MATERNAL CARDIAC AUTONOMIC FUNCTION AND FETAL BEHAVIOUR IN HYPERTENSIVE AND OBESE PREGNANCIES

by

JENNIFER ANN VAN DER MEULEN

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ABSTRACT

Hypertension in pregnancy is associated with autonomic dysregulation whereas the effects of obesity in pregnancy on maternal cardiac autonomic function are poorly understood. Furthermore, hypertension in pregnancy is associated with placental insufficiency and fetal growth restriction, whereas obesity in pregnancy is associated with placental inflammation and macrosomia. Fetal growth restriction is associated with an increased risk for language deficits at 2-5 years of age. However, maternal cardiac autonomic function and fetal auditory processing in pregnancies complicated by hypertension compared to obesity have not been examined and are the focus of this study. Maternal short-term cardiac autonomic modulation in the supine and standing postures as well as spontaneous and auditory elicited fetal behaviours were compared in 61 mother-fetal pairs (n=20 hypertensive; n=20 overweight; n=21 normal weight comparison pregnancies) from 34 to 40 weeks gestation. Maternal cardiovascular measures included systolic arterial finger-cuff blood pressure and electrocardiographic recordings of heart rate. Spontaneous observations of fetal heart rate, body and breathing movements, muscle tone and an estimate of amniotic fluid were made. Finally, each fetus received a 2 min recording of their mother and the mother's voice in reverse (counterbalanced over subjects).

When standing (othostatic stress), all three groups of women exhibited a decrease in the average baroreflex slope, parasympathetic nervous system indicator and high frequency power compared to the supine position. In a 20 min observation of spontaneous behaviour in the maternal supine compared to the standing position, fetuses of hypertensive mothers had, on average, fewer heart rate accelerations $\geq$ 15 bpm while the mother was supine; fetuses in the normal weight comparison group experienced more accelerations while the mother was supine. The average number of heart rate accelerations did not change in the two maternal positions for fetuses in the obese group. Fetuses in the three groups showed differential responses to the

mother's voice played forward and backward. It was concluded that there were no differences in maternal heart rate variability measures in the group of mildly hypertensive women compared to those with obesity and the normal weight comparison group. Differential spontaneous fetal heart rate accelerations and responses to the mother's voice among the three groups needs further study with sufficient sample size to examine behaviour as a function of gestational age.

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LIST OF ABBREVIATIONS AND ACRONYMS

AFI	Amniotic fluid index
BMI	Body mass index
BP	Blood pressure
FHR	Fetal heart rate
GA	Gestational age
HRV	Heart rate variability
NE	Norepinephrine
NST	Non-stress test
PNS	Parasympathetic nervous system
SNS	Sympathetic nervous system

CHAPTER 1

Introduction

Over the past two decades, researchers and clinicians have developed an interest in human maternal autonomic nervous system regulation and fetal development and behaviour in pregnancies complicated by maternal hypertension and obesity. Even though both hypertension and obesity increase the risk of maternal and fetal morbidity and mortality, few have examined simultaneously the relationship between maternal and fetal factors, and the extent to which maternal autonomic system regulation affects fetal behaviour is unknown. Moreover, obesity increases the risk of hypertension and hypertension in pregnancy is often found in the presence of maternal obesity. However, the nature of the effects of maternal obesity in the absence of confounding disease on maternal cardiac autonomic regulation and fetal behaviour is unknown and the focus of this thesis. Specifically, the relationship between maternal autonomic regulation and fetal behaviour will be explored in the presence of maternal hypertension, maternal obesity, and in normal weight, normotensive pregnancies.

Five questions will be addressed: 1) What are the effects of maternal hypertension and/or excess body weight on maternal heart rate variability (HRV) when compared to HRV in uneventful, normal weight, normotensive pregnancies? 2) What is the effect of maternal posture (standing vs. supine) on maternal heart rate variability and fetal heart rate in hypertensive, overweight, and uneventful pregnancies? 3) What is the relationship between maternal heart rate variability and spontaneous fetal heart rate, body, and breathing movements in hypertensive, overweight and uneventful pregnancies? 4) Is there a relationship between maternal BP (systolic and/or diastolic), HRV, and baroreflex sensitivity and fetal spontaneous heart rate, body and breathing movements and auditory-elicited behaviour? 5) Is there a difference in auditory processing of the mother's voice (forward and/or backward) among fetuses of women with

hypertension, women who are overweight, and those with an uneventful, normal weight, normotensive pregnancy?

CHAPTER 2

Literature Review

Hypertension in Pregnancy

Hypertensive disorders are the most common medical complication of pregnancy, with a reported incidence ranging from 5-22 % (Bryson, Ioannou, Rulyak, & Critchlow, 2003; American College of Obstetricians and Gynecologists [ACOG], 2002). They are a leading cause of maternal, fetal and neonatal morbidity and mortality (Helewa et al., 1997). Hypertensive diseases in pregnancy were associated with an estimated 33% of all obstetrical deaths in Canada between 1971 and 1986 (Wittman, Murphy, Yuen, Shaw & Wittman, 1988) and are responsible for approximately 17.6% of current obstetrical deaths (ACOG, 2002). Women with pregnancies complicated by hypertension are more likely to experience abruptio placentae, acute renal dysfunction, and increased Caesarean delivery (Hauth et. al., 2000). Hypertension in pregnancy has long been associated with an increased risk of high blood pressure later in a woman's life (Svensson, Andersch, & Hansson, 1983; Sibai, El-Nazer, & Gonzalea-Ruiz, 1986). In long-term follow up studies (Arnadottir, Geirsson, Arngrimsson, Jonsdotter & Olafsson, 2005), an increased incidence of death from ischemic heart disease and cerebrovascular events in women who had experienced hypertension in pregnancy has been reported. Interestingly, Broughton and colleagues (Broughton Pipkin, Sharif, & Lal, 1998) found that a single systolic blood pressure reading $\geq$ 140 mmHg before 20 weeks' gestation was associated with an increased risk of later developing hypertension.

In addition to untoward maternal effects, there are negative effects on the fetus. Hypertension in pregnancy is associated with decreased and/or impaired uteroplacental blood flow (Brown, 1995), leading to decreased oxygen and nutrient transport to the fetus (Sapunar,

1996), restricting placental and fetal growth. These fetuses are at increased risk of low birth weight, preterm birth and death (Arnath, Peedicayil, & Savitz, 1995). Preterm birth is associated with respiratory distress syndrome and ventilator support (Hauth et al., 2000). Furthermore, the offspring of women who experience hypertension in pregnancy are at greater risk of developing cardiovascular disease in adulthood. Birth weight, which is affected by maternal hypertension, also has long-term implications for the offspring. In an epidemiological study, Barker, Winter, Osmond, Margetts, and Simmonds (1989) found that men with the lowest weights at birth and at 1 year of age had the highest rates of death from ischemic heart disease. Those who were thin at birth but caught up during infancy were at particular risk.

Presently there is no standardized classification, diagnostic criteria or nomenclature for hypertensive disorders in pregnancy (Lenfant, 2001). In 2007, at the onset of this study, the most widely accepted definition was a blood pressure (BP) $\geq$ 140/90 mmHg taken on two occasions at least 6 hours apart (ACOG, 2002); it was the criterion used in this study. Classifications of hypertensive disorders in pregnancy generally include: 1) chronic hypertension (any hypertension preceding pregnancy or diagnosed before the 20th week of gestation); 2) preeclampsia-eclampsia (increased BP accompanied by proteinuria of at least 0.3g of protein in a 24 hour urine specimen); 3) preeclampsia superimposed on chronic hypertension: a) hypertension and no proteinuria before 20 weeks' gestation with new-onset proteinuria, b) women with hypertension and proteinuria before 20 weeks' gestation with sudden increase in levels of proteinuria, and c) sudden increase in BP and/or with increased alanine aminotransferase or aspartate aminotransferase to abnormal levels); and 4) gestational hypertension (a BP elevation detected for the first time after 20 weeks' gestation with no proteinuria). To avoid the confound of the systemic disease associated with preeclampsia on interpretation of results, this study was limited to women experiencing chronic or pregnancy-induced hypertension, without the presence of

proteinuria (at least 0.3g of protein in a 24 hour urine specimen or repeated 1+ protein in urine determined by dip stick performed at clinic visits) at the time of testing. Women who develop hypertensive disease in pregnancy are often overweight or obese prior to pregnancy.

