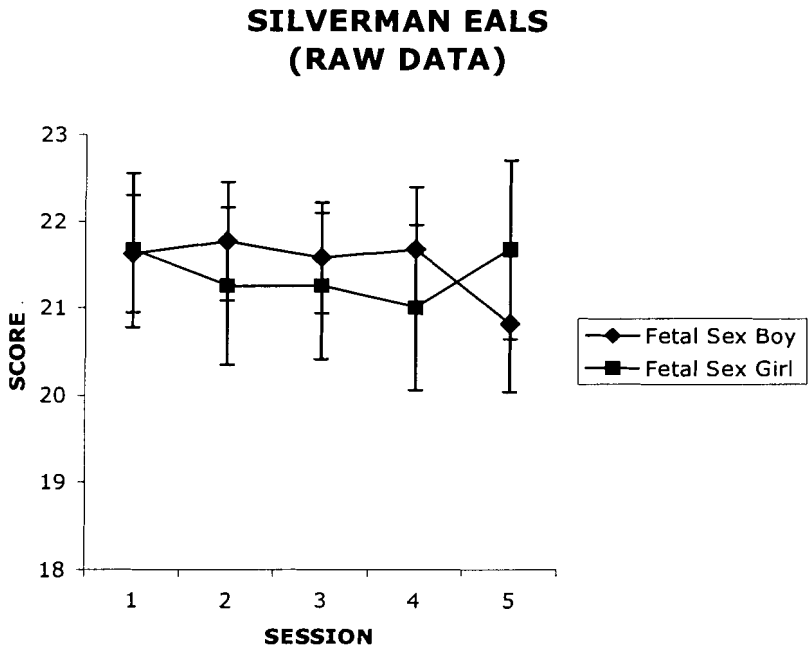
Test	Raw Data (21boys, 12 girls)	Replaced Data (29 boys, 16 girls)
Purdue Pegboard (Non-Dominant Hand)	Main Effect: Group F(1, 31) = 1.199, p= .282 Main Effect: Session F(4, 31) = 2.299, p= .063 Interaction Effect: Group x Session F(4, 31) = .478, p= .752	Main Effect: Group F(1,43) = 1.225, p= .274 Main Effect: Session F(4, 43) = 3.226, p= .014 Interaction Effect: Group x Session F(4, 43) = .986, p= .416

Figure 30: Boy-Moms to Girl-Moms: Symbol Search (Raw)



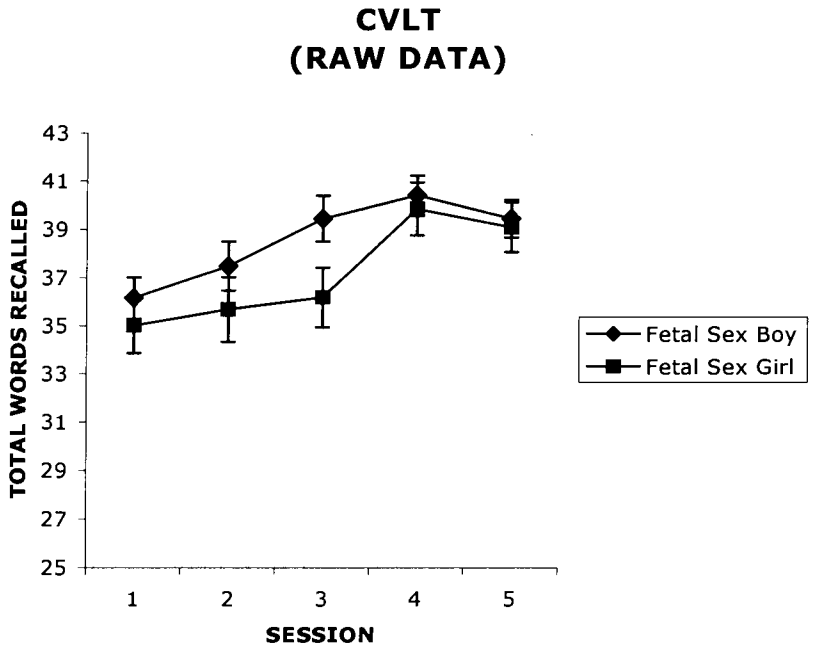
Test	Raw Data (21boys, 12 girls)	Replaced Data (29 boys, 16 girls)
Symbol Search	Main Effect: Group F(1,31) = 2.518, p= .123 Main Effect: Session F(4, 31) = 10.082, p< .001* Interaction Effect: Group x Session F(4, 31) = .717, p= .573	Main Effect: Group F(1.43) = 2.792, p=.102 Main Effect: Session F(4, 43) = 9.552, p< .001* Interaction Effect: Group x Session F(4, 43) = .150, p= .963

Figure 31: Boy-Moms to Girl-Moms: Silverman Eals (Raw)



Test	Raw Data (21boys, 12 girls)	Replaced Data (29 boys, 16 girls)
Silverman Eals Object. Location	Main Effect: Group F(1,31) = .018, p= .895 Main Effect: Session F(4, 31) = .143, p= .953 Interaction Effect: Group x Session F(4, 31) = .543, p= .682	Main Effect: Group F(1,43) = .069, p= .795 Main Effect: Session F(4, 43) = .332, p= .844 Interaction Effect: Group x Session F(4, 43) = .991, p= .411

Figure 32: Boy-Moms to Girl-Moms: CVLT (Raw)



Test	Raw Data (21boys, 12 girls)	Replaced Data (29 boys, 16 girls)
California Verbal LearningTask	Main Effect: Group F(1,31) = 2.007, p= .167 Main Effect: Session F(4, 31) = 9.634, p< .001• Interaction Effect: Group x Session F(4, 31) = .959, p= .428	Main Effect: Group F(1,43) = 1.576, p= .216 Main Effect: Session F(4, 43) = 14.209, p< .001* Interaction Effect: Group x Session F(4, 43) = 1.439, p= .225

Salivary Analyses

Salivary analyses are based entirely on raw data. This resulted in the Boy-Moms n being reduced from 29 to 21, and the n for the Girl-Moms falling from 16 to 12.

Analysis of Variance

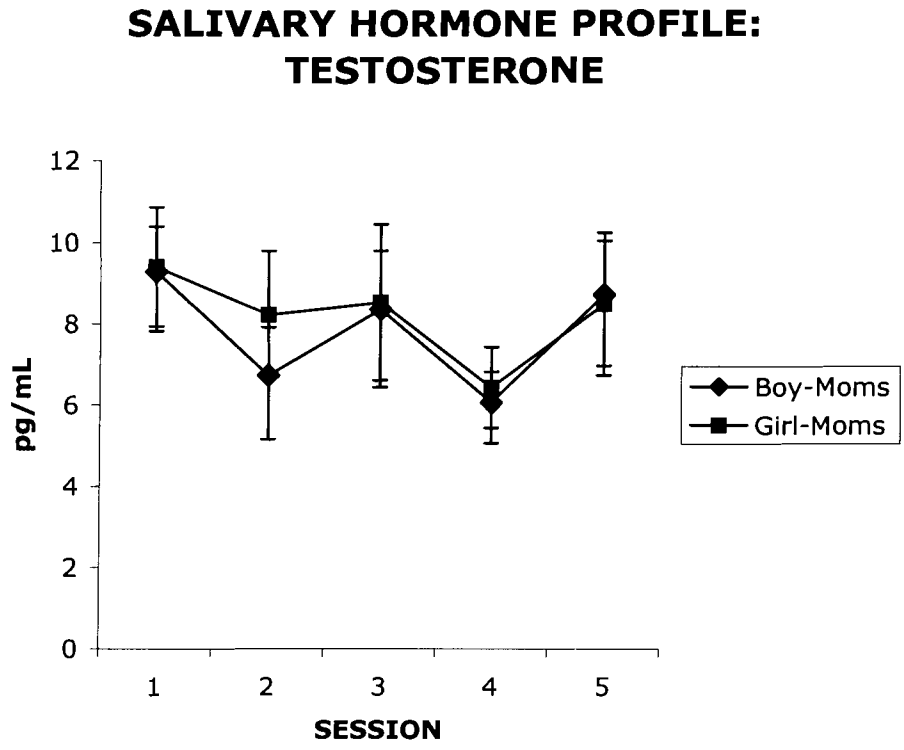
Group by Session Interactions and Main Effect of Group

No interaction effects, or group main effects were observed on any of the salivary hormone measures at the corrected alpha.

Main Effect of Session

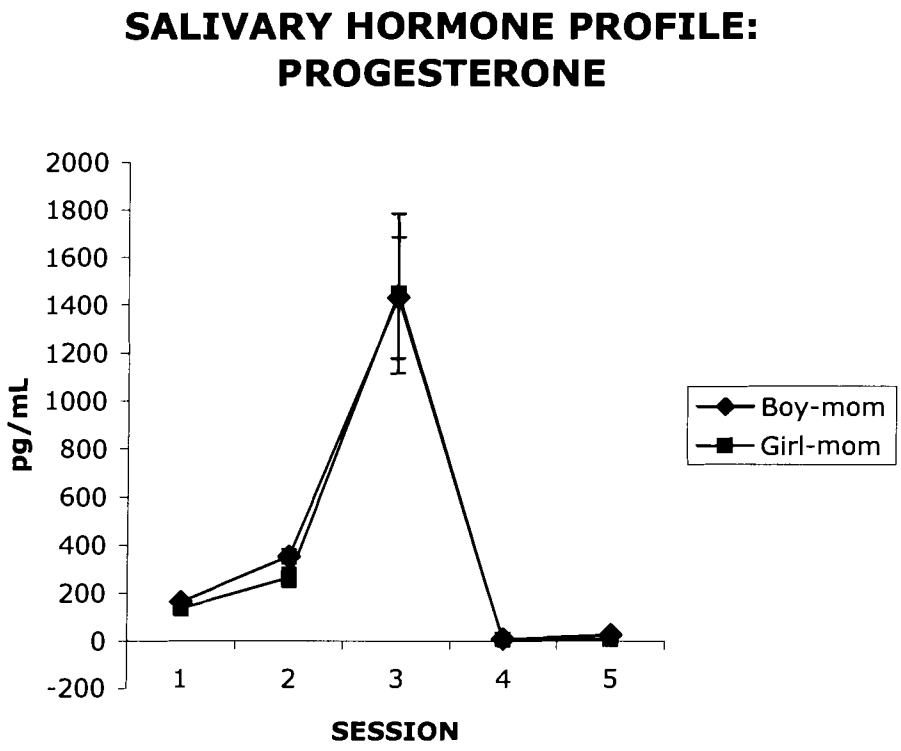
Six of the seven steroids showed a main effect of session. The only exception to this was testosterone. The effect of pregnancy was evident in progesterone, cortisol and the estrogens. Generally this followed a trend of low early pregnancy levels, which rose to a peak just prior to parturition and dropped precipitously during the postnatal period. Both Boy-Moms and Girl-Moms groups showed very similar trends in this regard. Levels of both androgens dropped from the first to the second trimester, with DHEAs remaining low until after parturition. A result that is consistent with current research in gestational steroidogenesis (Peter, Door & Sippell, 1994). Figures 33 to 39 summarises these results (with attendant ANOVAs). Descriptive statistics of the salivary hormones for the Boy-Moms and Girl-Moms are located in Appendix J.

Figure 33: Testosterone Profile: Boy-Moms to Girl-Moms



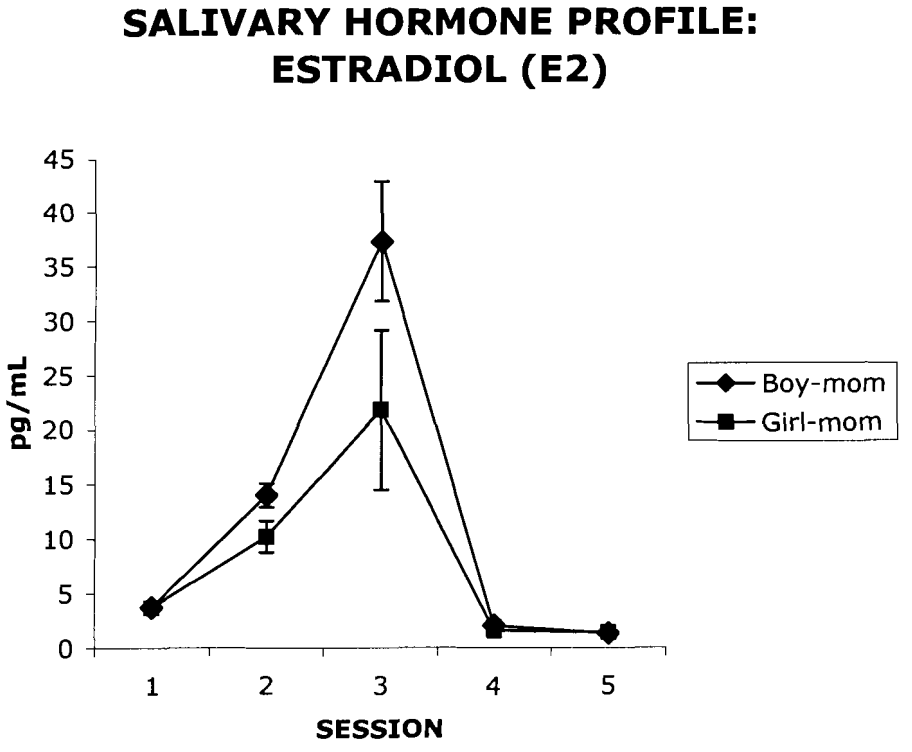
Testosterone Raw Data (21 Boy-Moms/12 Girl-Moms)	Main Effect: Group F(1, 31) = .097, p= .757 Main Effect: Session F(4, 31) = 1.938, p= .119 Interaction Effect: Group x Session F(4, 31) = .147, p= .948

Figure 34: Progesterone Profile: Boy-Moms to Girl-Moms



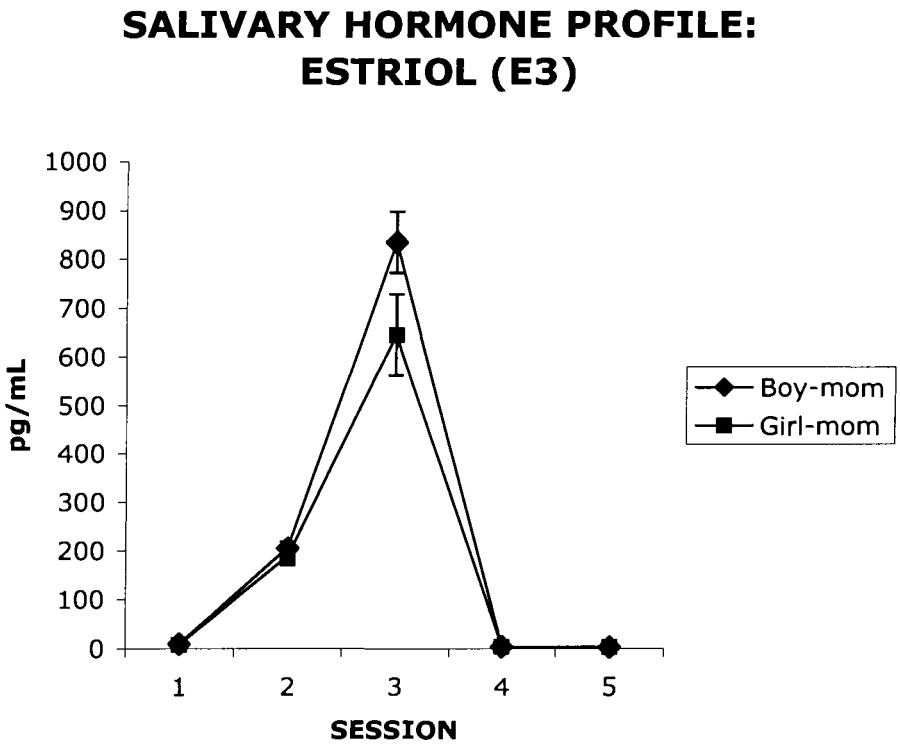
Progesterone Raw Data (21 Boy-Moms/12 Girl-Moms)	Main Effect: Group F(1, 31) = .067, p= .798 Main Effect: Session F(4, 31) = 42.363, p< .001• Interaction Effect: Group x Session F(4, 31) = .049, p= .841