Obesity in Pregnancy

Obesity is determined by several methods, the most commonly used being the body mass index (BMI). BMI is calculated by dividing body weight by the square of the height (kg/m^2) (Levario-Carillo et al., 2006). The risk of developing hypertension in pregnancy increases with increasing BMI classification (2.0 % for underweight, compared to 6.0 % for overweight; Belogolovkin et al., 2007). BMI alone accounts for at least some systolic BP variability (e.g., Broughton Pipkin et al., 1998). However, few studies examining the effects of maternal weight independent of other complicating factors on fetal development and pregnancy outcome could be found. The limited studies examining the effects of obesity and overweight in pregnancy have shown an increased incidence of adverse maternal complications including gestational diabetes, gestational hypertension, preeclampsia and eclampsia, Caesarean delivery which can have adverse complications for the mother and complications specific to the fetus such as macrosomia (> 4000 g), death and preterm delivery (i.e., before 32 weeks' gestation; Baeten et al., 2001). Baeten and colleagues reported that the risk of these complications increased with increasing weight. Furthermore, infants born to obese women are almost twice as likely as those born to women with a normal weight to die within the first year of life.

Currently, BMI is the most common method of categorizing weight; it is considered the most useful indicator to date of the health risks associated with being overweight or underweight. BMI is a more accurate measure of body fat than weight alone, as BMI takes into account height. A BMI of less than 18.5 $kg \cdot m^{-2}$ is classified as underweight, 18.5-24.9 $kg \cdot m^{-2}$ as normal weight, 25-29.9 $kg \cdot m^{-2}$ as overweight, 30-34.9 $kg \cdot m^{-2}$ as obese class I, 35-39.9 $kg \cdot m^{-2}$ as obese class II

and 40 $kg \cdot m^{-2}$ or more as obese class III. While there is a continuous relationship between BMI and health risk, these cut-off points have been established in the non-pregnant population in order to identify different gradations of risk (Health Canada, 2003). Individuals in the normal weight range are considered to be at the lowest relative risk for morbidity and mortality. In studies examining the general population (Calle, Thun, Petrelli, Rodriguez, & Heath, 1999), and female nurses (Hu et al., 2004), overweight and obesity were strongly associated with increased risk of developing and/or dying of diseases including heart disease, diabetes and cancer, with a positive relationship established between risk and increasing weight classification. In two previous studies in this laboratory examining fetal behaviour in hypertensive pregnancies, the hypertensive groups had a higher BMI prior to pregnancy (29.7 ± 6.1 vs. 23.8 ± 3.3 $kg \cdot m^{-2}$; Swansburg, Brown, Hains, Smith & Kisilevsky, 2005) and at time of testing (33.7 ± 4.2 vs. 28.8 ± 2.9 $kg \cdot m^{-2}$; Lee, Brown, Hains & Kisilevsky, 2007) than did the control groups. However, neither study was designed to untangle the influence of body weight and hypertension independently.

Long-term, even in the absence of pregnancy, overweight and obesity have become increasingly prevalent in Canadian adults. According to the 2004 Canadian Community Health Survey (Tjepkema, 2005), 23.1% of Canadians 18 years or older (approximately 5.5 million adults) had a BMI of 30.0 $kg \cdot m^{-2}$ or more. Another 36.1% (8.6 million) were overweight. While obesity rates remained relatively unchanged between 1978-1979 and 1986-1992 (Shields & Tjepkema, 2006), the rates have since gone up, particularly among men. A 2005 Statistics Canada report (Le Petit & Berthelot, 2005) demonstrated that approximately one-third of people (38% of men, 28% of women) who were classified as normal weight in 1994-1995 had become overweight by 2002-2003. Nearly one-quarter (20% of men, 28% of women) of those who were initially overweight were classified as obese after the eight-year period. Conversely, only 10% of those who were overweight in 1994-1995 had reduced to a normal weight by 2002-2003.

For women, the childbearing years from ages 25 to 34 are the period of greatest weight gain (Williamson, Kahn, Remington & Anda, 1990). Contrary to popular belief, the development of obesity is largely due to prepregnancy weight, pregnancy weight gain that is retained, and post-partum weight gain, rather than the pregnancy itself (Lederman, 2001). Although overweight and obese women gain less weight during pregnancy (Stephansson, Dickman, Johansson & Cnattingus, 2001), they retain more weight postpregnancy (Coitinho, Sichieri & D'Aquino Benico, 2001).

In summary, overweight and hypertension are issues negatively affecting pregnant women and their offspring. Excess body weight is a modifiable risk factor associated with the development of hypertension early in life. Though the relationship and etiologies are currently poorly understood, it is speculated that increasing body mass as a social trend may have increased the incidence of hypertension in pregnancy (Zhang, Meikle & Trumble, 2003). It has been postulated that examining changes in cardiac autonomic function in overweight and hypertensive pregnancies could provide insight into the development of hypertensive disease, not only during pregnancy but for those women who are at risk of subsequently developing cardiovascular disease.

Maternal Autonomic Function

The irregularity of the physiologic cardiac rhythm has been known for years. However, until relatively recently, beat-to-beat alterations in heart rate and blood pressure rhythms were not fully understood by health care providers. It was not until the discovery that a completely regular sinus rhythm is associated with negative outcome in the nonpregnant population that it became apparent that heart rate irregularity is not necessarily a pathologic event (Malik & Camm, 1995). Since this discovery, interest in heart rate and blood pressure variability has surged, particularly

for estimation of the degree of cardiovascular change/disease in a wide variety of patient populations.

Heart rate variability measures, such as the R-R interval, are being used increasingly for investigations of central regulation of autonomic state, as they serve as a non-invasive, quantitative marker of human autonomic function (Akselrod, Gordon, Ubel, Shannon, Barger & Cohen, 1981). Heart rate variability is the variation in the length of time between successive R-R intervals (in ms; the time between two successive ventricular contractions)

There are two methods of measuring heart rate variability. The time domain method is utilized for longer periods of recording (usually 24 hours), and evaluates beat-by-beat variations in heart rate (HR) from short-term 5 minute recordings. Because the time domain method will not be used in this study, no further explanation is warranted. Frequency domain spectral analysis was utilized in this study, because short recording periods (minutes rather than hours) will be used for data collection [Task Force of the European Society of Cardiology and the North American Society of Pacing and Electrophysiology (TFESCNASPE), 1996]. It uses power spectral analysis to reduce beat-by-beat HR signals in short recordings to frequency components and quantifies them in terms of variance (power; TFESCNASPE, 1996). Beat-by-beat variations in heart rate are evaluated to determine how power (variance) distributes as a function of frequency (of fluctuations in R-R interval). The main spectral components that are categorized in this method are ultra-low-frequency (≤ 0.003 Hz), very-low-frequency (0.003-0.04 Hz), low-frequency (0.04-0.15 Hz), and high-frequency (0.15-0.4 Hz) power (TFESCNASPE, 1996); the ratio of high-frequency to total power reflects parasympathetic (vagal) modulation of heart rate while the ratio of low-frequency to high-frequency power can be used to reflect sympathetic activity fluctuations (TFESCNASPE, 1996). While many of the studies in this review were

carried out in non-pregnant populations, the measurement, terminology and interpretations are the same in the pregnant population.

Short term maternal cardiovascular function is directed by a complex reciprocal interaction of the parasympathetic and sympathetic branches of the autonomic nervous system in order to maintain homeostasis. Both the parasympathetic and sympathetic nerves synapse on the SA node in order to influence heart rate. The parasympathetic branch also innervates the AV node and junction. The sympathetic fibres synapse on atrial and ventricular myocardial tissues and blood vessels (Levy & Pappano, 2007). In the healthy non-pregnant population the parasympathetic effects prevail over sympathetic at the SA node in the resting state, resulting in the predominance of the parasympathetic modulation of heart rate.

The parasympathetic nervous system (PNS) decreases heart rate by hyperpolarizing the cell membrane and decreasing the slope of pacemaker potential, inhibiting the excitability and conductivity of the sinoatrial node. Acetylcholine (ACh), which has a latency period of 100-400 ms (Levy & Pappano, 2007), binds to muscarinic cholinergic receptors and activates the transmembrane K+ channel (Hainsworth, 1996) to reach steady state very quickly. Acetylcholinesterase, which rapidly hydrolyzes acetylcholine, is found in abundance in the SA node, making any effects of the vagal impulse brief; heart rate returns to normal within 5 s of cessation of parasympathetic stimulation (Levy & Pappano, 2007).

In contrast, the sympathetic nervous system (SNS) accelerates heart rate via norepinephrine stimulated β1 receptor-mediated second messenger cascade of intracellular signals. The result is an increased slope of pacemaker potential (and a resultant increase in HR). Norepinephrine has a latency period of 3-5 s, and reaches full potential within 20-30 s (Akselrod et al., 1981). Because cardiac tissues metabolize norepinephrine slowly, sympathetic effects on heart rate are slow to decay, resulting in a longer period of recovery to normal heart rate

following cessation of sympathetic stimulation. It is well-established that rapid changes in heart rate are a result of parasympathetic modulation (e.g. Akselrod et al., 1981; Levy & Pappano, 2007; Hainsworth, 1996).

There are five main measures of heart rate variability. The low-frequency (LF) power of the heart period power spectrum (0.04-0.15 Hz) reflects modulation of both sympathetic and vagal tone by baroreflex activity, while high-frequency (HF) power (0.15-0.5 Hz) reflects vagal modulation of heart rate. Total power (TP) reflects the variance of the entire signal, and the ratio of high frequency to total power is understood to reflect vagal activity whereas the ratio of low frequency to high frequency power is used to indicate sympathetic activity [Task Force of the European Society of Cardiologists and the North American Society of Pacing (TFESCNASPE), 1996].

A major determining factor in the development of hypertension is related to the malfunction of the autonomic nervous system wherein the sympathetic nervous system prevails over the parasympathetic nervous system (Levy & Pappano, 2007). Further, alterations in autonomic modulation in pregnancy may explain, in part, inadequate cardiovascular adaptation to the profound hemodynamic changes (e.g., placenta, increased blood volume) that occur in pregnancy (Ekholm, Piha, Antilla, & Erkkola, 1994). Heart rate variability (HRV) measures oscillations in the interval between consecutive heart beats, specifically, variability in the intervals between R waves (i.e., the RR interval). Not to be confused with absolute heart rate, which is a measure of the number of beats per minute, the variability between consecutive R-R intervals can change, but heart rate may not. An indicator of the activity of autonomic regulation of circulatory function, reduced HRV has been associated with several pathological conditions, including hypertension. HRV is a non-invasive, accurate means of studying the beat-by-beat

autonomic control of the cardiovascular system, with serial recordings permitting the study of changing autonomic modulation in pregnancy (Stein, Bosner, Kleiger & Conger, 1993).

HRV and BRS in pregnancy

Just as with a non-pregnant population, there is considerable variation in individual heart rate and HRV changes during a normal pregnancy. Pregnancy results in profound changes in maternal hemodynamics, with a progressive increase of approximately 50% of total blood volume from the beginning of the second trimester to around the 36th week of gestation (Silver, Seebeck & Carlson, 1998). Heart rate and cardiac output also increase while mean arterial pressure decreases (Ekholm, Piha, Antilla & Erkkola, 1994). Ekholm and colleagues report a decrease in systemic vascular resistance in the first half of pregnancy followed by an increase in the last trimester. Furthermore, there is a progressive increase in peripheral vascular constriction after the early second trimester, resulting in an increase in blood pressure after 28 weeks' gestation (Paller, 1998).

Pregnancy associated changes in hemodynamics are speculated to be initiated by ovarian changes and placental hormones in first trimester, and later may be modified by placental and fetal endocrine factors (Avery, Wolfe, Amara, Davies & McGrath, 2001). Pregnancy is associated with decreased HRV, with a significant decrease in the second trimester which cannot be explained by pregnancy-induced respiratory changes (Ekholm & Erkkola, 1996). One proposed mechanism for this change in HRV is that the hypervolemia associated with pregnancy diminishes the large changes in blood pressure induced by a stimulus; the increased blood volume would continuously stretch the stretch receptors, resulting in reduced baroreceptor sensitivity (Thompson, Tatro, Ludwig & Convertino 1990); reduced baroreflex sensitivity in humans is associated with decreased BP variability (Mancia et al., 1986).

Blood pressure progressively decreases in the first half of pregnancy in both normotensive and chronically hypertensive pregnant women, reaching a mean of 15 mmHg lower than prepregnancy levels by the second trimester before returning to baseline in the third trimester (MacGillivray, Rose & Rowe, 1969; Paller, 1998). Though the exact nature and physiological mechanisms behind the changes are poorly understood, it is accepted that these adaptations are associated with autonomic nervous system changes which alter cardiac autonomic modulation (Airaksinen, Kirkinen & Takkunen, 1985; Stein, 1999).

HRV and BRS in hypertensive pregnancies

Though there are many hypotheses proposed to explain the etiology and progression of hypertensive disorders that develop in pregnancy, the exact causes are unknown. Pregnancies complicated by hypertension have a greater than normal increase in blood pressure due to increased vascular resistance (ACOG, 2002). Interestingly, while preeclampsia (a severe form of pregnancy-associated hypertensive disease) is associated with reduced total blood volume relative to that of the uncomplicated pregnancy, pregnancy-induced hypertension is not (Silver et al., 1998). In the absence of pregnancy, hypertension is associated with a progressive decrease in long-term (24 hour) sensitivity of the baroreceptor reflex; those with the most pronounced degree of hypertension have the most impaired sensitivity. Though the exact pathophysiological impairment causing the alterations in vascular activity observed in hypertension is unknown, there is evidence of autonomic dysregulation, where the reduced baroreceptor heart rate reflex is paired with the increased BP found in essential hypertension (Parati et. al., 1988). This is observed as increased sympathetic and decreased parasympathetic modulation of cardiac function and increased vasomotor sympathetic modulation (Souza et. al., 2001).

Studies of hypertensive pregnant women in this laboratory have shown no differences in maternal HRV or BRS measures between gestation and hypertensive status (hypertensive vs.

normotensive; Lee et al., 2007). However, in the preeclamptic population, an effect of diagnostic group (preeclamptic vs. normotensive) on systolic arterial finger-cuff BP was found (Swansburg, 2005). Effects of position (from supine to standing) also were found; increased TP, SNS indicator, systolic arterial finger-cuff BP and decreased PNS indicator and R-R interval were found for both groups when standing was compared to supine posture. Furthermore, HF power decreased in the preeclamptic group when these women with hypertension were in the standing position compared to the supine position but increased in the normotensive group. While both diagnostic groups demonstrated decreased PNS indicator in the standing compared to supine postures, the decrease was greater in the preeclamptic group than in the normotensive group (Swansburg).