Figure 35: Estradiol Profile: Boy-Moms to Girl-Moms



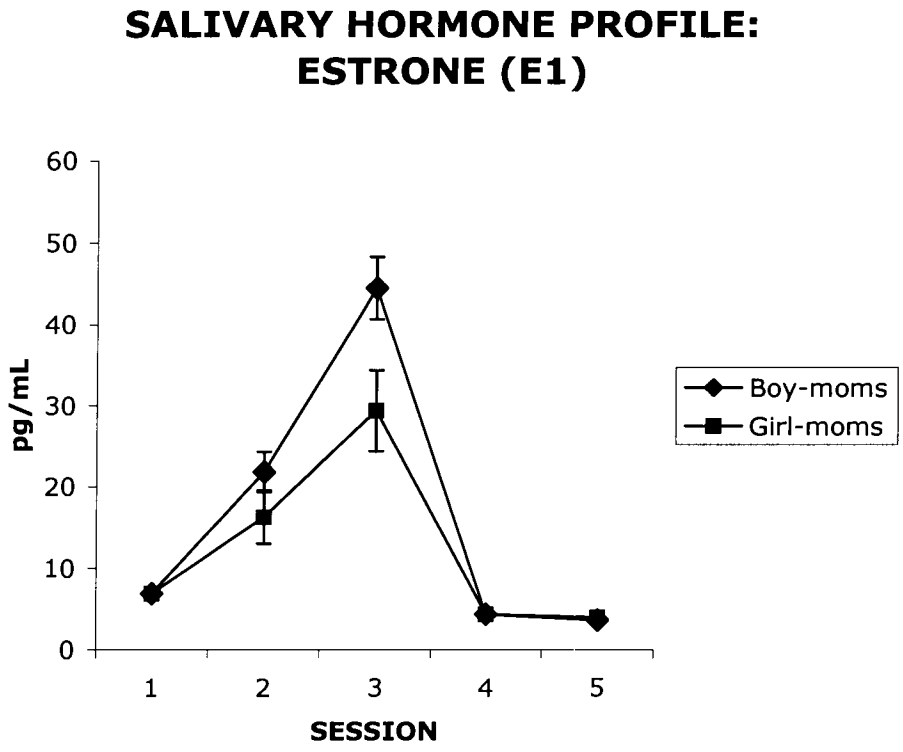
Estradiol (E2) Raw Data (21 Boy-Moms/12 Girl-Moms)	Main Effect: Group F(1, 31) = 3.145, p= .086 Main Effect: Session F(4, 31) = 35.958, p< .001* Interaction Effect: Group x Session F(4, 31) = 2.795, p= .100

Figure 36: Estriol Profile: Boy-Moms to Girl-Moms



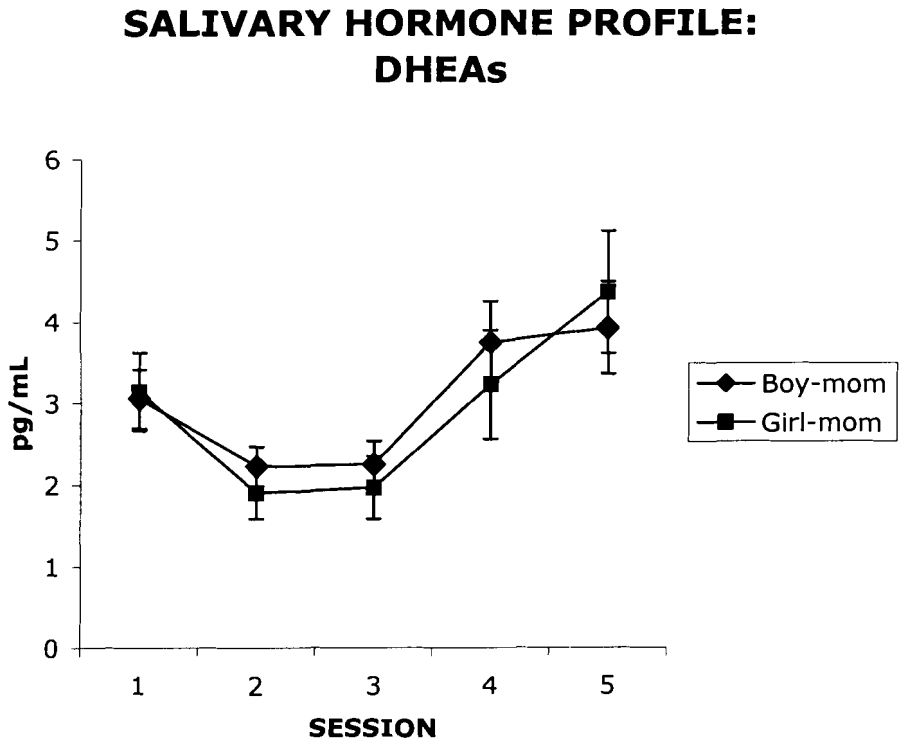
Estriol (E3) Raw Data (21 Boy-Moms/12 Girl-Moms)	Main Effect: Group F(1, 31) = 3.283, p= .080 Main Effect: Session F(4, 31) = 186.83, p< .001* Interaction Effect: Group x Session F(4, 31) = 3.147, p= .081

Figure 37: Estrone Profile: Boy-Moms to Girl-Moms



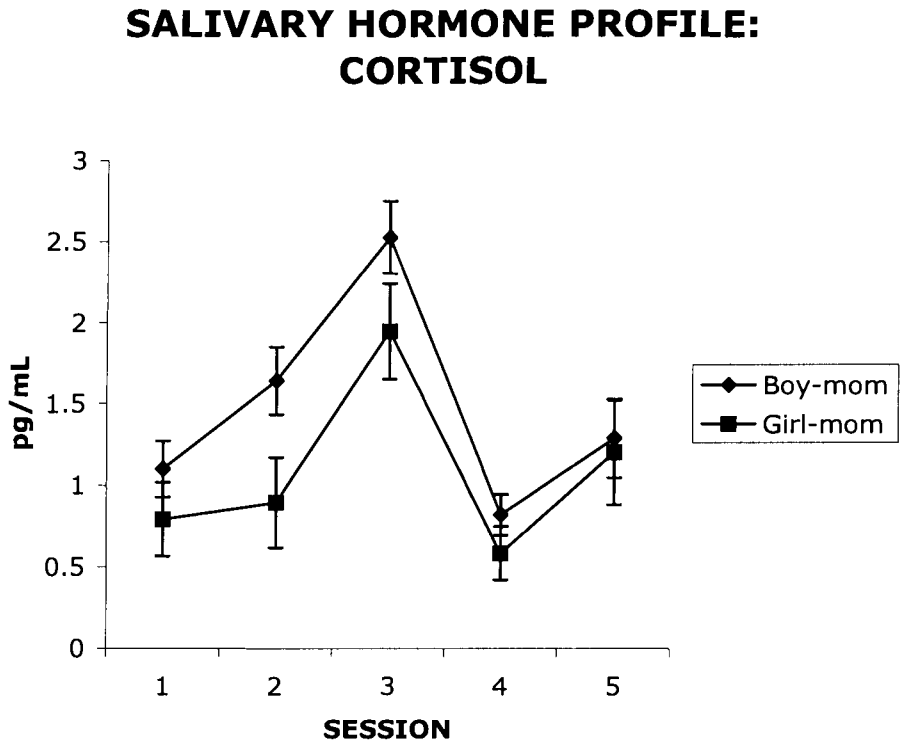
Estrone (E1) Raw Data (21 Boy-Moms/12 Girl-Moms)	Main Effect: Group F(1, 31) = 3.799, p= .060 Main Effect: Session F(4, 31) = 88.970, p< .001* Interaction Effect: Group x Session F(4, 31) = 4.930, p= .019

Figure 38: DHEAs Profile: Boy-Moms to Girl-Moms



DHEAs Raw Data (21 Boy-Moms/12 Girl-Moms)	Main Effect: Group F(1, 31) = .046, p= .832 Main Effect: Session F(4, 31) = 16.036, p< .001* Interaction Effect: Group x Session F(4, 31) = .726, p= .493

Figure 39: Cortisol Profile: Boy-Moms to Girl-Moms



Cortisol Raw Data (21 Boy-Moms/12 Girl-Moms)	Main effect: Group F(1, 31) = .3.712, p= .063 Main Effect: Session F(4, 31) = 16.429, p< .001* Interaction Effect: Group x Session F(4, 31) = .869, p= .480

Possible Relationships Between Dependent Measures and Salivary Hormone Profiles

When analyzed, specific steroid hormones did not reliably or consistently correlate with any of the dependent measures across the five test sessions. This was true for the overall correlations and also true when separate analyses were conducted for both the Boy-Moms and the Girl-Moms. There was one exception to this however, DHEAs consistently showed a positive relationship to MRT scores, with higher salivary DHEAs levels being associated with better MRT scores. This relationship was present from test session one and persisted until approximately session four. By session five the effect was no longer present. When the relationship was broken down and analysed by fetal sex, trends in the data suggest that the Boy-Moms were accounting for the DHEAs and MRT relationship. Table 15 lists the overall and by-group correlations for DHEAs and the Mental Rotation Task.

Table 15: Correlations for Salivary DHEAs Profile and MRT Score

Session	r =	p =
Boy-Moms and Girl-Moms combined:		
1	.484	.001
2	.531	.000
3	.346	.029
4	.353	.027
5	.254	.109
Boy-Moms only:		
1	.655	.000
2	.461	.018
3	.366	.072
4	.590	.002
5	.441	.024
Girl-Moms only:		
1	.215	.460
2	.801	.000
3	.194	.488
4	.020	.946
5	.288	.298

Possible Relationships Between Fetal Sex and Salivary Hormone Profiles

Some tentative trends in the data suggest a possible link between higher steroid levels and a male fetus, namely prenatal progesterone levels during the first ($F(1, 39) = 3.083$, $p = .087$) and second ($F(1, 39) = 5.530$, $p = .024$) trimesters. Higher salivary levels of cortisol during the second ($F(1, 40) = 6.804$, $p = .013$) and third ($F(1, 38) = 3.921$, $p = .055$) trimesters, and preparturition levels of estrone ($F(1, 38) = 5.573$, $p = .023$), but not estradiol ($F(1, 38) = 2.197$, $p = .147$) or estriol ($F(1, 38) = .624$, $p = .435$) were all associated with a male fetus.

Sleep and Mood

As with the salivary hormone results, raw data only was used in the analyses of both the sleep and mood scores.

Mood Measure

When the Profile of Mood States scores were analysed, no group by session interaction ($F(4, 31) = .907$, $p= .458$) or main effect of session ($F(4, 31) = 1.155$, $p= .334$) was observed. In addition, Boy-Mom mood scores did not significantly differ from Girl-Mom mood scores across the five test sessions ($F(1, 31) = .355$, $p= .556$). The Analysis of covariance revealed one significant effect of mood on just one of the dependent measures across the five test sessions, this being the CVLT during test session four. The proportion of variance explained by the POMS on the CVLT accounted for less than one percent of the D.V. variance ($R^2 = .0029$). In light of these negative findings, no further consideration will be given to the impact of mood on the overall Analysis 2 results. Appendix K lists the descriptive statistics for the mood scores across the five test sessions.

Sleep Measures

As with Analysis 1, six sleep measures were obtained from all women in the study at every test session. Sleep descriptors are identical to those used in Analysis 1.

Analysis of Variance

Group by Session Interactions/Main Effect of Group

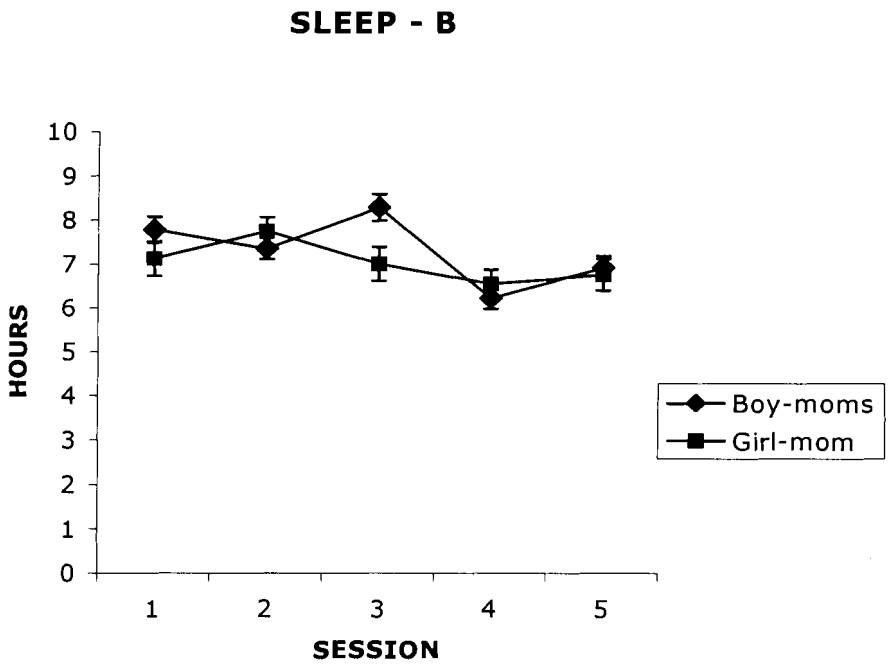
Analysis of variance results revealed no session by group interactions or group main effects for any of the sleep measures.

Main Effect of Session

A clear main effect of session is evident on four sleep measures. These were sleep measures B (average hours of night-time sleep last night), C (is the hours of sleep you obtained last night enough for you?), D (average hours of night-time sleep over the last week), and E (is the sleep you have been getting over the last week enough for you?). No main effect of session was evident for sleep measure F however (Karolinska Sleepiness Scale, current alertness rating), suggesting, as with Analysis 1, that although pregnant women had had less sleep prior to the test session, and had rated themselves as more sleepy, it did not affect their current subjective alertness score. Figure 40 and 41 provide a graphical representation of sleep measures B and D, and figure 42 depicts the by group current alertness rating across the test sessions (sleep F). Notice both groups show a trend for increasing subjective ratings of sleepiness.

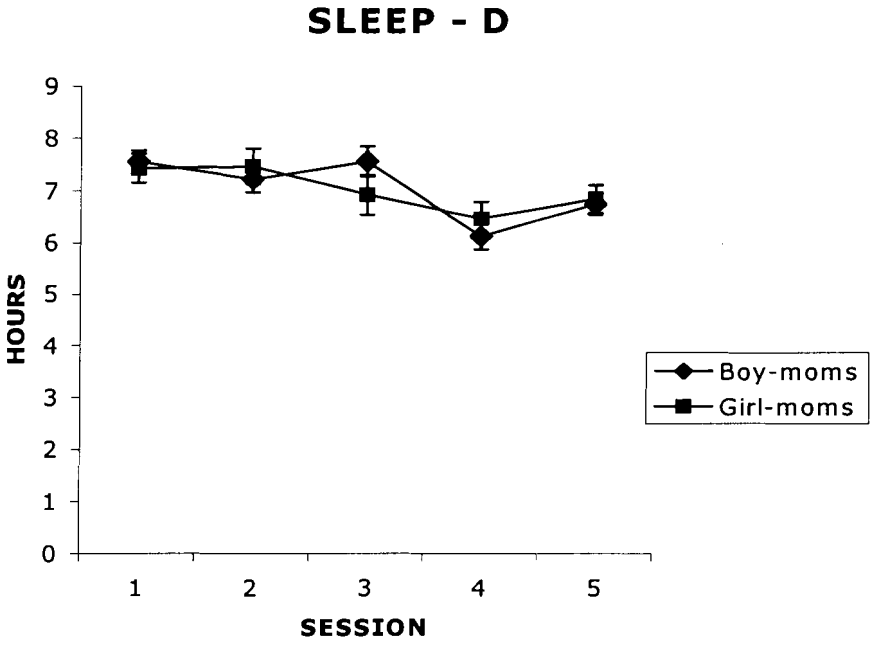
No interaction ($F(4, 31) = .358$, $p= .838$), session ($F(4, 31) = .701$, $p= .592$) or group ($F(1, 31) = 2.245$, $p= .144$) main effects were detected for sleep measure A *(morningingness/eveningness score)*.