HRV and BRS in Obesity

As previously noted, hypertension often occurs in the presence of obesity. However, few studies could be found that examined the effects of maternal excess body weight in the absence of other complications on cardiac autonomic regulation in pregnancy. One study in this laboratory (Schmidt-Stutzman) of the effects of exercise and body weight on HRV over gestation found no effect of weight group (overweight vs. normal weight) at 20 weeks gestation on maternal heart rate variability. However, LF power significantly decreased more during exercise vs. rest in a normal weight group compared to an overweight group at 36 weeks gestation, potentially reflecting lower sympathetic tone in the normal weight group (Schmidt-Stutzman, 2005). In non-pregnant obese subjects, conflicting results have been reported. In some studies, BMI and waist/hip ratio (Laederach-Hoffman, Mussgay and Ruddel, 2000) and body fat percentage (Peterson et al., 1988, Picrillo et al., 1996) were inversely related to sympathetic activity. Others found no difference between obese and normal weight populations in sympathetic activity levels (e.g. Rossi et al., 1989), while still others found that BMI was positively related to sympathetic

activity (Zahorska-Markiewicz, Kuagowska, Kucio & Klin, 1993). It should be noted that all of the aforementioned studies found indications of decreased vagal activity in obese compared to normal weight women. In addition, Zahora-Markiewicz and colleagues found that the circulatory response (changes in the cardiac and vascular functions in response to factors including emotional stress, physical exercise and temperature change) of the obese women to vagal stimulation during deep breathing and SNS stimulation during isometric handgrip exercises were less prominent following a weight loss treatment. In contrast, Picirillo and colleagues (1996) found lower indices of sympathetic response and higher indicators of vagal activity in obese compared to normal weight subjects. To date, the exact nature, and explanation for the mechanism behind the autonomic changes remains unclear. However, it has been speculated that resistance to the sympatho-excitatory effects of insulin might have a role in the development of obesity (Quillot, Zannad & Ziegler, 2005) and that low SNS activity/reactivity/sensitivity could be a cause of obesity. It has been proposed (Rossi et al., 1989) that understanding and detecting early autonomic changes can be potentially important in the management of obesity.

Postural change can affect maternal autonomic function in the pregnant and non-pregnant state. Standing from the supine position causes blood to pool in the veins in the legs. In the healthy non-pregnant population, this action results in decreased preload, stroke volume and cardiac output; the unloaded systemic baroreceptors reflexly increase heart rate. Heart rate returns to normal within 30 s (Ekholm, Piha, Antilla & Erkkola, 1994). However, in pregnancy, a reduced heart rate "recovery" in response to position change was observed, possibly indicating a diminished baroreflex-induced slowing of heart rate (Ekholm et al., 1994). Furthermore, the low- to high-frequency ratio was significantly increased by turning from left lateral recumbent position to supine after the 33rd week of gestation, indicating an increase in sympathetic nervous system function. However, as there were no significant changes in non-pregnant subjects, the authors

speculated that aortocaval compression syndrome might be the precipitating factor behind the observed differences (Speranza, Verlatto & Albiero, 1998). Only one study could be found examining the effects of postural change on HRV in obese subjects; no HRV response to postural change (supine to standing) was found in nonpregnant obese subjects (Kim et al., 2005).

Vagal stimulation results in a more rapid change in heart rate response than sympathetic stimulation. Furthermore, the acetylcholine released by the PNS is readily hydrolyzed by cholinesterase, making the effects of vagal stimulation diminish very rapidly following cessation of vagal activity. In contrast, as most norepinephrine released by the SNS is taken up by nerve terminals, the effects of sympathetic stimulation terminate very gradually following cessation of sympathetic activity (Levy & Pappano, 2007). Because of the slower onset and longer-acting results of sympathetic stimulation, examining parasympathetic cardiac control provides a more precise representation of cardiac autonomic modulation than does sympathetic activity.

Maternal Baroreflex Sensitivity

The arterial baroreflex is a negative feedback mechanism that is involved in short-term cardiovascular regulation in both pregnant and non-pregnant populations. Baroreflex control of efferent autonomic effects on R-R intervals are mediated by afferent carotid and aortic baroreceptors that respond to short-term systemic blood pressure variations. Arterial baroreceptors play a key role in the short-term adjustment of BP when the changes in cardiac output, blood volume and peripheral resistance are rapid, such as in exercise, by buffering abrupt fluctuations in blood pressure. Baroreceptor reflexes are especially relevant to heart rate variability because they can phasically operate within the short time period of the highest frequency heart rate rhythms. Arterial baroreceptors are stretch receptors located in the carotid sinuses and the aortic arch which respond to high pressures and provide one of the body's homeostatic mechanisms for blood pressure maintenance. In contrast, cardiopulmonary receptors

in the atria respond to low pressures, and are not responsible for short-term regulation. The arterial baroreceptors provide a negative feedback loop where elevated blood pressure causes distension in the aortic arch and carotid sinus, activating the stretch-sensitive mechanoreceptors. Resulting impulses travel up the sinus nerve, through the glossopharyngeal nerve (cranial nerve IX), ending in the nucleus of the tractus solitarus (NTS) in the medulla. The NTS is the central control site for chemoreceptors and baroreceptors. Stimulation of the NTS results in inhibition of SNS impulses to the heart and peripheral blood vessels, resulting in decreased heart rate, peripheral vasodilation (decreasing peripheral resistance) and decreased BP. Stimulation of the vagal nuclei (cranial nerve X) in the medulla contributes to a reduction in heart rate, and ultimately the lowering of cardiac output and BP through reduced heart rate. Hypertension results in diminished baroreceptor sensitivity; as the carotid sinus becomes stiffer and less sensitive due to high intra-arterial pressures, the outcome being any increase in carotid sinus pressure elicits a smaller decrease in systemic vascular resistance than it would at normal levels of BP (Levy & Pappano, 2007). The baroreceptor-cardiac reflex is measured as the R-R response (in ms) to a change in BP in the same direction for three or more beats (See Appendix B; Blaber, Yamamoto & Hughson, 1995; see appendix B).

Spontaneous baroreflex sensitivity measurement involves the computer scanning of values obtained from continuous recordings of spontaneously fluctuating BP, which are accompanied by electrocardiogram sequences of parallel beat-by-beat fluctuations in R-R interval. The degree of pulse interval response to any given sequence of spontaneous BP fluctuation is used to calculate the baroreflex slope. The mean of the slopes of the sequences is used to quantify the average baroreflex sensitivity during the period of data collection (Parlow, 1993). Though there are other means of measuring baroreflex sensitivity, the spontaneous baroreflex method is most useful due to its non-invasive methodology. The non-invasive nature

of HRV and spontaneous baroreflex data collection methods are of particular interest to researchers working with pregnant populations. They provide a method for examining short-term autonomic nervous system modulation in the presence of maternal cardiovascular complications with no risk to mother or fetus.

Influence of Respiration on Maternal Autonomic Regulation

As respiration modulates autonomic activity, the strongest component of vagal modulation of R-R interval variability is related to respiratory activity. In general, inspiration results in decreased R-R interval and accelerated heart rate as a result of increased SNS activity, whereas expiration results in increased R-R interval and decelerated heart rate due to increased PNS activity (Haggenmiller et al., 1996). Studies examining the effect of controlled respiration on HRV are conflicting. Some authors (Cooke et al., 1998) argue that voluntary control of breathing is the most efficient means of studying short-term HRV, whereas others (Patwardhan, Evans, Bruce, Eckberg & Knapp, 1995) argue that vagal tone and modulation of heart rate is not altered during metronomic breathing and that metronomic breathing is the best method available to interpret high-frequency power in the heart rate spectrum. Others (Pinna, Maestri, La Rovere, Gobbi & Fanfulla, 2006) found evidence that paced breathing does not alter cardiovascular autonomic function when compared with spontaneous breathing. Still others (Mallani, Pagani, Lombardi & Cerutti, 1991; Ori, Monir, Weiss, Sayhouni & Singer, 1992) have found evidence that controlled breathing to a metronome increases high-frequency power in heart rate spectra, which suggests enhanced vagal heart rate modulation or increased vagal tone. In one study in the nonpregnant population, low frequency arterial pressure oscillations were not influenced by respiration rate or type of breathing (i.e., spontaneous, hyperventilation, fixed frequency), suggesting an independence of low frequency rhythms from respiratory activity (Badra et al., 2001).