Figure 40: Night-time Sleep: Boy-Moms to Girl-Moms



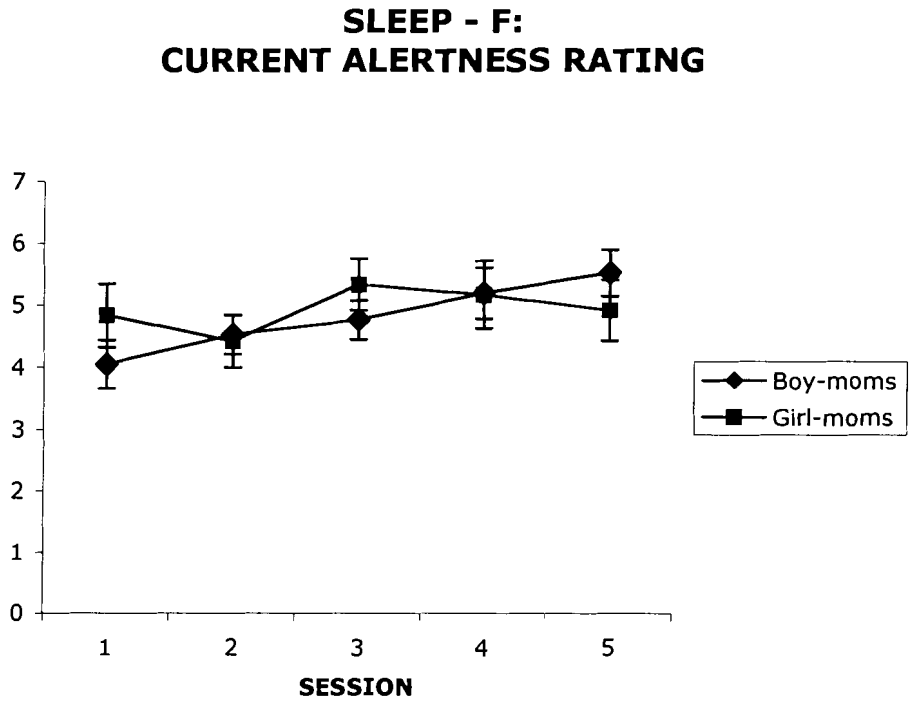
SLEEP – B Hours of sleep last night Raw Data (21 Boy-Moms/12 Girl-Moms)	Main Effect: Group F(1, 31) = .814, p= .374 Main Effect: Session F(4, 31) = 8.677, p< .001* Interaction Effect: Group x Session F(4, 31) = 3.614, p= .008
SLEEP – C Enough for you?	Main Effect: Group F(1, 31) = .004, p= .952 Main Effect: Session F(4, 31) = 7.501, p< .001* Interaction Effect: Group x Session F(4, 31) = 3.042, p= .021

Figure 41: ***Average Hours of Night-time Sleep in Last Week: Boy-Moms to Girl-Moms***



SLEEP – D Average nightly sleep over the last week Raw Data (21 Boy-Moms/12 Girl-Moms)	Main Effect: Group F(1, 31) = .003, p= .955 Main Effect: Session F(4, 31) = 10.309, p< .001* Interaction Effect: Group x Session F(4, 31) = 1.624, p= .183
SLEEP – E Enough for you?	Main Effect: Group F(1, 31) = 454, p= .505 Main Effect: Session F(4, 31) = 6.054, p< .001* Interaction Effect: Group x Session F(4, 31) = 1.425, p= .236

Figure 42: Karolinska Sleepiness Scale: Boy-Moms to Girl-Moms



SLEEP – F Current alertness rating 1 = very alert 9 = very sleepy Raw Data (21 Boy-Moms/12 Girl-Moms)	Main Effect: Group F(1, 31) = .097, p= .757 Main Effect: Session F(4, 31) = 2.323, p= .060 Interaction Effect: Group x Session F(4, 31) = 1.221, p= .305

Post Hoc Comparisons of Sleep Measures

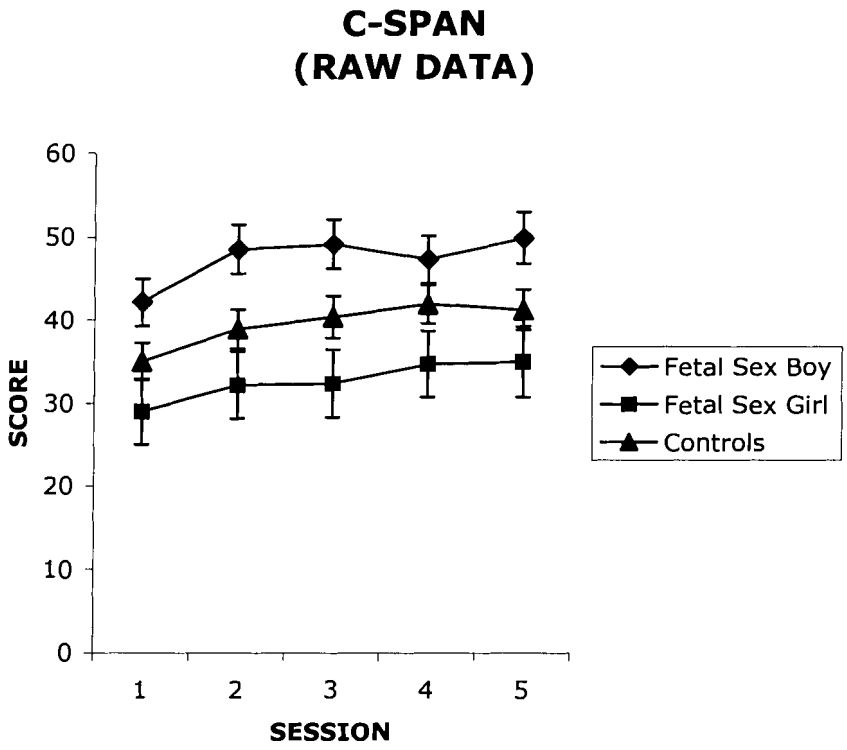
When the six sleep scores were evaluated over the five sessions, their existed no significant difference between Boy-Moms and Girl-Moms on any of these measures. Specifically, women carrying and ultimately delivering boys did not differ from those carrying and delivering girls on; number of hours sleep the night before the test session (SLEEP1B), average nightly sleep over the last week (SLEEP1D), current level of alertness - Karolinska Sleepiness Scale (SLEEP1F) and subjective ratings of quality of recent sleep (SLEEP1C (last night) & SLEEP1E (over the last week)). There were also no differences between these two groups on the subjective ratings of morning-active/evening-active - Morningness/Eveningness Composite Scale (Smith, Reilly & Midkiff, 1989) (SLEEP 1A). Finally, Analysis of covariance indicated none of the seven sleep measures were related to any of the dependent variables. Appendix L provides a summary of all t-test by group comparisons for each of the 30 sleep measures (6 measures x 5 test sessions).

Improvement or Decrement?
Comparing the 'Boy-Moms' and the 'Girl-Moms' to the Control Group

Although not generally attaining significance at the corrected alpha, when data from control women were compared to both Boy-Moms and Girl-Moms a trend emerged on the three tasks that had initially revealed a significant fetal sex difference. Cognitive performance of control women fell somewhere in between that of performance of the Boy-Moms and the Girl-Moms. Boy-Moms however, tended to perform a little better

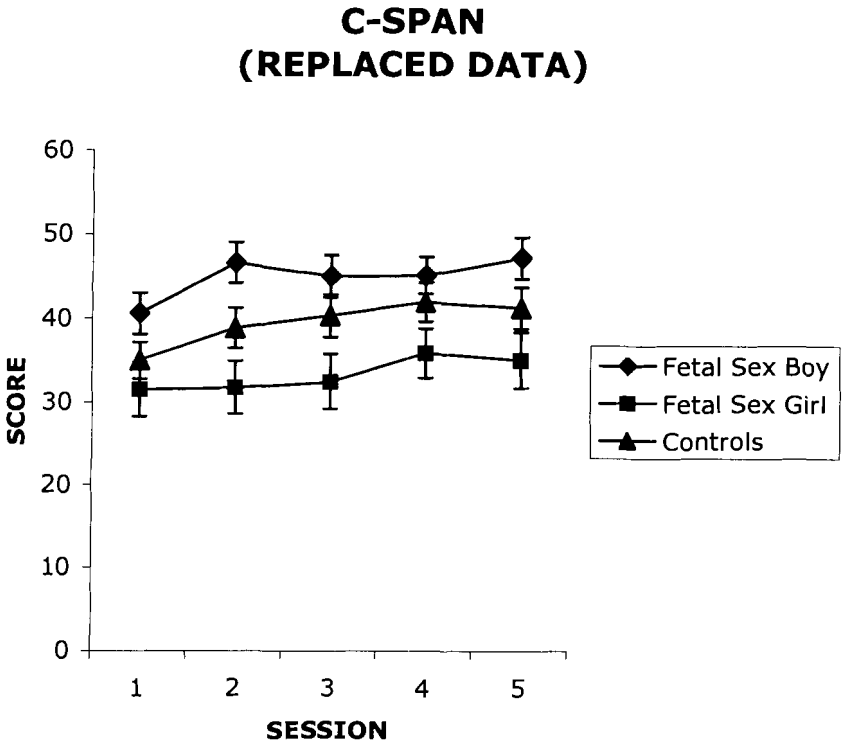
than both Girl-Moms and Controls, while the performance of Girl-Moms was more similar to that of the control women (Figures 43-48). This effect was only identified on the three working memory tasks of the nine-test battery. The span tasks showed the highest correlations of all the dependent measures ($r = .64$, $p < 001$*). This correlation coefficient is consistent with reported values for these two tasks of approximately $r = .60$ (Salthouse & Babcock, 1990). The MRT did not correlate with either the C-Span ($r = .30$, $p = .058$) or the L-Span ($r = .24$, $p = .125$) tasks. However this task does trigger activation of the prefrontal cortex (Duff & Hampson, 2001), a structure previously implicated in tasks related to working memory (see Goldman-Rakic, 1987, for a review).

Figure 43: Boy-Moms and Girl-Moms to Control Women: C-Span (Raw)



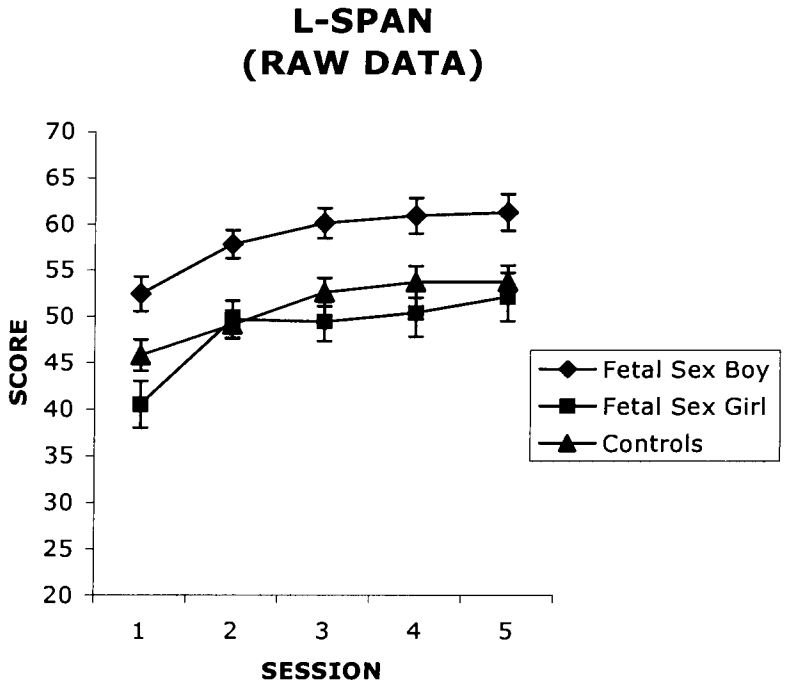
Computation Span "Boy-Moms" to Controls Raw Data 21 "Boy-Moms"/ 35 Controls	Main Effect: Group F(1, 54) = 4.966, p=.030 Main Effect: Session F(4, 54) = 19.896, p< .001* Interaction Effect: Session x Group F(4, 54) = 1.772, p= .137
Computation Span"Girl-Moms" to Controls Raw Data 11 "Girl-Moms" 35 Controls	Main Effect: Group F(1, 44) = 2.817, p= .10 Main Effect: Session F(4, 44) = 10.594, p< .001* Interaction Effect: Session x Group F(4, 44) = .247, p= .904

Figure 44: Boy-Moms and Girl-Moms to Control Women: C-Span (Replaced)



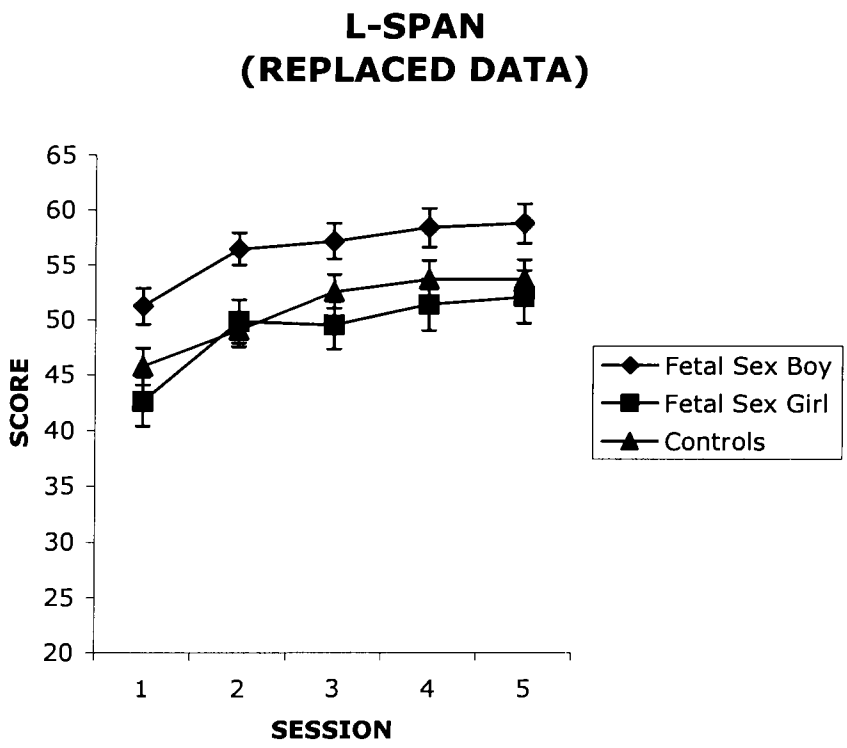
Computation Span "Boy-Moms" to Controls Replaced Data 29 "Boy-Moms"/ 45 Controls	Main Effect: Group F(1, 72) = 4.021, p= .049 Main Effect: Session F(4, 72) = 14.727, p< .001* Interaction Effect: Session x Group F(4, 72) = 1.758, p= .141
Computation Span "Girl-Moms" to Controls Replaced Data 16 "Girl-Moms"/ 45 Controls	Main Effect: Group F(1, 59) = 3.453, p= .068 Main Effect: Session F(4, 59) = 8.927, p< 001* Interaction Effect: Session x Group F(4, 59) = .837, p= .491

Figure 45: Boy-Moms and Girl-Moms to Control Women: L-Span (Raw)