There remains a discrepancy in the literature regarding the exact respiratory rate affecting respiratory sinus arrhythmia, and inconsistent methodologies between studies with standardized breathing protocols in respect to respiratory rates used exacerbates the difficulty in comparing the results of studies. Furthermore, there is convincing argument that conscious control over respiration exerts a small but significant increase in mean heart rate and a decrease in respiratory-associated variation in heart rate. Padwardhan and colleagues (1995b) demonstrated that voluntary control of breathing reduces R-R interval spectral power. Wallin and colleagues (2005) demonstrated that mental stress increased arterial pressure, heart rate, muscle SNS activity and cardiac norepinephrine spillover; it is assumed that voluntary control of breathing would require more mental effort than spontaneous breathing. In the pregnant population, Schmidt-Stutzman (2005) found that spontaneous resting respiratory rate did not influence any resting BRS outcomes in women at 20 or 36 weeks gestation.

Effects of Maternal Hypertension/Obesity on the Fetus

As the fetus is physically dependant on its mother via the placenta for growth and development, it is logical to presume that maternal factors such as cardiac autonomics strongly influence fetal health and development. Examining maternal and fetal factors together could provide insight into the reciprocal relationship between the two, allowing for a better understanding of fetal health and well-being. Typically, the mother and fetus are examined separately.

The principal influence on birth weight, the placenta is the vector for all maternal-fetal gas, nutrient and waste exchange. Initiation of development occurs when the blastocyst initiates invasion of the endometrium on day 6 or 7 post conception, and results in complete fetal-placental circulation by five weeks post conception. Complete fetal-placental-maternal circulation is not established until 10 weeks post conception, and prior to this time, substances in the

maternal blood must diffuse through extracellular fluid in order to reach the embryo. Anatomically, physiologically and pathologically unique, the human placenta is characterized by the absence of maternal tissues so that maternal blood comes into direct contact with the trophoblast, and resembles placenta from only a few primate species. Providing the sole means of gas and nutrient supply to the fetus, any damage or disease involving the placenta can have profound effects on the fetus. Maternal hypertension is associated with decreased placental perfusion (Brown, 1995), whereas maternal obesity is associated with an accumulation of macrophages and inflammation within the placenta (Challier et al., 2008), and increased placental weight (Swanson & Bewtra, 2008).

In clinical practice today, two standardized tests of fetal well-being have been developed. They are the nonstress test (NST) and biophysical profile (BPP). Both of these tests employ observations of spontaneous behaviour in order to determine the current health status of the fetus and guidelines have been established for their conduct and interpretation (SOGC, 2007). The nonstress test (NST) measures spontaneous fetal heart rate changes continuously over 20 min while the mother is at rest. The test depends on transient fetal heart rate accelerations in response to fetal movement, with 2 FHR accelerations of greater than 15 beats per min above baseline lasting 15 seconds or more considered normal in fetuses 32 weeks GA or older. Mean FHR gradually decreases from about 175 bpm in the ninth week of gestation, until the baseline FHR near term varies between 110 and 150 bpm (Nijhuis et al., 1998; Pillai & James, 1990; Rooth, Huch & Huch, 1987). It is generally accepted that the FHR decrease is mediated by increased parasympathetic tone which overrides the accelerating influence of the sympathetic activity, which develops first (eg. Nijhuis et al.). Changes in vagal function can furthermore be expected to lead to an increase in heart rate variability, such as the increase in measures of short- and long-term variability observed by Van Leeuwen and colleagues (1999).

Like the heart rate of adults, FHR is controlled through the reciprocal action of the parasympathetic and sympathetic branches of the autonomic nervous system. FHR normally fluctuates by 5 to 15 bpm around the mean. Only after the introduction of electronic means of monitoring fetal heart rate in the 1960s was tracing and observation of the subtle variations made possible. In a study comparing intrapartum fetal heart rate patterns in hypertensive and normotensive pregnancies, 20.5% of fetuses of women with hypertension had ominous FHR patterns compared to only 6.5% of matched control fetuses of normotensive women. "Ominous" FHR tracings were defined as those with baseline FHR > 160 bpm with a silent pattern (i.e., decreased FHR variability) or prolonged (> 5 minutes) FHR decelerations, or repetitive variable decelerations (frequently occurring FHR decelerations ≥ 15 bpm of varying severity observed on the NST; Montan & Ingemarsson, 1989). In a sheep model, chronic placental insufficiency was associated with a 30% decrease in the number of fetal heart rate accelerations 21 days after embolization. Control fetuses experienced a gradual increase in heart rate variability with advancing gestational age, whereas the fetal heart rate variability of the embolized fetuses remained unchanged, and was 20% lower than that of controls 21 days following embolization (Murotsuki, Bocking & Gagnon, 1997). In both fetal sheep (Kardon, Peterson, & Bishop, 1974; Cohn et al., 1974) and monkey (Martin, 1978), an increased HRV was found in response to acute hypoxemia. It is apparent that insufficient placental oxygenation is related to alterations in FHR variability; however, the differences in response to acute vs. chronic hypoxemia could reflect fetal adaptation to placental insufficiency over time.

In the single study that could be found comparing fetal heart rate in the standing and supine positions, no positional differences in FHR were found in uneventful pregnancies (Van Katwijk & Wladimiroff, 1991). However, no studies to date could be found examining the effect

of maternal HRV on FHR in the standing position, or the effect of standing on FHR in overweight or hypertensive pregnant women.

The BPP includes a number of variables that reflect the current fetal condition. These include at least 3 body movements, good muscle tone and 30 s of continuous breathing in a 30 min observation, and one that reflects fetal condition over a longer time span [amniotic fluid index (which varies over gestational age and reflects fetal kidney function)].

In the near-term sheep fetus, short-term, moderate hypoxemia results in a distinct decrease in movement, including forelimb, eye, and breathing movements (Boddy, Dawes, Fisher, Pinter & Robinson, 1974; Natale, Clewlow & Dawes, 1981). However, if hypoxemia is maintained in the absence of metabolic acidemia, movement activity returns to baseline after several hours (Bocking, Gagnon, Milne, & White, 1988). Further, upon stepwise reduction of oxygenation over several days in both human (Bekedam, Mulder, Snijders & Visser, 1991; Gagnon, Hunse & Vijan, 1990) and sheep (Richardson, Carmichael, Homan, & Patrick, 1992) fetuses, a marked decrease in fetal movement is observed only when the hypoxemia is severe enough that acidemia develops. This is suggestive of an adaptive response which mitigates the effects of hypoxemia below certain levels.

Though fetal behaviour is assumed to reflect the development and function of the central nervous system (Hepper, 1995), the NST and BPP only reflect the most fundamental properties of the brain stem necessary for survival, such as heart rate and breathing. As these functions are critical for life, it is hypothesized that they may be maintained at the expense of the development of other nonessential systems and account for the fact that the tests are not predictive (Kisilevsky & Hains, 2005).

A focus on fetal response to acoustic stimulation as an augment to the NST began after Murphy and Smyth (1962) reported that two fetuses of diabetic women responded to pure tones

with increased heart rate at 30 weeks GA, failed to respond to the tones at 34 weeks GA and were subsequently stillborn. From this observation, Read and Miller (1977) speculated that fetal response to sound might have prognostic value in the assessment of fetal well-being. Subsequently, various investigators have examined fetal response to sound as a method of assessing fetal health. To date, however, no standardized stimuli or protocol have been developed and study remains experimental.

Technological advances in ultrasound and image processing techniques have allowed for a more thorough study of fetal behaviour over the past two decades. After a half-century of debate, indisputable evidence for fetal hearing emerged in the mid-1980's (see review by Kisilevsky & Low, 1998). As a result, sensory studies moved to in utero from the newborn, thus enhancing the use of response to sensory stimuli to map early brain development. Kisilevsky, Muir and Low (1989) reported that the reliable threshold for FHR acceleration in response to airborne high-pass filtered white noise in term fetuses is between 105 and 110 dB. Subsequently, they characterized the onset of hearing at 30 (± 1) weeks GA and the maturation of the heart rate and body movement response over gestation (Kisilevsky, Pang & Hains, 2000).

Development of the Fetal Auditory System

The first signs of the developing ear can be seen by the 22nd day of gestation as a thickening of the tissues on either side of the rhombencephalon. The cochlea of the inner ear develops from the otocyst and begins to curl in the 6th week of gestation, appears functional by 18 weeks and reaches its full adult size by the 20th week. Within the cochlea, the organ of Corti begins to develop within the 8th gestational week. While none are functional, the first inner hair cells and the three rows of outer hair cells are differentiated by the 11th gestational week, and their final positioning on the basilar membrane is complete at the 14th week (Pujol, 1993 original in French; cited in Lecanuet & Schaal, 1996 in English). Because the fetal inner ear and the external

auditory meatus are filled with amniotic fluid and fluid is present on both sides of the tympanic and round widow membranes, it is unlikely that sound can be effectively transmitted through inducing vibrations of the tympanic membrane. Therefore, it is suggested that sounds in the amniotic fluid may be transmitted to the fetal inner ear through bone conduction (Gerhardt et al., 1996). It has been demonstrated that the inner ear can be excited by a bone vibrator applied to the skull bone or to the contents of the cranial cavity (e.g., through the fontanel or a craniotomy; Sohmer, Freeman, Geal-Dor, Adelman, & Savion, 2000)

The human brainstem auditory pathway is relatively mature by term. However, only the most superficial layers of the cortex possess mature axons (Moore, 2002). The neurofilament content of brain stem auditory axons becomes adult-like between 16 and 28 weeks GA (Moore, Guan & Shi, 1997). Myelination of the axons is initiated between 26 and 28 weeks GA (Moore, Perazzo, & Braun, 1995), and evidence of rapid synchronous conduction in brain stem pathways is detected by 29 weeks (Ponton, Moore & Eggermont, 1996).

Several authors (Barden, Peltzman & Graham, 1968; Scibetta, Rosen, Hochberg & Chick, 1971; Staley, Iragui & Spitz, 1990) have established that auditory evoked potentials (AEPs; a measure of sensory functioning) are not consistently detectable in premature infants at 24-25 weeks GA. However, the AEPs become stable by 30-32 weeks GA; the sound thresholds required to elicit a brainstem response gradually decrease with development, until by 35 weeks GA, the thresholds are only 10-20 dB different from the threshold of adults. These findings are supported by Holst et al. (2005) using fetal magnetoencephalgraphy. They found a decrease in response latency over increasing age for normal fetuses at 29 weeks GA to term and newborns. This indicates a continuous development of the auditory system, auditory processing capabilities and related brain development, and supports the assertion that fetuses can hear and process external environmental sounds from the beginning of the third trimester.

The fetal sound environment is attenuated by a variety of mechanisms. External sounds are physically attenuated by maternal fluids and tissues. Higher frequency sounds are attenuated by about 35-40 dB, while lower frequency sounds are only slightly reduced (e.g., Querleu et al., 1988).

Fetal hearing is affected by the relatively hypoxic state of placental oxygenation. The fetus receives oxygen by placental diffusion from the maternal circulation. The placenta is much less efficient at oxygen diffusion than is the pulmonary system by a factor of 0.09 (Longo & Ching, 1977). Thus, when the arterial oxygen concentration of the mother is 14.3% that of the umbilical vein (blood returning from the placenta to the fetus) is only 8.6% (Metcalfe, Bartels & Moll, 1967). Furthermore, the anatomy of fetal circulation allows for a mixture of venous blood from the lower parts of the fetal body with the blood of the umbilical vein, which travels to the upper body, further reducing the oxygen concentration. When similar hypoxic conditions were examined in animal models, an auditory nerve-brainstem evoked response threshold elevation of 20 dB was found. It is hypothesized that the threshold elevation is a result of a hypoxia-induced depression of the magnitude of the endocochlear potential (Freeman, Goitein, Attias, Furst & Sohmer, 1995). A decrease in this potential leads to an elevated auditory threshold. This suggestion is supported in human experiments, where human fetal movement response to sound occurred at lower stimulus intensity (thresholds) when the mother was breathing oxygen than when she was breathing room air (Sohmer, Geal-Dor, & Weinstein, 1994).

Placental insufficiency associated with maternal hypertension affects auditory and nervous system function and development. For example, very low birth weight and growth restricted fetuses/newborns are at increased risk of impaired auditory function including sensorineural hearing loss (e.g. Kurtzberg, Hilpert, Kreuzer & Vaughan, 1984; Cone-Wesson Kurtzberg & Vaughan, 1987). As well, small for gestational age infants of mothers who had

hypertension in pregnancy have shown differential auditory brainstem responses (Sarda, Dupuy, Boulot, & Rieu, 1992). In guinea pigs, it has been demonstrated that chronic placental insufficiency initiated in the second half of gestation results in subtle functional alterations in the auditory pathway, including longer latency periods as a function of stimulus rate, suggesting that the auditory brainstem is more susceptible to adaptation in animals affected by placental insufficiency. In fetal sheep, a deficiency of large myelinated fibres and a slowed conduction velocity of the peroneal nerve was demonstrated in fetuses affected by placental insufficiency (Rees, Proske & Harding, 1989). Building on this research, preliminary results have indicated that prenatally compromised guinea pigs possess compromised auditory nerve axonal diameter and myelin sheath thickness, and smaller ganglion cells at term (Rees, unpublished data in Rehn et al., 2002).

In summary, development of the fetal auditory system begins early in gestation, and continues well after birth. It is well established that placental insufficiency impedes auditory system development, and evidence exists demonstrating atypical voice processing in fetuses of hypertensive women (Lee et al., 2007).

Language and the Fetus

Not only can late term fetuses hear, but there is emerging evidence that they learn ubiquitous sounds. Hepper (1991) found that term (37-39 weeks GA) fetuses exhibited changes in movement when they heard a piece of music they had previously been exposed to. However, term fetuses did not demonstrate learning when the music was played backwards. There were no differences in response between 29-31 week GA fetuses that had and had not been previously exposed to the music, indicating a "learning" response rather than a response to the music itself. DeCasper and colleagues (1994) found that fetal heart rate decreased in response to a recording of a female stranger reciting a rhyme their mother had recited during the previous 4 weeks but heart

rate did not change in response to a recording of a control rhyme their mother had never recited. Kisilevsky and colleagues (2003) demonstrated that fetuses can tell the difference between their mother's voice and that of a female stranger's. They showed that fetuses of low-risk, uneventful term pregnancies respond to a tape-recording of their own mother's voice with an increase in heart rate (5 beats per min, bpm) and to a recording of a female stranger's voice with a heart rate decrease (4 bpm). These findings indicate that auditory processing and the learning of speech, language, and voice characteristics begins prior to birth.

Although few studies have examined fetal speech/language learning, a number of studies have examined language learning in the newborn. DeCasper and Fifer (1980) found that newborn infants learned to produce a recording of their own mother's voice and produced it more often than a recording of a female stranger's voice through sucking on a nonnutritive nipple in different ways. In studies employing similar methods, Moon, Cooper and Fifer (1993) found that two day old infants demonstrated a preference for their native language over a foreign one, and DeCasper and Spence (1986) found that newborns showed a preference for a passage they had been exposed to in utero.