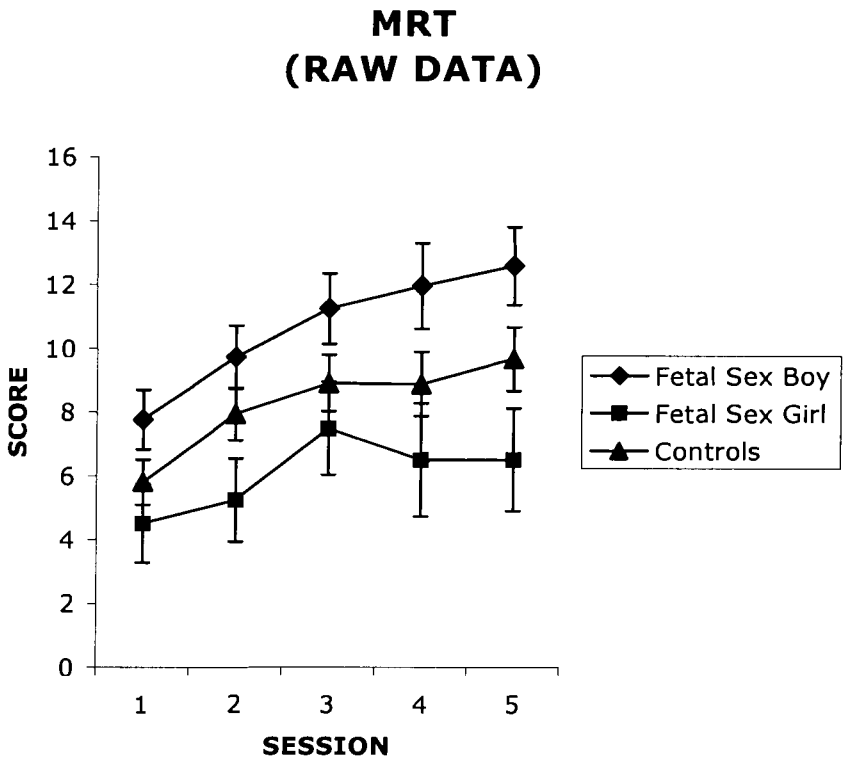
Listening Span "Boy-Moms" to Controls Raw Data 21 "Boy-Moms"/ 35 Controls	Main Effect: Group F(1, 54) = 10.248, p= .002* Main Effect: Session F(4, 54) = 30.033, p< .001* Interaction Effect: Session x Group F(4, 54) = .348, p= .814
Listening Span "Girl-Moms" to Controls Raw Data 12 "Girl-Moms"/ 35 Controls	Main Effect: Group F(1, 45) = .828, p= .368 Main Effect: Session F(4, 45) = 24.020, p< 001* Interaction Effect: Session x Group F(4, 45) = 1.894, p= .127

Figure 46: Boy-Moms and Girl-Moms to Control Women: L-Span (Replaced)



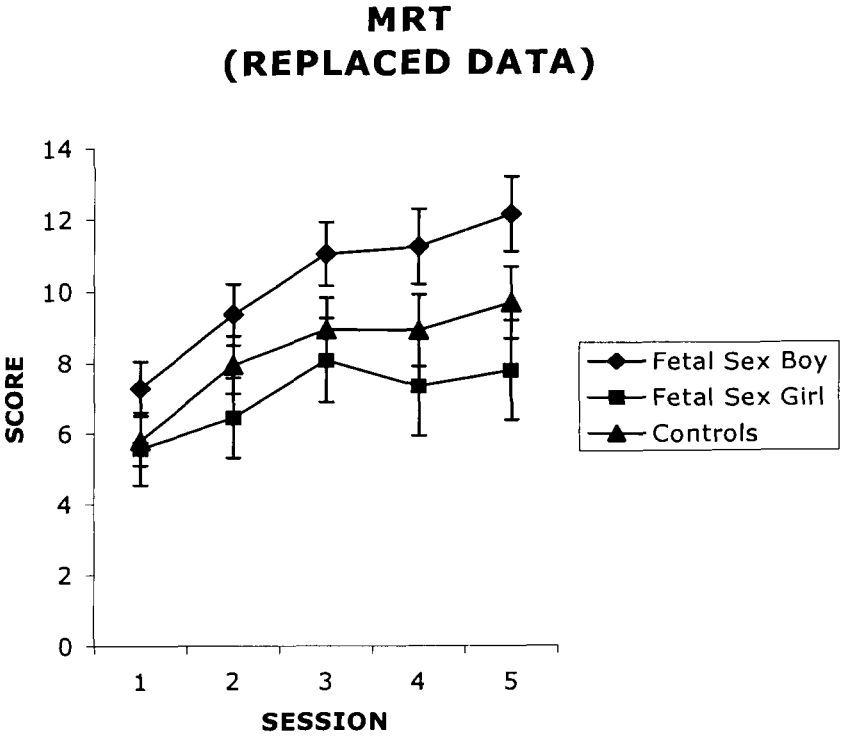
Listening Span "Boy-Moms" to Controls Replaced Data 29 "Boy-Moms"/ 45 Controls	Main Effect: Group F(1, 72) = 6.732, p= .011 Main Effect: Session F(4, 72) = 28.636, p< 001* Interaction Effect: Session x Group F(4, 72) = .800, p= .504
Listening Span "Girl-Moms" to Controls Replaced Data 16"Girl-Moms"/ 45 Controls	Main Effect: Group F(1, 59) = .921, p= .341 Main Effect: Session F(4, 59) = 23.377, p< .001* Interaction Effect: Session x Group F(4, 59) = 1.363, p= .248

Figure 47: Boy-Moms and Girl-Moms to Control Women: MRT (Raw)



Mental Rotation Task "Boy-Moms" to Controls Raw Data 21 "Boy-Moms"/ 35 Controls	Main Effect: Group F(1,54) = 3.730, p= .059 Main Effect: Session F(4, 54) = 21.849, p< .001* Interaction Effect: Session x Group F(4, 54) = .612, p= .647
Mental Rotation Task "Girl-Moms" to Controls Raw Data 12 "Girl-Moms"/ 35 Controls	Main Effect: Group F(1, 45) = 2.354, p= .132 Main Effect: Session F(4, 45) = 7.883, p< .001* Interaction Effect: Session x Group F(4, 45) = .785, p= .536

Figure 48: Boy-Moms and Girl-Moms to Control Women: MRT (Replaced)



Mental Rotation Task "Boy-Moms" to Controls Replaced Data 29 "Boy-Moms"/ 45 Controls	Main Effect: Group F(1, 72) = 1.918, p= .170 Main Effect: Session F(4, 72) = 22.697, p< .001* Interaction Effect: Session x Group F(4, 72) = 1.220, p= .302
Mental Rotation Task "Girl-Moms" to Controls Replaced Data 16"Girl-Moms"/ 45 Controls	Main Effect: Group F(1, 59) = 2.046, p=.158 Main Effect: Session F(4, 59) = 7.017, p< .001* Interaction Effect: Session x Group F(4, 59) = .351, p= .835

ANALYSIS 2: DISCUSSION

Dependent Measures

Women pregnant/delivering daughters showed significantly greater cognitive impairment than women pregnant/delivering sons. This effect was only evident on the three working memory tasks in the test battery namely, the Listening Span, Computation Span and the Shepard-Metzler Mental Rotation Task. Although utilized in other populations (Salthouse & Babcock, 1990), this is the first time the C-Span and L-Span have been used to assess working memory in a sample of pregnant women.

The Boy-Mom advantage was present from the first test and persisted until the final postnatal session. The dependability of this result is strengthened by a number of factors related to the internal validity of the study. Firstly, women were recruited before the sex of their fetuses was known, and most women opted against obtaining this information at the second trimester ultrasound so, at least for the initial three testing sessions, the participants and experimenter were both blind to the experimental condition. Furthermore, the two groups of women did not differ on any of the control measures, mood or sleep scores, making it unlikely that the observed group differences were attributable in any simple way to pre-existing differences between the two groups of mothers. The three tests that exhibited a fetal sex effect unlike other tests in the battery, presented a selective challenge to working memory, the short-term memory system that is employed for the temporary storage and manipulation of information during complex cognitive processing (Baddeley & Hitch, 1973; Baddeley, 2000).

When viewing the graphs of the effects (figures 43 to 48) it is evident that the scores from the control women fall intermediate between the women pregnant/delivering boys and that of the women pregnant/delivering girls. This assortment by sex of the fetus for the women who had originally comprised the experimental group appears to explain the initial non-significant differences seen between this group and the control group on these three tasks in Analysis 1.

Existing research in the area of cognitive change during pregnancy is variable and inconsistent (Buckwalter et al, 1999; Casey, 2000; Crawley, Dennison & Carter, 2003; Keenan et al, 1998; McDowall & Moriarty, 2000; Sharp et al, 1984). If fetal sex selectively affects working memory as shown here, and tasks designed to evaluate working memory are routinely included in some studies of gestation-related cognitive change but not others, mixed findings would result. This would result in a research literature that is peppered with both positive and negative findings, a result completely consistent with this particular area of discovery.

Failures of working memory have previously been identified as the subjective experience of forgetfulness or absentmindedness (Reason, 1982). It is not unreasonable to expect this same interpretation of working memory to apply to pregnant woman. In light of this, the reported results suggest some interesting interpretations for the experience of gestation on the subjective accounts of working memory during gestation. Let us assume a woman was pregnant with a son or a daughter but her daily task load did not routinely tax her working memory, then she might report minimal forgetfulness during her pregnancy. The woman pregnant with a son whose schedule caused her to encounter tasks that challenged working memory on a regular basis might also report minimal decrements. However, the woman who may notice and report

significant forgetfulness would be the woman pregnant with a daughter whose daily tasks and responsibilities challenged her working memory. If the findings reported here accurately mimic real-world settings, then it would be these women who would report being forgetful and absentminded. This suggests a clear interaction between fetal sex and challenges to working memory.

It is possible that the effect of fetal sex seen on the C-Span, L-Span and MRT may be both related to the type of task administered (i.e. working memory) as well as task difficulty. Based on numerous anecdotal reports from both pregnant and control women participating in the study, these three tasks were the least liked in the battery because they were perceived to be very hard. Indeed, on test sessions beyond the first, many women readily remembered these tasks and repeatedly reported with considerable disdain how difficult they found them to be. Although statistical quantification of task difficulty was not evaluated in this study, future research could address this question. If task difficulty was found to interact with fetal sex, it might provide another explanation as to why some women report little or no cognitive impairment in pregnancy and others note considerable decrements (see Crawley, Dennison & Carter, 2003 for a review).

In beginning to interpret the possible causal mechanisms of the fetal sex difference, two overarching explanations are possible. The first would be that some form of diffusible factor of fetal origin is infiltrating maternal physiology and altering maternal cognitive performance. An alternate explanation is related to the mother, where some component of maternal physiology, either pre-existing or specific to gestation is causing or linked to this result. Put more simply, is it a fetal effect or a maternal effect?

Possible Mechanisms: It's the Presence of the Fetus

Given the wealth of literature demonstrating that sex steroids affect cognitive functions in adults (Kimura, 2002) it is tempting to attribute the present results to fetal steroids crossing the placenta and affecting the mother. As mentioned above, the notion that the conceptus may affect the maternal nervous system via placental-derived steroid hormones is not a new idea, and it is similarly plausible that steroids originating from the fetal gonads might be able to alter maternal cognitive processing in a similar way. However, several considerations temper this suggestion. First, the observed difference between Boy-Moms and Girl-Moms is evident even early in gestation (around 12 weeks since last menstrual period, or approximately 10 weeks of fetal age; and although gonadal differentiation has occurred by this point, testosterone secretion by male fetuses doesn't peak until 15-18 weeks (the gonads of female fetuses are comparatively quiescent). Furthermore, radioimmunoassay studies of maternal serum have detected little (Meulenberg & Hofman, 1991) or no change (Glass & Klein, 1981) in free or total testosterone attributable to fetal sex (but see Gitau, Adams, Fisk & Glover, 2005). And in any case, it is not clear by what mechanism fetal sex steroids could account for maternal cognitive differences that persist well beyond parturition; presumably, any fetal steroids in the maternal circulation would have been cleared well before the final test session. Yet whatever the proximate mechanisms may be, convergent evidence indicates that fetal sex can indeed produce long-lasting changes in maternal physiology. For example, there appears to be a birth order effect on sexual orientation (Blanchard & Bogaert, 1996), in which the likelihood of homosexuality in men is reliably correlated with the number of older brothers (but not older sisters) that individuals have. Somehow --

perhaps through progressive maternal immune responses to Y-linked histocompatibility antigens -- mothers' bodies record the sex of fetuses that they have carried. It is possible that a similar mechanism accounts for the durability of the fetal sex-related differences in maternal cognitive acuity.

Some tentative trends in the data suggest a possible link between higher steroid levels and a male fetus, namely prenatal progesterone levels during the first and second trimesters; higher salivary levels of cortisol during the second and third trimesters; and preparturition levels of estrone, but not estradiol or estriol, were all associated with a male fetus. Although largely speculative at this stage, it would be interesting to see if this effect persisted with a significantly bigger n, which would clarify these findings by reducing within-group variability. Others have shown this type of variability is often seen in salivary steroid hormone profiles and appears to be attributed to interlab variability (Rinaldi, et al, 2001) and/or normal individual variation (Bachmann et al, 2002; Shirtcliff et al, 2000; Speroff, Glass & Kase, 1999).

Salivary DHEAs was positively related to MRT scores, an effect that seems to be linked primarily to the Boy-Moms. The potential association between this neurosteroid and spatial performance has not been reported before. Although previously implicated in cognitive function, results to date have been varied and inconclusive (see Dubrovsky (2005) for a review). It has been hypothesised that this variability may be due in part to DHEAs' metabolism into testosterone and/or estradiol (Hirshman et al, 2004). Recall these steroids have been shown to differentially affect performance of spatial and verbal tasks (Kimura, 1999). However, unlike other major steroids, a receptor for DHEAs has not been definitively isolated, and it is currently

unclear if this product has a biological role other than as an androgen precursor (Dubrovsky, 2005; Widstrom & Dillon, 2004).

Memory enhancing effects of DHEAs has been observed in aging mice (Flood & Roberts, 1988), however, research in aging humans has been less conclusive; with some authors identifying improvements (Berr et al, 1996), while others have not (Huppert & Van Niekerk, 2001). Nevertheless, DHEA and DHEAs can be converted to more potent androgens such as testosterone (Nelson, 2000) and perhaps it is via this mechanism that it is capable of affecting maternal cognition. Although in the results reported here testosterone levels did not correlate with MRT scores, in other studies a clear link has been demonstrated between this androgen and improvements in cognitive function (Cherrier et al, 2005; Moffat, Zonderman, Metter, Blackman, Harman & Resnick, 2002).

There is a known fetal sex-related difference in maternal serum human chorionic gonadotropin (hCG) titres: hCG is significantly elevated in women pregnant with female fetuses, compared with women carrying male fetuses (Obiekwe & Chard, 1982). This difference is consistently observed across all three trimesters (Obiekwe & Chard, 1982; Santolaya-Forgas, Meyer, Burton &, Scommegna, 1997) and is evident as early as three weeks post-fertilization (Yaron et al, 2002). Furthermore, hCG readily traverses the blood-brain barrier and interacts with neuronal recognition sites in limbic structures such as the hippocampus (Lei, Rao, Kornyei, Licht & Hiatt, 1993). Given that the hippocampus is widely implicated in memory performance, it seems plausible that modulations of maternal hCG levels may contribute to the effect reported here.

The ratio of male to female births in analysis 1 suggests some interesting interpretations. Once fetal sexes were revealed (at parturition), it was found that almost

twice as many participants had been carrying male fetuses (n=29) as had been carrying female fetuses (n=16). As previously discussed, although not a significant deviation from the expected 50%:50% ratio, it could however suggest the possibility that a subgroup of women carrying female fetuses selected themselves out of the study. This may be related to the elevated hCG profile observed in women pregnant with female fetuses; high levels of hCG are associated with hyperemesis gravidarum (severe "morning sickness") (Kauppila, Huhtaniemi & Ylikorkala, 1979) and women suffering from this phenomenon during pregnancy disproportionately deliver daughters (Askling, Erlandsson, Kaijser, Akre & Ekbom, 1999). If this is the case, then women who chose to exclude themselves from the study may have been those that were most affected by hCG, either by direct action on neural substrates or as a consequence of pregnancy sickness, in which case the present data could be a conservative estimate of the variability in maternal cognition associated with fetal sex.

Possible Mechanisms: It's Something About Mom

Instead of taking the view that this effect is exclusively linked to fetal effects, an alternative perspective would be to relate this finding to a pre-existing condition in the mother that is linked *both* to her cognitive profile and her propensity to deliver sons or daughters. Trivers and Willard (1973) have argued that reproductive success might be enhanced in parents who could manipulate the sex of their offspring in response to availability of resources necessary for survival. They suggested it would be advantageous, under certain conditions for healthy females with good access to these resources to produce male offspring, and females in poor condition with suboptimal

access to deliver female offspring. Trivers and Willard (1973) made this assumption based on their conclusion that the survival of male offspring is most strongly influenced by maternal care. A number of subsequent publications have both supported (Clutton-Brock, Albon & Guinness 1984; Teitelbaum & Mantel, 1971) and refuted this hypothesis (Brown, 2001; Leimar, 1996; Myers 1978). However, one attempt to reconcile the divergent data, which is relevant here, is the maternal dominance hypothesis (Grant, 2003). Under this theory the link between maternal condition and sex ratio may be spurious primarily because good condition could simply be an indicator of relative dominance; where the more dominant females generally have priority access to resources. Instead, according to this theory, the key variable here would be the biological underpinnings of dominance, namely androgens, specifically testosterone.

Research with spotted hyenas *(Crocuta crocuta)* is consistent with the suggestion that testosterone may be positively related to dominance. In this species top-ranking individuals of both sexes have been shown to exhibit high serum androgen concentrations (Frank, Davidson & Smith, 1985;Yalcinkaya et al, 1993). Indeed, the primary tenant of the recently proposed "challenge hypothesis" states increases in testosterone levels in male animals during the breeding season is directly proportional to the extent of intrasexual competition for mates or resources experienced by that individual (Wingfield, Hegner, Duffy Jr, & Ball, 1990). Although research is less clear in females of the species (Davis & Marler, 2003), this effect has been observed in higher primates (Marshall & Hohmann, 2005). In women, serum and salivary testosterone levels have been shown to be positively correlated with social status. Professional, managerial and technical workers have higher levels than clerical workers and

housewives (Purifoy & Koopmans, 1979), and levels are higher in female attorneys than they are in female teachers and nurses (Schindler, 1979).

While recognizing the basic function of X- and Y- chromosome-bearing spermatozoa and its primary determination of fetal sex, the maternal dominance hypotheses proposes an additional component to fertilization by suggesting some kind of maternal discriminatory role. Although no clear proximate mechanism is given, under this explanation, the mother could selectively advantage either an X- or Y-spermatozoon, depending on which sex offspring she is at that time and place more suited to raise. Because testosterone levels have been shown to respond to environmental influences (Booth, Shelley, Mazur, Tharp & Kittok, 1989; Mazur & Booth, 1998; Rose, Holaday & Bernstein, 1971; Gray 1992; Kemper, 1990), circulating levels of this steroid could provide a physiological indicator at conception of which sex would be more advantaged.

Testosterone, like other steroid hormones has also been linked to improved cognitive function in women. In the past this finding has mostly been attributed to the effects of estrogen (Hampson & Kimura, 1988; Kampen & Sherwin, 1994; Sherwin, 1988; Smith, McCleary, Murdock, Wilshire, Buckwalter & Bretsky, 1999), however there exists a small unfolding body of research suggesting a link between enhanced cognitive performance and testosterone (Aleman, Bronk, Kessels, Koppeshaar & van Honk, 2004; Celec et al, 2005; Wolf & Kirschbaum, 2002). According to the maternal dominance hypothesis, women with higher testosterone would disproportionately deliver sons, due to ambient conditions surrounding conception and perhaps one consequence of these higher testosterone levels would be enhancements in specific aspects of cognitive function.

A check of this hypothesis in this study would simply be to correlate the obtained salivary testosterone profiles with fetal sex and performance on the three working memory tests in the battery – namely the L-Span, C-Span and MRT. When this analysis was completed there existed no link between these variables however. This failure to find a relationship however does not necessarily negate the explanatory power of the maternal dominance hypothesis for two reasons. First, as outlined earlier, steroid hormone within-group variability tends to be very high for both salivary and serum profiles (Rinaldi et al, 2001). This could serve to inflate the size of the error term and perhaps wash out any potential between group effects; a confound that is generally addressed with a larger sample size than the one seen in this study. Second, commercial assay kits for androgens were generally designed to estimate the much higher levels of testosterone found in men (Davison & Davis, 2003). As the androgen profile of women is approximately $1/10^{th}$ that of a man (Judd, Judd, Lucas & Yen, 1974), the very small quantities found in women often challenge even the most sensitive kits, resulting in the potential for unreliable values at the lower end of the assay spectrum (Bachmann et al, 2002).

Analysis 2: Summary

Women pregnant and delivering sons selectively and consistently outperformed women pregnant and delivering daughters. This effect was only evident on the three working memory tasks included in the battery. On several other cognitive tests the sex of the fetus was unrelated to maternal performance. This result was present across all test sessions, and persisted independent of sleep, mood and biodemographic measures.

Two salivary hormone levels consistently correlated positively with a male pregnancy, however *post hoc* analyses failed to detect a relationship between these hormones and the working memory tasks. MRT scores correlated positively with DHEAs, an effect that appears to be related specifically to the Boy-Moms.

GENERAL DISCUSSION

As briefly outlined in Analysis 2, the finding that fetal sex appears to interact with aspects of maternal cognitive function may be able to explain some of the wide discrepancy in this area of research. In using tasks that reportedly tax similar components of cognition, different researchers have observed dissimilar outcomes (see Brett and Baxendale, 2001 for a review). In the past this discrepancy has been attributed to methodological concerns such as differing sample sizes, expectancy effects and research design limitations (Christensen et al, 1999; Crawley, Dennison & Carter, 2003; Gross & Pattison, 1994; Harris et al, 1996; Jarrahi-Zadeh et al, 1969). However, to date no published study has explored the possibility that the sex of the fetus may differentially affect maternal cognitive performance (but see Vanston & Watson, 2005). This may be related to the general inability thus far to link any fetal-derived diffusible factors such as steroids, to aspects of maternal cognitive function (Buckwalter et al, 1999; Silber et al, 1990); despite the knowledge that many of these sex hormones readily cross the blood-brain barrier, and interact with neural recognition sites in brain regions known to involve cognitive processing (Nelson, 2000).

The effect of fetal sex on working memory as tested by the C-Span, L-Span and MRT persisted right up to and including the final test session. In light of this it is currently unknown for how long the Boy-Mom advantage (or Girl-Mom disadvantage) persists. The interval between the fourth (six weeks postnatal) and the final test session ranged between four and eighteen months but averaged around eight to twelve months. In an attempt to clarify the long term survivability of this phenomenon a follow-up study is needed. Cross-sectional research could readily address this by testing women who had

delivered sons in the last year or so (and were not currently pregnant or nursing) and comparing this result to women who have delivered daughters.

Although the research reported here provides no direct mechanism of how the conceptus is able to modify aspects of maternal cognitive function in a specific sexually dimorphic way, some potential mechanisms are discussed. Human Chorionic Gonadotropin is an excellent candidate for future research in this area. This peptide derived from the conceptus, shows a reliable sex difference from very early in pregnancy (Meyer, Burton &, Scommegna, 1997; Obiekwe & Chard, 1982; Santolaya-Forgas, 1997; Yaron et al, 2002) and studies have already shown it readily binds a common luteinizing hormone receptor in limbic, cortical and hypothalamic (among other) brain structures (Lei et al, 1993). To date one animal study has failed to find a link between this product and spatial memory tasks (Lukacs, Hiatt, Lei & Rao, 1995), however research addressing the relationship between levels of this hormone and working memory in women are yet to be completed.

Like HCG, Progesterone is also a candidate for further research on maternal cognitive function. Older studies have identified a link between this steroid and cognitive performance in the infant. Work conducted in the 1960s and 1970s revealed that pregnancy toxaemia could be reduced in some cases by progesterone supplementation (Dalton, 1962; Dalton, 1976). An important discovery as it had been suggested there existed a link between maternal toxaemia and diminished intelligence in the child of that pregnancy (Baker & Edwards, 1967). This led to some British physicians to prescribe large doses of this steroid to treat early toxaemia symptoms between gestation weeks 16 to 28. Among children whose mothers received a regimen of prophylactic progesterone a noted advancement in development at one year and enhanced

educational attainment at 9-10 years (Dalton, 1968) and 17-20 years (Dalton, 1976) was observed. Consistent with is result was the finding that children suffering from congenital adrenogenital syndrome, a condition where they are exposed to excessive quantities of endogenous progesterone in prenatal life had higher IQ scores (Ehrhardt & Money, 1967).

The cognitive function of the mothers of the "progesterone children" is not known, however, based on the current understanding of steroidal effects (Nelson, 2000), it is not implausible to conclude that progesterone like other sex hormones, is not only capable of organizing the fetal nervous system during prenatal life, but at the same time could exert an activational effect on maternal nervous tissues. It has been shown that this neuroactive steroid (Dubrovsky, 2005) readily traverses the blood-brain barrier and is capable of interacting with specific receptors within limbic and cortical structures (Maggi & Perez, 1985). Although only the most tenuous link was found between progesterone and fetal sex in this study, it would provide a sound basis for subsequent research. Women prescribed transdermal progesterone therapy to boast endogenous levels of this hormone for luteul support of early pregnancy (Kleinstein, 2005) would be an ideal subject pool for this type of research.

Like progesterone, trends in the salivary data suggest cortisol levels also correlate positively with a male fetus. Other than the results reported here, to date there appears to be no observed fetal-sex difference in levels of this hormone when serum levels were evaluated (Haning, Curet, Poole, Boehnlein, Kuzma & Meier, 1989). Higher levels of this steroid have consistently been associated with cognitive impairments, which appear to be mediated by damage to hippocampal structures (Nelson, 2000); an effect that has also been observed neonatally, where higher corticosteroids have been

shown to permanently affect brain morphology, physiology and behaviour (Henry, Kabbaj, Simon, Le Moal & Maccari, 1994).

The results of DHEAs and its relationship to maternal age in Analysis 1 (negative) and MRT scores in Analysis 2 (positive) require further discussion. As reported here, with age comes a decline in pregnancy levels of this steroid. This occurs against a backdrop of already low gestation levels, levels lower than those seen during the ovarian cycle. Both results are consistent with existing research in this area (Peter, Door & Sippell, 1994; Zumoff, Rosenfeld, Strain, Levin & Fukushima, 1980). However, if higher levels of DHEAs were positively correlated with scores on a spatial task, then it would be expected that the control women would also do well on this task. They did not however, no significant relationship emerged for the MRT scores and salivary DHEAs levels in the control group. This was true for both the raw and replaced data sets. Matters are complicated further when it is noted that the relationship between DHEAs and MRT scores are largely linked to the Boy-Moms and not the mothers of girls. Moreover, no fetal sex difference was observed between salivary levels of this hormone. So what might be accounting for this effect? One possible explanation is the existence of an optimal steroid range for this hormone necessary for maximal cognitive performance on a spatial task like the MRT. This effect has already been observed with another androgen, namely testosterone. Gouchie and Kimura (1991) and others (Shute, Pellegrino, Hubert and Reynolds, 1983) have shown that the adult testosterone levels in the low normal range are associated with the best spatial performance. This cannot be the complete explanation however, as DHEAs levels of Boy-Moms and Girl-Moms did not differ here. However the correlations between the MRT scores and the DHEAs levels do suggest this effect is linked to a male fetus and not a female fetus. This

suggests it is something about the male fetus that appears to be linked to DHEAs is conferring the spatial advantage seen in the Boy-Moms. Moreover, it appears to be independent of aromatization effects to testosterone or estrogen, as these hormones did not correlate with any dependent measures let alone the Shepard-Metzler Mental Rotation Task.

It may not be the case that the fetal-sex effect is being caused by a unitary mechanism, i.e. a diffusible factor or a maternal trait. It is possible that the fetal sex effect observed here may be caused by two, or more temporarily discrete mechanisms. Indeed the fetal sex effect on working memory might well be attributed to gestational hormones, however the persistence of this effect into the postnatal period may be due to a different mechanism. If we assume a pregnant woman is given a working memory task to complete that she finds difficult, but she perceives her performance to be good, it may serve as a motivator for her to try harder. Further, with repeated exposures she may perceive improvements in performance, which might also serve to motivate her to continue to work hard on this difficult task. Conversely, if a pregnant women is given a working memory task that she finds difficult, and she perceives her performance to be poor, she may be less motivated to work has hard when completing this task during subsequent exposures. As women received no feedback on their performance on any of the tests used in the cognitive battery, their perceptions were the only performance indicators available to them. If a diffusible factor that differs in type and kind between male and female fetuses is capable of advantaging maternal cognition such that a pregnant woman can perform well on a task that she perceives to be difficult, this effect may still persist postnatally in the absence product. That is to say, differences between the Boy-Moms and the Girl-Moms may in fact be caused by a fetal-derived product,

however the persistence of this into the postnatal period may caused by a different cognitive mechanism, namely volition; where Boy-Moms will try harder because their perceived earlier good performance is motivating subsequent effort on the task. Whereas Girl-Moms may lack this drive to try hard, as there earlier subjective experiences with the task were related to a perception of poor performance.

Beliefs of cognitive impairments in pregnancy are widespread in popular culture such as books (Ellison, 2005) and magazines (Moore, 1997) and lay terms are common for this phenomenon (Brett & Baxendale, 2001). It is therefore plausible that some women may embark on a pregnancy (or participate in a pregnancy and cognition study) with a prior expectation that cognitive deterioration is an inevitable accompaniment to pregnancy. Should this be the case, any study that provides even subtle clues as to purpose of the research could accidentally introduce significant expectancy effects. Moreover, even very careful solicitation of participants for this type of research could inadvertently alert the pregnant woman as to the study's objectives simply by the types of tests included in the battery (i.e. memory tasks). Research design can become even more complicated when the morphological state of human gestation is considered. A double-blind design is often impossible in this regard simply because of the very obvious differences that exist between a gestating woman and the generally more svelte control, at least in the latter stages of pregnancy. Any pregnancy and cognition study runs the risk of bias in the data based on these effects and Analysis 1 is no exception. However, based on the results reported in Analysis 2, it seems that expectancy effects did not interfere with these results in any systematic way. That is to say, it is extremely unlikely that Girl-Moms responded to expectancy effects while Boy-Moms did not. Moreover, the

selectivity of the finding specific only on the working memory tasks also precludes this explanation.

Quite possibly the most significant weakness of the two studies is the absence of prepregnancy baseline data. Although some conclusions have been made based on the assumption that gestation is the causal factor in the reported effects, this research has actually not directly tested this interpretation. As mentioned in the Discussion section of Analysis 2, it is unclear if the reported effects are directly related to fetal effects or a pre-existing feature or trait of the mother. Although the most obvious interfering variables have been addressed such as education, parity and age, it is possible other unconsidered variables may account for this effect. In discussing the results of Analysis 2 some possible mechanisms have been outlined, for example the maternal dominance hypothesis (Grant, 2003), however, subsequent research which tests women prior to pregnancy is necessary to clarify these findings further.

Although the earliest iterations of the research proposal for these studies had included a prepregnancy baseline testing session, it quickly became an impracticality. Despite extensive early advertising, women intending on becoming pregnant were not forthcoming and among those who did volunteer there was no obvious guarantee these women would end up pregnant. This created a problem on two fronts. Wide variability was emerging between the first (prepregnancy, baseline) and second (first trimester) test sessions; and some women were just not conceiving. Recall these women were around thirty years of age, and probably were experiencing reduced fertility. This is a suggestion consistent with current research in this area, which acknowledges as women move through the third decade of life their probability of successfully conceiving declines (Speroff, Glass & Kase, 1999).

To guard against potential type I errors a Bonferroni correction was used in Analysis 1 and Analysis 2. This correction divides the test-wise significance level (in this case 0.05) by the number of tests administered (Bonferonni, 1936). This resulted in the significance level being set at 0.005. In spite of its simplicity, the Bonferroni correction has attracted some criticism as an ultra conservative test. By controlling the group-wise error rate, each individual test is held to an unreasonably high standard. This increases the probability of a Type II error, and makes it more likely that legitimately significant results will fail to be detected (Benjamini & Hochberg, 1995; Hochberg, 1988; Holm, 1979; Hommel, 1988). Given the use of this type of correction in Analysis 1 and 2, their remains the possibility of a type two error on some of the dependent measures. The failure of the MRT to achieve significance at .005 may be due to the use of this very conservative correction. In addition, it is for this reason some non-significant (at .005) data trends are on occasion discussed at length.

Prior to beginning this longitudinal study a power analysis was conducted to estimate effect sizes and establish the necessary sample size. When evaluating the tests used in previous studies to generate the power analysis, it was clear that the methodology used in previous research on gestation-related cognitive change was extremely variable and inconsistent (see Brett & Baxendale (2001) for a review). In some cases authors used tests that showed an effect in some studies (Brindle et al, 1991), while in others no effect was detected (McDowall & Moriarty, 2000). In addition, some tests were not used in a consistent fashion across studies (Brindle et al, 1991; Janes et al, 1999) or tests used were poorly described or extremely obscure making them impossible to trace (Jarrahi-Zadeh et al, 1969). Sample sizes suffered similar problems, with unclear reporting of final numbers and attrition rates that accounted for

more than 80% of the original n (Casey, 2000; Eidelman et al, 1993; Keenan et al, 1998; Schneider, 1989). In one study extremely heterogeneous experimental and control groups included not only normal pregnancies, but also high-risk pregnancies across all gestation phases (Eidelman et al, 1993). In light of this, although a power analysis was feasible, it would have generated an effect size that would have potentially been very inaccurate. Because of this, the power analysis was based on previous work conducted evaluating cognitive change across the menstrual cycle. In this area of research experimental and control groups are more homogenous and studies use similar tests and administer them in a more consistent fashion (Hampson, 1990a; Hampson, 1990b; Hampson & Kimura, 1988). Based on these studies, a power analysis estimated a medium effect size with an n of approximately 50 women per group. However, this effect size and the sample size assumed the current study was a single session design and not a longitudinal study. In light of this the estimate of power may have been less predictive across the five test sessions. As it turns out, power was not a concern and effect sizes for the three tests ranged from medium (for the MRT) to large (for the L-Span).