Several hypotheses attempting to explain how young infants discriminate between languages have been presented. One, the rhythm-based language discrimination hypothesis is the result of evidence that newborns respond to the intonation and rhythmic properties of language. It is suggested that newborns sort sentences into sets based on timing and rhythmic properties. Ramus and colleagues (2000) examined language discrimination in human newborns, and found that newborns demonstrated signs of discrimination between Dutch and English sentences, but not if the sentences were played backwards. Nazzi, Bertoncini and Mehler (1998) observed newborn language discrimination only when English and Dutch sentences were contrasted with Spanish and Italian. Building on these studies, Tincoff et al. (2005) found that tamarin monkeys

could discriminate Polish from Japanese (different rhythmic classes), but failed to discriminate English and Dutch (same rhythmic class), and failed to discriminate backward utterances from different and same rhythmic classes. These results provide further evidence that language discrimination is facilitated by rhythmic differences between languages, although such discriminations are not uniquely human as non-human primates demonstrate these abilities as well.

Pena and colleagues (2003) found an increase in left cerebral hemisphere blood volume compared to the right hemisphere when neonates listened to a woman reading a passage in their own language. The same infants showed no difference in blood volume between hemispheres when the passage was played in reverse, or during a silent control trial. The authors speculated that backwards speech disrupts the spectral patterns contained in natural speech utterances, reflecting the articulatory dynamics of the speaker's vocal tract and aiding the listener in detecting distinct linguistic units from the continuous acoustic signal. Previous studies (e.g., Nazzi et al., 1998) have established that newborns use prosodic and rhythmic cues to distinguish language; playing a voice in the reverse disrupts the natural prosody and rhythm of the language. It is speculated that some property of forward speech is required to activate the areas of the left cerebral hemisphere involved in speech processing, and it has been suggested (Nazzi & Ramus, 2003) that it is sensitivity to rhythm, rather than language recognition, that supports language recognition.

No studies to date have examined language discrimination across different vocal classes by fetuses and only one study (unpublished master's thesis, Gilmour 2004) could be found that examined fetal response to a voice played in the reverse. While the fetuses of overweight and normal weight women responded to the playing of their mother's voice with heart rate accelerations, they responded with a FHR deceleration immediately following the offset of the

reverse voice (Gilmour, 2004). In the proposed study, fetal response to the mother's voice played forward and reverse will be examined in order to further understand the nature of the response.

Over the past six year period, the Kisilevsky laboratory has been examining fetal response to the maternal voice in low-risk pregnancies. Preliminary analyses of data aggregated over studies have demonstrated a maturation of fetal response to maternal voice in low-risk pregnancies. Fetuses from 32 to 37 weeks GA respond to their mother's voice with an initial decrease followed by an increase in fetal heart rate. After 37 weeks GA there is an initial heart rate increase (Kisilevsky & Hains, 2008 March). The initial decrease in FHR response may indicate a cardiac orientating response to the stimulus, the physiological correlate of cognitive processing originally described by Sokolov (1963). The cardiac orientating response is elicited by low-intensity stimuli and is associated with a HR deceleration (Sokolov). Groome and colleagues (1999) found that term fetuses demonstrated decreased mean FHR in response to the playing of single syllables; interestingly, a greater decrease was observed while fetuses were in quiet as opposed to active sleep (Groome et al., 1999).

While fetal spontaneous and sound elicited behaviour have been characterized in low-risk uneventful pregnancies, few studies have examined fetal spontaneous and sensory induced responses in pregnancies complicated by maternal hypertension or excess body weight. In the few studies that have been reported, atypical response to sensory stimulation has been the most consistent finding. No significant differences in examining spontaneous behaviour were found between fetuses of overweight and normal weight mothers (Gilmour, 2004), or those of hypertensive and normotensive mothers (Lee et al., 2007). However, both hypertensive (Warner et al., 2001) and overweight (Gilmour, 2004) groups of women had significantly higher average amniotic fluid index than did the control (normotensive/normal weight) groups. Examining fetal response to sensory stimulation, Warner and colleagues (2001) found that fetuses of hypertensive

women had fewer body movements, a lower magnitude of fetal heart rate accelerations, and a lack of cardiac-body movement coupled responses to a vibroacoustic stimulus (a compound stimulus including sound and vibration) than did fetuses of normotensive mothers. Lee and colleagues (2007) observed that fetuses of normotensive mothers demonstrated a heart rate increase during the playing of their own mother's voice while fetuses of hypertensive mothers showed a brief response limited to the first few seconds following maternal voice offset. Furthermore, they observed that in both groups of fetuses, a greater fetal heart rate change was observed when the amniotic fluid index was above compared to below the median (i.e., 150 mm), indicating that amniotic fluid index could be an independent moderator of fetal auditory sensitivity. It was hypothesized that differential fetal responding to the mother's voice in pregnancies complicated by maternal hypertension may be attributed to a functional elevation of the sensorineural threshold or a delay in auditory system maturation, signifying functional differences during fetal life or subtle differences in the development of the central nervous system at a level higher than the brainstem.

In a meta-analysis, Kisilevsky and Hains (2005) found no significant differences in the number of spontaneous fetal heart rate accelerations between fetuses in pregnancies complicated by chronic or pregnancy-induced hypertension versus normotensive pregnancies. However, in a study of fetal behaviour in fetuses of preeclamptic (the most severe form of hypertension during pregnancy) and normotensive pregnancies, Swansburg, Brown, Hains, Smith and Kisilevsky (2005) found an association between maternal preeclampsia and parasympathetic nervous system indicator as well as their interaction on the number of fetal heart rate accelerations observed during non-stress testing. These findings may reflect the severity of the maternal disease and its effect on the fetus. In light of the contrasting finding between the two groups, perhaps the maternal autonomic effect on the fetus only manifests in severe disease, as the hypertensive

mothers in the earlier study had evidence of hypertension without kidney (i.e., multi-organ) involvement.

Examining fetuses in pregnancies complicated by obesity but not hypertension, Gilmour (2004) found that fetuses of overweight women showed greater fetal heart rate acceleration to the playing of a recording of their mother's voice reading a passage than did fetuses of normal weight women. Furthermore, Schmidt-Stutzman (2005) found that fetuses of overweight women who participated in a walking program (compared to overweight and normal weight women not enrolled in the walking program and normal weight women participating in the walking program) showed an increased FHR in response to the maternal voice as well as following the offset of the maternal voice. The reason for this response is a matter of speculation. The author hypothesized that this differential response could be attributed to sound enhancement as it passes through the maternal tissues.

In summary, studies in this laboratory of fetal behaviour in pregnancies complicated by maternal hypertension (Brown, Lee, Hains, & Kisilevsky, 2008; Lee et al., 2007; Swansburg et al., 2005; Warner et al., 2001) and/or overweight (Gilmour, 2004; Schmidt-Stutzman, 2005) have consistently demonstrated atypical sensory-elicited fetal behaviour as compared to those in low-risk, normotensive, normal weight pregnancies. However, as hypertensive women tend to be overweight, the condition responsible for the difference in behaviour is poorly understood. To date, no studies could be found which compared fetal behaviour in hypertensive and overweight pregnant women. Furthermore, though differences in cardiac autonomic control in obese non-pregnant subjects have been demonstrated (e.g. Laederach-Hoffman, Mussgay & Ruddel, 2000; Rossi et al., 1989), only one study to date has explored cardiac autonomic function in overweight pregnant women independent of hypertension. Moreover, only one study has examined the effects of maternal posture (standing vs. supine) on FHR, and none have looked at the effects of posture

on FHR in high-risk populations. Understanding the relationship between maternal weight, blood pressure and HRV/BRS in pregnancy may provide more comprehensive insight into the nature of the effects of overweight and hypertensive disease in pregnancy. The ultimate goal of this field of autonomic research is the detection of early indicators or prognostic indices of the development of pregnancy-induced complications, including gestational hypertension. Furthermore, understanding the relationship between maternal cardiac autonomic function and fetal behaviour will help to determine which pregnancy complications associated with maternal hypertension are attributable to the hypertension itself, and which are attributable to the maternal overweight (a modifiable risk factor). Such information may ultimately be useful in the development of more definitive tests of fetal well-being and/or interventions to aid in weight reduction which will moderate maternal blood pressure.