Finally, attrition rates have always been a source of confounds in longitudinal research with some rates as high as 50% (Pedhazur & Pedhazur-Schmelkin, 1991). Problems are compounded when individuals who drop out are somehow different from those who remain in the study (Cozby, 2001). For this reason, attrition has always been a major problem for longitudinal research. The attrition rates for Analysis 1 and Analysis 2 was approximately 10%; A rate that is generally considered to be quite low in this type of research (Pedhazur & Pedhazur-Schmelkin, 1991).

My candle burns at both ends;
It will not last the night;
But ah, my foes, and oh my friends –
It gives a lovely light!

Edna St. Vincent Millay (1920)
A Few Figs fromThistles

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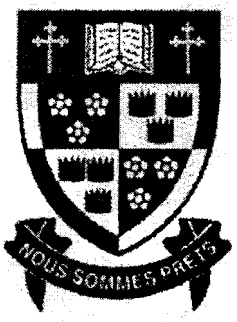
APPENDICES

APPENDIX A: ADVERTISMENT FOR CONTROL PARTICIPANTS

Now Let Me Think...



The Behavioural Neuroendocrinology Lab in the Dept. of Psychology at Simon Fraser University is conducting a study to evaluate how hormones affect thought processes.

We welcome your participation in our study if you are a woman between the age of 22 and 42 years and are currently not using oral contraceptives.

Your involvement would include five one-hour test sessions conducted approximately every three months. Your complete anonymity is assured

If you would like to participate, or require additional information, please leave a voice message on the following ***confidential*** *voice mail.*

604-450-7171

This study has been approved by the SFU Research Ethics Review Committee.

APPENDIX B: ADVERTISEMENT FOR EXPERIMENTAL PARTICIPANTS

DOES PREGNANCY CHANGE THE WAY YOU THINK?

The Behavioural Neuroendocrinology Lab in the Dept. of Psychology at Simon Fraser University is conducting a study to evaluate the effects of pregnancy and parenthood on general cognitive function.

We are interested in testing women throughout their pregnancy and into the postnatal period. We welcome your participation in our study if you are either intending on becoming pregnant in the next three months, or are within the first twelve weeks of pregnancy.

Your involvement would include five one-hour test sessions conducted across your pregnancy and during the postnatal period. With your permission, to minimize inconvenience, test sessions would be completed in your home at a time suitable to you. Your complete anonymity is assured.

If you would like to participate, or require additional information, please leave a voice message on the following confidential voice mail.

(604) 450 7171

Should you require any additional information about our research please call 450-7171.

This study has been approved by the SFU Research Ethics Review Committee

Primary Researcher:
Claire Vanston B.A. (Hons.), M.Sc.
Department of Psychology, SFU
Ph: (604) 291 3354

Project Director:
Dr. Neil Watson Ph.D.
Department of Psychology, SFU
Ph: (604) 291-3354

APPENDIX C: ANCOVA (ANALYSIS 1)

Test	Raw Data (33 exptal, 35 control)	Replaced Data (45 exptal, 45 control)
Digit Symbol Coding	Main Effect: Group F(1, 52) = .498, p= .484 Main Effect: Session F(4, 52) = 1.579, p= .181 Interaction Effect: Group x Session F(4, 52) = .303, p= .876	Main Effect: Group F(1, 74) = .000, p= .995 Main Effect: Session F(4, 74) = .460, p= .758 Interaction Effect: Group x Session F(4, 74) = .489, p= .736
Symbol Search	Main Effect: Group F(1, 52) = .051, p= .822 Main Effect: Session F(4, 52) = .979, p= .420 Interaction Effect: Group x Session F(4, 52) = 1.262, p= .286	Main Effect: Group F(1, 74) = .910, p= .343 Main Effect: Session F(4, 74) = 2.715, p= .030 Interaction Effect: Group x Session F(4, 74) = 1.787, p= .131
CVLT	Main Effect: Group F(1, 52) = 3.826, p= .056 Main Effect: Session F(4, 52) = 2.043, p= .090 Interaction Effect: Session x Group F(4, 52) = 1.442, p= .221	Main Effect: Group F(1, 74) = 1.884, p= .174 Main Effect: Session F(4, 74) = .793, p= .531 Interaction Effect: Session x Group F(4, 74) = 1.071, p= .371
Silverman Eals Obj. Location	Main Effect: Group F(1, 52) = .042, p= .838 Main Effect: Session F(4, 52) = 1.283, p= .278 Interaction Effect: Session x Group F(4, 52) = .494, p= .740	Main Effect: Group F(1, 74) = .098, p= .755 Main Effect: Session F(4, 74) = 1.567, p= .183 Interaction Effect: Session x Group F(4, 74) = .191, p= .943

Purdue Pegboard (Dominant Hand)	Main Effect: Group F(1, 52) = .658, p= .421 Main Effect: Session F(4, 52) = .464, p= .762 Interaction Effect: Session x Group F(4, 52) = .699, p= .593	Main Effect: Group F(1, 74) = 1.517, p= .222 Main Effect: Session F(4, 74) = .675, p= .610 Interaction Effect: Session x Group F(4, 74) = .517, p= .723
Purdue Pegboard (Non-Dominant Hand)	Main Effect: Group F(1, 52) = 5.316, p= .463 Main Effect: Session F(4, 52) = 1.259, p= .287 Interaction Effect: Session x Group F(4, 52) = 2.335, p= .057	Main Effect: Group F(1, 74) = 2.156, p= .146 Main Effect: Session F(4, 74) = .930, p= .447 Interaction Effect: Session x Group F(4, 74) = 1.673, p= .156
Mental Rotation Task	Main Effect: Group F(1, 52) = .004, p= .951 Main Effect: Session F(4, 52) = 2.653, p= .034 Interaction Effect: Session x Group F(4, 52) = 1.033, p= .391 Covariate: Cattell **F(4, 52) = 11.557, p< .001* (R^2 = 0.04)**	Main Effect: Group F(1, 74) = 1.833, p= .180 Main Effect: Session F(4, 74) = .954, p= .433 Interaction Effect: Session x Group F(4, 74) = 1.200, p= .311 Covariate: Cattell **F(4, 74) = 20.686, p< .001***
Computation Span	Main Effect: Group F(1, 51) = .260, p= .612 Main Effect: Session F(4, 51) = .728, p= .574 Interaction Effect: Session x Group F(4, 51) = .831, p= .507	Main Effect: GroupF(1, 74) = .034, p= .855 Main Effect: Session F(4, 74) = 1.573, p= .181 Interaction Effect: Session x Group F(4, 74) = .882, p= .475

Listening Span	Main Effect: Group F(1, 52) = 355, p= .554 Main Effect: Session F(4, 52) = 1.062, p= .377 Interaction Effect: Session x Group F(4, 52) = 1.966, p= .101 Covariate: Vocab Test **F(4, 52) = 12.482, p< .001*** **(R^2 = 0.02)**	Main Effect: Group F(1, 74) = .144, p= .705 Main Effect: Session F(4, 74) = 1.503, p= .203 Interaction Effect: Session x Group F(4, 74) = 1.671, p= .158 Covariate: Vocab Test **F(4, 74) = 12.256, p= .001***

APPENDIX D: DESCRIPTIVE STATISTICS OUTPUT OF DEPENDENT VARIABLES (ANALYSIS 1)

DIGIT SYMBOL (RAW DATA)

	SESSION 1			SESSION 2			SESSION 3			SESSION 4			SESSION 5		
GROUP	Exptal	Control	Total	Exptal	Control	Total	Exptal	Control	Total	Exptal	Control	Total	Exptal	Control	Total
Mean	84.1	80.7	82.4	89.8	84.0	86.8	89.7	85.0	87.3	92.8	88.0	90.3	94.3	89.3	91.8
Std Dev.	13.8	12.0	12.9	12.9	13.5	13.4	13.8	14.8	14.4	16.2	12.3	14.4	13.8	14.0	14.0
N	33.0	35.0	68.0	33.0	35.0	68.0	33.0	35.0	68.0	33.0	35.0	68.0	33.0	35.0	68.0

DIGIT SYMBOL (REPLACED DATA)

	SESSION 1			SESSION 2			SESSION 3			SESSION 4			SESSION 5		
GROUP	Exptal	Control	Total	Exptal	Control	Total	Exptal	Control	Total	Exptal	Control	Total	Exptal	Control	Total
Mean	84.9	82.2	83.6	89.0	85.4	87.2	88.3	87.1	87.7	92.0	89.0	90.5	93.0	89.7	91.4
Std. Dev.	13.3	13.9	13.6	13.0	13.8	13.4	12.3	15.3	13.8	14.2	11.4	12.9	12.3	12.4	12.4
N	45.0	45.0	90.0	45.0	45.0	90.0	45.0	45.0	90.0	45.0	45.0	90.0	45.0	45.0	90.0

SYMBOL SEARCH (RAW DATA)

	SESSION 1			SESSION 2			SESSION 3			SESSION 4			SESSION 5		
GROUP	Exptal	Control	Total	Exptal	Control	Total	Exptal	Control	Total	Exptal	Control	Total	Exptal	Control	Total
Mean	35.9	35.0	35.4	37.7	37.8	37.8	39.6	39.1	39.4	41.3	40.6	40.9	41.7	40.2	40.9
Std. Dev.	5.9	8.0	7.0	6.9	7.2	7.0	7.3	6.8	7.0	6.4	7.5	7.0	6.6	6.5	6.5
N	33.0	35.0	68.0	33.0	35.0	68.0	33.0	35.0	68.0	33.0	35.0	68.0	33.0	35.0	68.0

SYMBOL SEARCH (REPLACED DATA)

	SESSION 1			SESSION 2			SESSION 3			SESSION 4			SESSION 5		
GROUP	Exptal	Control	Total	Exptal	Control	Total	Exptal	Control	Total	Exptal	Control	Total	Exptal	Control	Total
Mean	36.5	35.8	36.1	38.0	38.9	38.4	39.4	39.6	39.5	40.7	40.5	40.6	41.4	40.3	40.8
Std. Dev.	6.0	8.2	7.2	7.1	7.5	7.3	6.4	6.7	6.5	6.0	6.9	6.4	6.1	5.7	5.9
N	45.0	45.0	90.0	45.0	45.0	90.0	45.0	45.0	90.0	45.0	45.0	90.0	45.0	45.0	90.0

C-SPAN (RAW DATA)

	SESSION 1			SESSION 2			SESSION 3			SESSION 4			SESSION 5		
GROUP	Exptal	Control	Total	Exptal	Control	Total	Exptal	Control	Total	Exptal	Control	Total	Exptal	Control	Total
Mean	37.6	35.0	36.3	42.9	38.9	40.8	43.4	40.3	41.8	43.0	41.9	42.4	44.8	41.3	42.9
Std. Dev.	14.4	11.6	13.0	15.4	12.4	13.9	15.6	14.1	14.8	14.3	12.8	13.5	15.6	13.2	14.4
N	32.0	35.0	67.0	32.0	35.0	67.0	32.0	35.0	67.0	32.0	35.0	67.0	32.0	35.0	67.0

C-SPAN (REPLACED DATA)

	SESSION 1			SESSION 2			SESSION 3			SESSION 4			SESSION 5		
GROUP	Exptal	Control	Total	Exptal	Control	Total	Exptal	Control	Total	Exptal	Control	Total	Exptal	Control	Total
Mean	37.3	35.2	36.3	41.3	38.1	39.7	40.5	39.7	40.1	41.8	41.2	41.5	42.9	41.5	42.2
Std. Dev.	13.7	11.9	12.8	14.6	11.8	13.3	14.5	12.9	13.7	12.4	12.2	12.3	14.4	11.6	13.0
N	45.0	45.0	90.0	45.0	45.0	90.0	45.0	45.0	90.0	45.0	45.0	90.0	45.0	45.0	90.0

L-SPAN (RAW DATA)

	SESSION 1			SESSION 2			SESSION 3			SESSION 4			SESSION 5		
GROUP	Exptal	Control	Total	Exptal	Control	Total	Exptal	Control	Total	Exptal	Control	Total	Exptal	Control	Total
Mean	48.1	45.8	46.9	54.8	49.1	51.9	56.2	52.6	54.3	57.0	53.7	55.3	57.9	53.7	55.8
Std. Dev.	10.3	9.8	10.0	8.0	9.8	9.4	9.0	9.2	9.2	10.1	10.2	10.2	9.9	10.8	10.5
N	33.0	35.0	68.0	33.0	35.0	68.0	33.0	35.0	68.0	33.0	35.0	68.0	33.0	35.0	68.0

L-SPAN (REPLACED DATA)

	SESSION 1			SESSION 2			SESSION 3			SESSION 4			SESSION 5		
GROUP	Exptal	Control	Total	Exptal	Control	Total	Exptal	Control	Total	Exptal	Control	Total	Exptal	Control	Total
Mean	48.2	46.5	47.3	54.1	49.5	51.8	54.4	52.7	53.6	55.9	53.7	54.8	56.4	53.9	55.2
Std. Dev.	9.7	9.8	9.7	8.4	9.4	9.2	9.3	8.4	8.9	9.9	9.3	9.6	10.0	9.5	9.7
N	45.0	45.0	90.0	45.0	45.0	90.0	45.0	45.0	90.0	45.0	45.0	90.0	45.0	45.0	90.0

PURDUE - DOMINANT HAND (RAW DATA)

	SESSION 1			SESSION 2			SESSION 3			SESSION 4			SESSION 5		
GROUP	pregnant	Control	Total	Exptal	Control	Total	Exptal	Control	Total	Exptal	Control	Total	Exptal	Control	Total
Mean	17.4	16.9	17.1	17.6	17.6	17.6	17.7	17.5	17.6	18.1	17.7	17.9	18.1	17.7	17.9
Std. Dev.	1.8	1.7	1.8	1.6	1.7	1.6	1.9	1.6	1.8	1.6	1.7	1.6	1.6	1.8	1.7
N	33.0	35.0	68.0	33.0	35.0	68.0	33.0	35.0	68.0	33.0	35.0	68.0	33.0	35.0	68.0

PURDUE - DOMINANT HAND (REPLACED DATA)

	SESSION 1			SESSION 2			SESSION 3			SESSION 4			SESSION 5		
GROUP	Exptal	Control	Total	Exptal	Control	Total	Exptal	Control	Total	Exptal	Control	Total	Exptal	Control	Total
Mean	17.4	16.9	17.1	17.5	17.6	17.5	17.5	17.5	17.5	18.0	17.8	17.9	18.1	17.7	17.9
Std. Dev.	1.7	1.6	1.7	1.7	1.6	1.6	1.8	1.4	1.6	1.5	1.5	1.5	1.6	1.6	1.6
N	45.0	45.0	90.0	45.0	45.0	90.0	45.0	45.0	90.0	45.0	45.0	90.0	45.0	45.0	90.0

PURDUE - NON-DOMINANT HAND (RAW DATA)

	SESSION 1			SESSION 2			SESSION 3			SESSION 4			SESSION 5		
GROUP	Exptal	Control	Total	Exptal	Control	Total	Exptal	Control	Total	Exptal	Control	Total	Exptal	Control	Total
Mean	16.4	15.8	16.1	16.7	15.8	16.2	16.6	16.0	16.3	17.0	16.0	16.5	17.0	16.2	16.6
Std. Dev.	1.6	1.6	1.6	1.5	1.7	1.6	1.6	1.6	1.7	1.6	1.8	1.7	1.5	1.7	1.6
N	33.0	35.0	68.0	33.0	35.0	68.0	33.0	35.0	68.0	33.0	35.0	68.0	33.0	35.0	68.0

PURDUE - NON-DOMINANT HAND (REPLACED DATA)

	SESSION 1			SESSION 2			SESSION 3			SESSION 4			SESSION 5		
GROUP	Exptal	Control	Total	Exptal	Control	Total	Exptal	Control	Total	Exptal	Control	Total	Exptal	Control	Total
Mean	16.2	15.7	15.9	16.6	16.0	16.3	16.4	16.1	16.3	16.9	16.1	16.5	16.7	16.3	16.5
Std. Dev.	1.4	1.5	1.5	1.5	1.6	1.6	1.6	1.5	1.6	1.6	1.6	1.6	1.5	1.5	1.5
N	45.0	45.0	90.0	45.0	45.0	90.0	45.0	45.0	90.0	45.0	45.0	90.0	45.0	45.0	90.0

MRT (RAW DATA)

	SESSION 1			SESSION 2			SESSION 3			SESSION 4			SESSION 5		
GROUP	Exptal	Control	Total	Exptal	Control	Total	Exptal	Control	Total	Exptal	Control	Total	Exptal	Control	Total
Mean	6.6	5.8	6.2	8.1	7.9	8.0	9.9	8.9	9.4	10.0	8.9	9.4	10.4	9.7	10.0
Std. Dev.	4.5	3.9	4.2	5.0	4.7	4.8	5.3	5.2	5.2	6.6	5.2	5.9	6.2	5.6	5.9
N	33.0	35.0	68.0	33.0	35.0	68.0	33.0	35.0	68.0	33.0	35.0	68.0	33.0	35.0	68.0

MRT (REPLACED DATA)

	SESSION 1			SESSION 2			SESSION 3			SESSION 4			SESSION 5		
GROUP	Exptal	Control	Total	Exptal	Control	Total	Exptal	Control	Total	Exptal	Control	Total	Exptal	Control	Total
Mean	6.7	6.5	6.6	8.3	8.7	8.5	10.0	9.6	9.8	9.8	9.3	9.6	10.6	9.8	10.2
Std. Dev.	4.2	4.3	4.2	4.7	5.2	5.0	4.9	5.4	5.1	5.9	5.0	5.4	5.9	4.9	5.4
N	45.0	45.0	90.0	45.0	45.0	90.0	45.0	45.0	90.0	45.0	45.0	90.0	45.0	45.0	90.0

SILVERMAN EALS (RAW DATA)

	SESSION 1			SESSION 2			SESSION 3			SESSION 4			SESSION 5		
GROUP	Exptal	Control	Total	Exptal	Control	Total	Exptal	Control	Total	Exptal	Control	Total	Exptal	Control	Total
Mean	21.6	20.5	21.1	21.6	20.6	21.1	21.5	20.9	21.2	21.4	20.9	21.2	21.1	21.1	21.1
Std. Dev.	3.0	2.3	2.7	3.1	2.4	2.8	2.9	3.2	3.0	3.3	3.3	3.3	3.5	3.2	3.3
N	33.0	35.0	68.0	33.0	35.0	68.0	33.0	35.0	68.0	33.0	35.0	68.0	33.0	35.0	68.0

SILVERMAN EALS (REPLACED DATA)

	SESSION 1			SESSION 2			SESSION 3			SESSION 4			SESSION 5		
GROUP	Exptal	Control	Total	Exptal	Control	Total	Exptal	Control	Total	Exptal	Control	Total	Exptal	Control	Total
Mean	21.6	20.7	21.1	21.6	21.1	21.3	21.6	21.1	21.4	21.6	21.1	21.4	21.0	21.1	21.1
Std. Dev.	2.7	2.3	2.5	3.3	2.4	2.9	2.8	2.9	2.9	3.0	2.9	2.9	3.5	2.8	3.1
N	45.0	45.0	90.0	45.0	45.0	90.0	45.0	45.0	90.0	45.0	45.0	90.0	45.0	45.0	90.0

CVLT (RAW DATA)

	SESSION 1			SESSION 2			SESSION 3			SESSION 4			SESSION 5		
GROUP	Exptal	Control	Total	Exptal	Control	Total	Exptal	Control	Total	Exptal	Control	Total	Exptal	Control	Total
Mean	35.7	31.9	33.7	36.8	35.2	36.0	38.2	36.9	37.5	40.2	36.1	38.1	39.3	36.2	37.7
Std. Dev.	3.9	4.1	4.4	4.7	5.1	4.9	4.5	5.3	5.0	3.7	6.7	5.8	3.5	6.6	5.5
N	33.0	35.0	68.0	33.0	35.0	68.0	33.0	35.0	68.0	33.0	35.0	68.0	33.0	35.0	68.0

CVLT (REPLACED DATA)

	SESSION 1			SESSION 2			SESSION 3			SESSION 4			SESSION 5		
GROUP	Exptal	Control	Total	Exptal	Control	Total	Exptal	Control	Total	Exptal	Control	Total	Exptal	Control	Total
Mean	34.5	32.8	33.7	36.1	35.4	35.7	37.2	36.9	37.0	39.6	36.4	38.0	38.2	36.4	37.3
Std. Dev.	4.7	5.1	4.9	4.9	5.0	5.0	4.7	4.9	4.8	4.0	6.0	5.3	4.2	5.8	5.1
N	45.0	45.0	90.0	45.0	45.0	90.0	45.0	45.0	90.0	45.0	45.0	90.0	45.0	45.0	90.0

APPENDIX E: DESCRIPTIVE STATISTICS OUTPUT OF ASSAYED STEROID HORMONES (ANALYSIS 1)

TESTOSTERONE

Session	Exptal Mean	exptal s.d.	Control Mean	control s.d.
1	9.18	4.95	9.04	5.41
2	7.97	5.12	9.78	4.57
3	8.69	6.44	9.56	4.09
4	6.66	3.78	9.49	3.73
5	8.60	6.01	12.41	10.56

PROGESTERONE

Session	Exptal Mean	exptal s.d.	Control Mean	control s.d.
1	157.27	62.69	9.11	6.66
2	332.85	147.55	12.22	13.52
3	1441.05	1052.76	12.51	14.57
4	9.63	10.03	12.50	10.66
5	17.38	48.25	13.18	11.33

ESTRADIOL

Session	Exptal Mean	exptal s.d.	Control Mean	control s.d.
1	3.65	1.17	1.84	0.75
2	13.19	5.29	1.52	0.81
3	32.69	26.07	1.30	0.59
4	1.85	1.95	1.23	0.51
5	1.39	0.73	1.19	0.32

ESTRIOL

Session	Exptal Mean	exptal s.d.	Control Mean	control s.d.
1	8.40	5.14	4.31	3.13
2	198.33	57.16	3.54	1.86
3	797.37	362.17	2.78	1.60
4	3.24	1.18	3.16	1.62
5	2.59	1.55	3.57	2.75

ESTRONE

Session	Exptal Mean	exptal s.d.	Control Mean	control s.d.
1	7.11	2.58	4.87	1.39
2	19.75	11.04	4.22	1.62
3	38.95	18.99	3.65	1.17
4	4.42	1.36	4.33	4.10
5	3.75	1.05	3.51	1.19

DHEAS

Session	Exptal Mean	exptal s.d.	Control Mean	control s.d.
1	3.06	1.55	4.03	1.80
2	2.19	1.04	4.16	2.35
3	2.13	1.25	4.03	2.73
4	3.70	2.29	4.19	2.65
5	4.22	2.49	4.65	2.96

CORTISOL

Session	Exptal Mean	exptal s.d.	Control Mean	control s.d.
1	0.88	0.75	0.73	0.47
2	1.43	1.02	0.98	0.60
3	2.48	1.20	0.88	0.63
4	0.79	0.65	1.19	0.85
5	1.17	1.01	2.78	8.08

APPENDIX F: DESCRIPTIVE STATISTICS OUTPUT OF POMS SCORES (ANALYSIS 1)

	Session 1			Session 2			Session 3			Session 4			Session 5		
GROUP	Exptal	Control	Total	Exptal	Control	Total	Exptal	Control	Total	Exptal	Control	Total	Exptal	Control	Total
Mean	28.9	31.2	30.1	24.3	35.2	29.9	31.7	51.0	41.6	22.8	39.6	31.5	28.1	45.6	37.1
Std. Dev.	26.9	32.9	30.0	23.3	34.7	30.0	25.0	42.6	36.3	20.9	41.8	34.1	25.9	37.8	33.5
N	33	35	68	33	35	68	33	35	68	33	35	68	33	35	68

APPENDIX G: *POST HOC* T-TESTS FOR SLEEP MEASURES (ANALYSIS 1)

	t	df	Sig	
SLEEP1A	0.815	84	0.42	
SLEEP1B	0.741	84	0.46	
SLEEP1C	0.557	84	0.58	
SLEEP1D	1.375	84	0.17	
SLEEP1E	1.001	84	0.32	
SLEEP1F	0.366	84	0.72	
SLEEP2A	-0.089	81	0.93	
SLEEP2B	0.860	81	0.39	
SLEEP2C	0.795	81	0.43	
SLEEP2D	0.785	81	0.44	
SLEEP2E	0.551	81	0.58	
SLEEP2F	-1.181	81	0.24	
SLEEP3A	0.558	77	0.58	
SLEEP3B	1.783	77	0.08	
SLEEP3C	-1.461	77	0.15	
SLEEP3D	1.468	77	0.15	
SLEEP3E	0.118	77	0.91	
SLEEP3F	0.065	77	0.95	
SLEEP4A	0.105	74	0.92	
SLEEP4B	**-4.072**	**74**	**0.00**	*
SLEEP4C	**4.621**	**74**	**0.00**	*
SLEEP4D	**-2.880**	**74**	**0.01**	*
SLEEP4E	**3.426**	**74**	**0.00**	*
SLEEP4F	1.685	74	0.10	
SLEEP5A	0.584	74	0.56	
SLEEP5B	-1.119	74	0.27	
SLEEP5C	1.362	74	0.18	
SLEEP5D	-0.461	74	0.65	
SLEEP5E	0.830	74	0.41	
SLEEP5F	0.000	74	1.00	

APPENDIX H: ANCOVA (ANALYSIS 2)

Test	Raw Data (12 girl-moms, 21 boy-moms)	Replaced Data (16 girl-moms, 29 boy-moms)
Digit Symbol Coding	Main Effect: Group F(1, 16) = 1.833, p= .195 Main Effect: Session F(4, 16) = .695, p= .598 Interaction Effect: Group x Session F(4, 16) = 3.080, p= .022	Main Effect: Group F(1, 28) = 3.532, p= .071 Main Effect: Session F(4, 28) = .538, p= .708 Interaction Effect: Group x Session F(4, 28) = 1.414, p= .234
Symbol Search	Main Effect: Group F(1, 16) = .299, p= .592 Main Effect: Session F(4, 16) = .169, p= .953 Interaction Effect: Group x Session F(4, 16) = .786, p= .539	Main Effect: Group F(1, 28) = 2.205, p= .149 Main Effect: Session F(4, 28) = .055, p= .994 Interaction Effect: Group x Session F(4, 28) = .205, p= .935
CVLT	Main Effect: Group F(1, 16) = .306, p= .588 Main Effect: Session F(4, 16) = 1.716, p= .157 Interaction Effect: Session x Group F(4, 16) = 1.760, p= .148	Main Effect: Group F(1, 28) = .006, p= .941 Main Effect: Session F(4, 28) = .713, p= .585 Interaction Effect: Session x Group F(4, 28) = .787, p= .536
Silverman Eals Object Location	Main Effect: Group F(1, 16) = .196, p= .664 Main Effect: Session F(4, 16) = 1.147, p= .343 Interaction Effect: Session x Group F(4, 16) = .443, p= .777	Main Effect: Group F(1, 28) = .228, p= .637 Main Effect: Session F(4, 28) = 1.689, p= .158 Interaction Effect: Session x Group F(4, 28) = .943, p= .442
Purdue Pegboard (Dominant Hand)	Main Effect: Group F(1, 16) = .029, p= .867 Main Effect: Session F(4, 16) = .288, p= .885 Interaction Effect: Session x Group F(4, 16) = .598, p= .665	Main Effect: Group F(1, 28) = .007, p= .935 Main Effect: Session F(4, 28) = .279, p= .891 Interaction Effect: Session x Group F(4, 28) = .791, p= .534

Purdue Pegboard (Non-Dominant Hand)	Main Effect: Group F(1, 16) = .081, p= .780 Main Effect: Session F(4, 16) = 1.550, p= .198 Interaction Effect: Session x Group F(4, 16) = .509, p= .729	Main Effect: Group F(1, 28) = .120, p= .732 Main Effect: Session F(4, 28) = 2.010, p= .098 Interaction Effect: Session x Group F(4, 28) = 1.048, p= .386
Mental Rotation Task	Main Effect: Group F(1, 16) = 3.978, p= .063 Main Effect: Session F(4, 16) = 1.698, p= .161 Interaction Effect: Session x Group F(4, 16) = .996, p= .417 Covariate: Cattell F(1, 16) = 6.299, p= .023	Main Effect: Group F(1, 28) = 6.490, p= .017 Main Effect: Session F(4, 28) = 1.246, p= .296 Interaction Effect: Session x Group F(4, 28) = .822, p= .514 Covariate: Cattell **F(4, 28) = 9.367, p= .005* (R^2= .044)**
Computation Span	Main Effect: Group F(1, 15) = 4.271, p= .056 Main Effect: Session F(4, 15) = .714, p= .586 Interaction Effect: Session x Group F(4, 15) = .810, p= .524	Main Effect: Group **F(1, 28) = 10.507, p= .003*** Main Effect: Session F(4, 28) = 1.020, p= .400 Interaction Effect: Session x Group F(4, 28) = 1.487, p= .211
Listening Span	Main Effect: Group F(1, 16) = 5.014, p= .040 Main Effect: Session F(4, 16) = .073, p= .990 Interaction Effect: Session x Group F(4, 16) = 1.749, p= .150	Main Effect: Group F(1, 28) = 5.517, p= .026 Main Effect: Session F(4, 28) = .142, p= .966 Interaction Effect: Session x Group F(4, 28) = .708, p= .588

APPENDIX I: DESCRIPTIVE STATISTICS OUTPUT OF DEPENDENT VARIABLES (ANALYSIS 2)

DIGIT SYMBOL (RAW DATA)

	SESSION 1			SESSION 2			SESSION 3			SESSION 4			SESSION 5		
GROUP	girl	boy	Total	girl	boy	Total	girl	boy	Total	girl	boy	Total	girl	boy	Total
Mean	79.5	86.8	84.1	85.7	92.2	89.8	83.5	93.3	89.7	84.8	97.3	92.8	88.0	98.0	94.3
Std. Dev	10.5	14.9	13.8	9.9	14.0	12.9	8.7	15.0	13.8	11.0	17.2	16.2	7.7	15.3	13.8
N	12	21	33	12	21	33	12	21	33	12	21	33	12	21	33

DIGIT SYMBOL (REPLACED DATA)

	SESSION 1			SESSION 2			SESSION 3			SESSION 4			SESSION 5		
GROUP	girl	boy	Total	girl	boy	Total	girl	boy	Total	girl	boy	Total	girl	boy	Total
Mean	80.6	87.2	84.9	84.5	91.5	89.0	82.9	91.2	88.3	86.7	94.9	92.0	87.1	96.3	93.0
Std. Dev	11.0	14.0	13.3	10.9	13.6	13.0	8.1	13.4	12.3	10.6	15.2	14.2	7.4	13.3	12.3
N	16	29	45	16	29	45	16	29	45	16	29	45	16	29	45

SYMBOL SEARCH (RAW DATA)

	SESSION 1			SESSION 2			SESSION 3			SESSION 4			SESSION 5		
GROUP	girl	boy	Total	girl	boy	Total	girl	boy	Total	girl	boy	Total	girl	boy	Total
Mean	34.3	36.8	35.9	36.5	38.4	37.7	37.6	40.8	39.6	38.0	43.2	41.3	39.9	42.7	41.7
Std. Dev	5.6	6.0	5.9	7.2	6.8	6.9	7.6	7.0	7.3	6.5	5.8	6.4	4.1	7.6	6.6
N	12	21	33	12	21	33	12	21	33	12	21	33	12	21	33

SYMBOL SEARCH (REPLACED DATA)

	SESSION 1			SESSION 2			SESSION 3			SESSION 4			SESSION 5		
GROUP	girl	boy	Total	girl	boy	Total	girl	boy	Total	girl	boy	Total	girl	boy	Total
Mean	35.0	37.2	36.5	36.4	38.9	38.0	37.6	40.5	39.4	38.5	41.9	40.7	39.9	42.2	41.4
Std. Dev	5.3	6.3	6.0	7.4	6.9	7.1	6.9	6.1	6.4	6.0	5.7	6.0	4.4	6.8	6.1
N	16	29	45	16	29	45	16	29	45	16	29	45	16	29	45

C-SPAN (RAW DATA)

	SESSION 1			SESSION 2			SESSION 3			SESSION 4			SESSION 5		
GROUP	girl	boy	Total	girl	boy	Total	girl	boy	Total	girl	boy	Total	girl	boy	Total
Mean	29.0	42.1	37.6	32.2	48.5	42.9	32.4	49.1	43.4	34.7	47.3	43.0	35.0	49.9	44.8
Std. Dev	10.1	14.4	14.4	11.0	14.5	15.4	11.9	14.3	15.6	10.8	14.2	14.3	11.0	15.4	15.6
N	11	21	32	11	21	32	11	21	32	11	21	32	11	21	32

C-SPAN (REPLACED DATA)

	SESSION 1			SESSION 2			SESSION 3			SESSION 4			SESSION 5		
GROUP	girl	boy	Total	girl	boy	Total	girl	boy	Total	girl	boy	Total	girl	boy	Total
Mean	31.5	40.6	37.3	31.8	46.6	41.3	32.5	45.0	40.5	35.9	45.1	41.8	35.1	47.2	42.9
Std. Dev	11.0	14.1	13.7	9.4	14.4	14.6	10.5	14.6	14.5	9.3	12.8	12.4	10.1	14.7	14.4
N	16	29	45	16	29	45	16	29	45	16	29	45	16	29	45

L-SPAN (RAW DATA)

	SESSION 1			SESSION 2			SESSION 3			SESSION 4			SESSION 5		
GROUP	girl	boy	Total	girl	boy	Total	girl	boy	Total	girl	boy	Total	girl	boy	Total
Mean	40.5	52.4	48.1	49.7	57.8	54.8	49.4	60.1	56.2	50.3	60.9	57.0	52.1	61.2	57.9
Std. Dev	7.2	9.3	10.3	5.8	7.6	8.0	7.2	7.6	9.0	8.6	9.0	10.1	8.5	9.2	9.9
N	12	21	33	12	21	33	12	21	33	12	21	33	12	21	33

L-SPAN (REPLACED DATA)

	SESSION 1			SESSION 2			SESSION 3			SESSION 4			SESSION 5		
GROUP	girl	boy	Total	girl	boy	Total	girl	boy	Total	girl	boy	Total	girl	boy	Total
Mean	42.6	51.2	48.2	49.9	56.4	54.1	49.5	57.2	54.4	51.4	58.4	55.9	52.1	58.8	56.4
Std. Dev	8.5	9.0	9.7	7.4	8.1	8.4	7.2	9.4	9.3	7.9	10.1	9.9	7.5	10.5	10.0
N	16	29	45	16	29	45	16	29	45	16	29	45	16	29	45

MRT (RAW DATA)

	SESSION 1			SESSION 2			SESSION 3			SESSION 4			SESSION 5		
GROUP	girl	boy	Total	girl	boy	Total	girl	boy	Total	girl	boy	Total	girl	boy	Total
Mean	4.5	7.8	6.6	5.3	9.7	8.1	7.5	11.2	9.9	6.5	12.0	10.0	6.5	12.6	10.4
Std. Dev	3.9	4.4	4.5	3.5	5.0	5.0	4.1	5.4	5.3	6.2	6.1	6.6	5.7	5.5	6.2
N	12	21	33	12	21	33	12	21	33	12	21	33	12	21	33

MRT (REPLACED DATA)

	SESSION 1			SESSION 2			SESSION 3			SESSION 4			SESSION 5		
GROUP	girl	boy	Total	girl	boy	Total	girl	boy	Total	girl	boy	Total	girl	boy	Total
Mean	5.6	7.3	6.7	6.4	9.3	8.3	8.1	11.0	10.0	7.3	11.2	9.8	7.8	12.1	10.6
Std. Dev	4.2	4.1	4.2	4.4	4.7	4.7	3.9	5.1	4.9	5.7	5.6	5.9	6.0	5.4	5.9
N	16	29	45	16	29	45	16	29	45	16	29	45	16	29	45

PURDUE PEGBOARD DOMINANT HAND (RAW DATA)

	SESSION 1			SESSION 2			SESSION 3			SESSION 4			SESSION 5		
GROUP	girl	boy	Total	girl	boy	Total	girl	boy	Total	girl	boy	Total	girl	boy	Total
Mean	17.5	17.4	17.4	17.5	17.6	17.6	17.6	17.7	17.7	18.4	18.0	18.1	18.1	18.1	18.1
Std. Dev	1.2	2.0	1.8	1.8	1.6	1.6	1.7	2.1	1.9	1.7	1.5	1.6	1.6	1.7	1.6
N	12	21	33	12	21	33	12	21	33	12	21	33	12	21	33

PURDUE PEGBOARD DOMINANT HAND (REPLACED DATA)

	SESSION 1			SESSION 2			SESSION 3			SESSION 4			SESSION 5		
GROUP	girl	boy	Total	girl	boy	Total	girl	boy	Total	girl	boy	Total	girl	boy	Total
Mean	17.5	17.4	17.4	17.5	17.6	17.5	17.3	17.6	17.5	18.3	17.9	18.0	18.0	18.1	18.1
Std. Dev	1.2	1.9	1.7	1.8	1.6	1.7	1.7	1.9	1.8	1.6	1.4	1.5	1.5	1.6	1.6
N	16	29	45	16	29	45	16	29	45	16	29	45	16	29	45

PURDUE PEGBOARD NON-DOMINANT HAND (RAW DATA)

	SESSION 1			SESSION 2			SESSION 3			SESSION 4			SESSION 5		
GROUP	girl	boy	Total	girl	boy	Total	girl	boy	Total	girl	boy	Total	girl	boy	Total
Mean	16.0	16.6	16.4	16.6	16.7	16.7	16.2	16.9	16.6	16.7	17.2	17.0	16.5	17.2	17.0
Std. Dev	1.5	1.6	1.6	1.6	1.4	1.5	1.9	1.5	1.6	1.8	1.5	1.6	1.3	1.6	1.5
N	12	21	33	12	21	33	12	21	33	12	21	33	12	21	33

PURDUE PEGBOARD NON-DOMINANT HAND (REPLACED DATA)

	SESSION 1			SESSION 2			SESSION 3			SESSION 4			SESSION 5		
GROUP	girl	boy	Total	girl	boy	Total	girl	boy	Total	girl	boy	Total	girl	boy	Total
Mean	15.9	16.3	16.2	16.6	16.6	16.6	16.0	16.7	16.4	16.6	17.1	16.9	16.3	16.9	16.7
Std. Dev	1.3	1.5	1.4	1.7	1.5	1.5	1.9	1.4	1.6	1.7	1.5	1.6	1.5	1.5	1.5
N	16	29	45	16	29	45	16	29	45	16	29	45	16	29	45

SILVERMAN EALS OBJECT LOCATION (RAW DATA)

	SESSION 1			SESSION 2			SESSION 3			SESSION 4			SESSION 5		
GROUP	girl	boy	Total	girl	boy	Total	girl	boy	Total	girl	boy	Total	girl	boy	Total
Mean	21.7	21.6	21.6	21.3	21.8	21.6	21.3	21.6	21.5	21.0	21.7	21.4	21.7	20.8	21.1
Std. Dev	3.7	2.7	3.0	2.7	3.3	3.1	3.6	2.4	2.9	2.6	3.6	3.3	2.0	4.2	3.5
N	12	21	33	12	21	33	12	21	33	12	21	33	12	21	33

SILVERMAN EALS OBJECT LOCATION (REPLACED DATA)

	SESSION 1			SESSION 2			SESSION 3			SESSION 4			SESSION 5		
GROUP	girl	boy	Total	girl	boy	Total	girl	boy	Total	girl	boy	Total	girl	boy	Total
Mean	21.8	21.5	21.6	21.6	21.6	21.6	21.7	21.5	21.6	21.1	21.8	21.6	21.7	20.6	21.0
Std. Dev	3.2	2.5	2.7	3.4	3.3	3.3	3.4	2.5	2.8	2.5	3.2	3.0	2.7	3.8	3.5
N	16	29	45	16	29	45	16	29	45	16	29	45	16	29	45

CVLT (RAW DATA)

	SESSION 1			SESSION 2			SESSION 3			SESSION 4			SESSION 5		
GROUP	girl	boy	Total	girl	boy	Total	girl	boy	Total	girl	boy	Total	girl	boy	Total
Mean	35.0	36.1	35.7	35.7	37.5	36.8	36.2	39.4	38.2	39.8	40.4	40.2	39.1	39.4	39.3
Std. Dev	4.0	3.9	3.9	5.0	4.4	4.7	4.9	4.0	4.5	3.5	3.9	3.7	2.6	4.0	3.5
N	12	21	33	12	21	33	12	21	33	12	21	33	12	21	33

CVLT (REPLACED DATA)

	SESSION 1			SESSION 2			SESSION 3			SESSION 4			SESSION 5		
GROUP	girl	boy	Total	girl	boy	Total	girl	boy	Total	girl	boy	Total	girl	boy	Total
Mean	34.6	34.4	34.5	34.5	37.0	36.1	35.5	38.1	37.2	38.9	40.0	39.6	37.9	38.4	38.2
Std. Dev	3.5	5.3	4.7	5.1	4.7	4.9	4.6	4.6	4.7	4.1	4.0	4.0	3.3	4.7	4.2
N	16	29	45	16	29	45	16	29	45	16	29	45	16	29	45

APPENDIX J: DESCRIPTIVE STATISTICS OUTPUT OF ASSAYED STEROID HORMONES (ANALYSIS 2)

Testosterone

		N	Mean	Std. Dev
Session 1	girl	14	9.98	4.28
	boy	27	8.76	5.29
	Total	41	9.18	4.95
Session 2	girl	16	9.28	6.65
	boy	26	7.17	3.84
	Total	42	7.97	5.12
Session 3	girl	15	8.89	7.23
	boy	25	8.57	6.08
	Total	40	8.69	6.44
Session 4	girl	14	7.31	4.32
	boy	25	6.29	3.48
	Total	39	6.66	3.78
Session 5	girl	15	9.65	5.64
	boy	26	7.98	6.24
	Total	41	8.60	6.01

Estriol (E3)

		N	Mean	Std. Dev
Session 1	girl	14	7.19	5.50
	boy	27	9.03	4.92
	Total	41	8.40	5.14
Session 2	girl	16	186.29	47.20
	boy	26	205.73	62.22
	Total	42	198.33	57.16
Session 3	girl	15	738.71	349.79
	boy	25	832.56	371.93
	Total	40	797.37	362.17
Session 4	girl	14	3.18	1.06
	boy	25	3.27	1.26
	Total	39	3.24	1.18
Session 5	girl	15	2.47	1.13
	boy	26	2.67	1.76
	Total	41	2.59	1.55

Progesterone

		N	Mean	Std. Dev
Session 1	girl	14	133.99	55.24
	boy	27	169.33	63.85
	Total	41	157.27	62.69
Session 2	girl	16	268.09	116.36
	boy	26	372.71	152.46
	Total	42	332.85	147.55
Session 3	girl	15	1443.89	1331.80
	boy	25	1439.34	875.41
	Total	40	1441.05	1052.76
Session 4	girl	14	7.76	3.42
	boy	25	10.68	12.24
	Total	39	9.63	10.03
Session 5	girl	15	9.83	7.15
	boy	26	21.73	60.35
	Total	41	17.38	48.25

Estrone (E1)

		N	Mean	Std. Dev
Session 1	girl	14	7.41	2.71
	boy	27	6.96	2.56
	Total	41	7.11	2.58
Session 2	girl	16	16.19	4.16
	boy	26	21.94	13.28
	Total	42	19.75	11.04
Session 3	girl	15	30.29	10.09
	boy	25	44.14	21.25
	Total	40	38.95	18.99
Session 4	girl	14	4.34	1.35
	boy	25	4.47	1.39
	Total	39	4.42	1.36
Session 5	girl	15	3.97	1.34
	boy	26	3.62	0.85
	Total	41	3.75	1.05

Estradiol (E2)

		N	Mean	Std. Dev
Session 1	girl	14	3.71	1.21
	boy	27	3.63	1.16
	Total	41	3.65	1.17
Session 2	girl	16	11.53	3.45
	boy	26	14.22	6.00
	Total	42	13.19	5.29
Session 3	girl	15	24.92	12.37
	boy	25	37.35	30.90
	Total	40	32.69	26.07
Session 4	girl	14	1.64	0.72
	boy	25	1.96	2.39
	Total	39	1.85	1.95
Session 5	girl	15	1.43	0.68
	boy	26	1.37	0.77
	Total	41	1.39	0.73

DHEA

		N	Mean	Std. Dev
Session 1	girl	14	3.30	1.29
	boy	27	2.93	1.67
	Total	41	3.06	1.55
Session 2	girl	16	2.11	0.75
	boy	26	2.23	1.20
	Total	42	2.19	1.04
Session 3	girl	15	1.96	0.83
	boy	25	2.23	1.45
	Total	40	2.13	1.25
Session 4	girl	14	3.78	2.36
	boy	25	3.66	2.30
	Total	39	3.70	2.29
Session 5	girl	15	4.88	3.10
	boy	26	3.84	2.04
	Total	41	4.22	2.49

CORTISOL

		N	Mean	Std. Dev
CORTIS1	girl	14	0.75	0.63
	boy	27	0.95	0.81
	Total	41	0.88	0.75
CORTIS2	girl	16	0.94	0.59
	boy	26	1.73	1.12
	Total	42	1.43	1.02
CORTI3	girl	15	2.01	0.91
	boy	25	2.76	1.29
	Total	40	2.48	1.20
CORTI4	girl	14	0.77	0.76
	boy	25	0.80	0.61
	Total	39	0.79	0.65
CORTI5	girl	15	1.19	1.05
	boy	26	1.16	1.01
	Total	41	1.17	1.01

APPENDIX K: DESCRIPTIVE STATISTICS OUTPUT OF POMS SCORES (ANALYSIS 2)

Session	Session 1		Session 2		Session 3		Session 4		Session 5	
GROUP	girl	boy	girl	boy	girl	boy	girl	boy	girl	boy
Mean	30.5	32.4	27.9	24.3	39.1	35.0	20.1	29.6	27.3	32.7
Std. Dev	28.0	28.4	24.4	21.2	30.8	25.7	20.5	22.9	27.3	28.1
N	14	27	16	26	15	25	14	25	15	26

APPENDIX L: *POST HOC* T-TESTS FOR SLEEP MEASURES (ANALYSIS 2)

SESSION	T-TEST	DF	SIGN
SLEEP1A	1.631	39	0.111
SLEEP1B	-1.151	39	0.257
SLEEP1C	0.127	39	0.899
SLEEP1D	-0.639	39	0.526
SLEEP1E	-0.095	39	0.925
SLEEP1F	1.462	39	0.152
SLEEP2A	1.792	40	0.081
SLEEP2B	0.87	40	0.389
SLEEP2C	-1.43	40	0.161
SLEEP2D	0.742	40	0.462
SLEEP2E	-1.947	40	0.059
SLEEP2F	0.032	40	0.975
SLEEP3A	1.033	38	0.308
SLEEP3B	-2.109	38	0.042
SLEEP3C	1.329	38	0.192
SLEEP3D	-0.807	38	0.425
SLEEP3E	0.56	38	0.579
SLEEP3F	1.124	38	0.268
SLEEP4A	0.55	37	0.585
SLEEP4B	0.615	37	0.542
SLEEP4C	-0.596	37	0.554
SLEEP4D	-0.067	37	0.947
SLEEP4E	0.178	37	0.860
SLEEP4F	0.336	37	0.739
SLEEP5A	0.626	39	0.535
SLEEP5B	0.236	39	0.815
SLEEP5C	0.789	39	0.435
SLEEP5D	0.266	39	0.792
SLEEP5E	0.556	39	0.582
SLEEP5F	-0.527	39	0.601