This study will examine the following research questions: 1) What are the effects of maternal hypertension and/or excess body weight on maternal heart rate variability (HRV) when compared to HRV in uneventful, normal weight, normotensive pregnancies? 2) What is the effect of maternal posture (standing vs supine) on maternal heart rate variability and fetal heart rate in hypertensive, overweight, and uneventful pregnancies? 3) What is the relationship between maternal heart rate variability and spontaneous fetal heart rate in hypertensive, overweight and uneventful pregnancies? 4) Is there a relationship between maternal BP (systolic and/or diastolic), HRV, and baroreflex sensitivity and fetal spontaneous heart rate, body and breathing movements and auditory-elicited behaviour? 5) Is there a difference in auditory processing of the mother's voice (forward and/or backward) among fetuses of women with hypertension, women who are overweight, and those with an uneventful, normal weight, normotensive pregnancy? Figure 1 outlines the possible relationships between the maternal and fetal factors associated with hypertension and obesity.

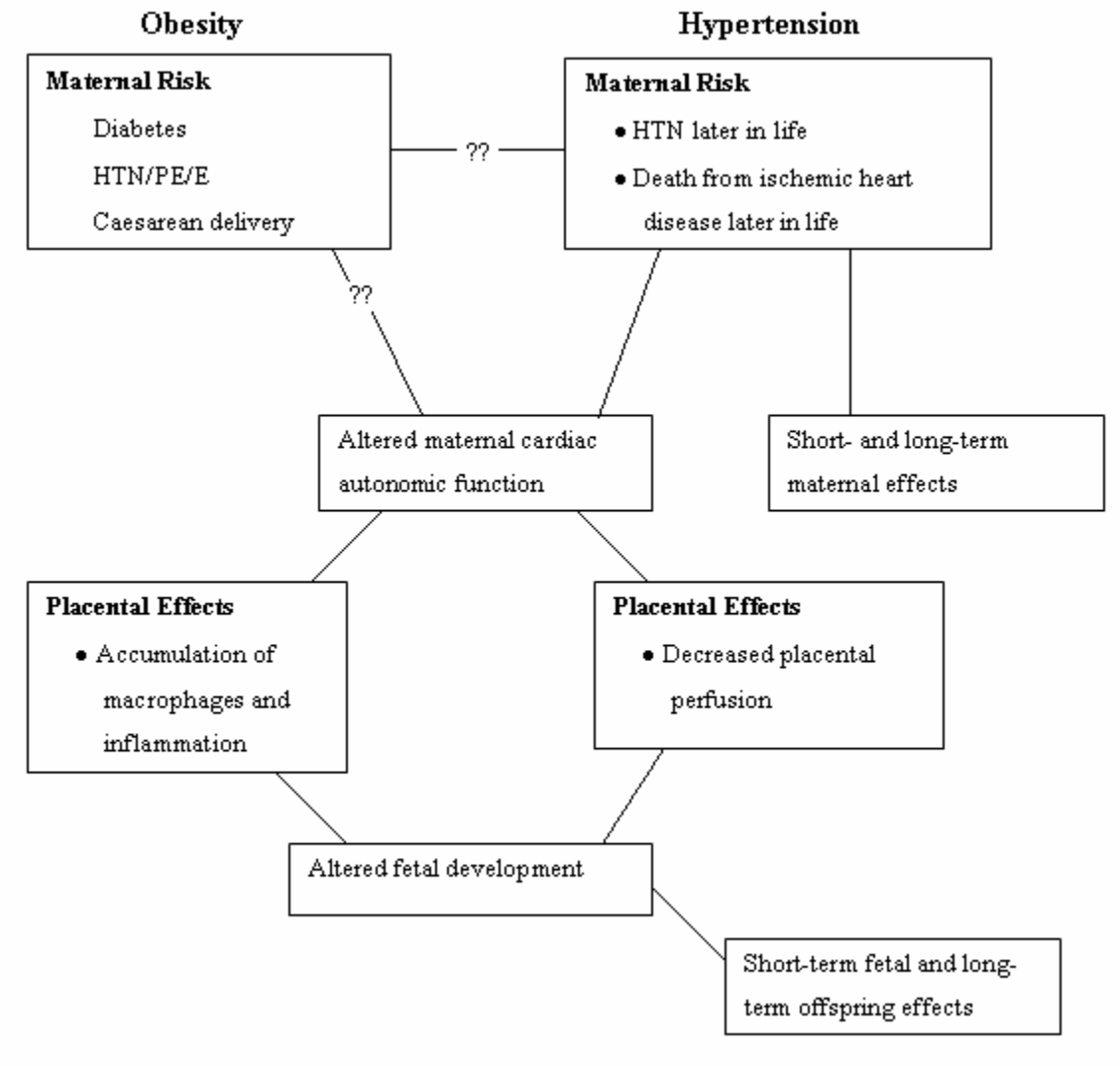

Figure 1: Model of the possible relationships between the maternal and fetal factors associated with hypertension and obesity.

CHAPTER 3
Methods

Participants

Sixty five pregnant women [n=21 hypertensive, n=20 overweight normotensive, n=24 uneventful, normal weight normotensive (normal weight comparison group)] at ≥ 35 weeks gestational age were recruited from the out-patient obstetrical clinics at Kingston General Hospital or by word of mouth for testing on one occasion. Gestational age was determined from the first day of the last menstrual period, if periods were reliable (accuracy rate of 75-85%) and/or from early ultrasound scan.

For all groups, the inclusion criteria were: maternal age of at least 16 years, absence of maternal systemic comorbidities (e.g., diabetes, thyroid disease), able to read, write, speak and understand English, experiencing a singleton pregnancy, at least 35 weeks GA. Information regarding medication usage during this pregnancy (e.g., antidepressants or asthma medications) was collected.

For the hypertensive group, the inclusion criteria were: pregnant women diagnosed with hypertension based on two clinic blood pressure (BP) readings of ≥ 140 systolic and/or 90 diastolic mmHg taken at least 6 hours apart. Four tested hypertensive subjects subsequently went on to develop preeclampsia following participation in the study. These subjects were included in data analysis. Women with proteinuria (at least 0.3g of protein in a 24 hour urine specimen) and/or preeclampsia at the time of testing were not recruited for the study in order to avoid the confound of systemic disease. Because antihypertensive medications (e.g., beta blockers) alter maternal HRV, and the effects on FHR characteristics are unknown (Waterman et al., 2004), women taking antihypertensive medications were excluded. However, it was found on the day of

testing that one hypertensive subject was taking propranolol for migraine prophylaxis. This subject's HRV data was lost due to experimenter error, but the spontaneous fetal behaviour data were within 2 SD of the mean of the data for the hypertensive group, and subsequently included in data analyses. The diagnostic criteria for hypertension in pregnancy changed in March 2008. Under the new criteria, hypertension in pregnancy is now defined as two diastolic BP readings ≥ 90 mmHg (SOGC, 2008). Eleven of the subjects in this study met the new diagnostic criteria for hypertension in pregnancy.

For the overweight group, the inclusion criteria were: a calculated prepregnancy/earliest recorded BMI ≥ 25 kg·m², and a BP < 140 systolic and 90 diastolic mmHg prior to testing. For the low-risk, normotensive, normal weight comparison group, the inclusion criteria were: a prepregnancy/earliest recorded BMI < 25 kg·m², experiencing an uncomplicated pregnancy and delivery of a healthy, full-term infant. When the earliest recorded weight was later than the early second trimester, women's self-reported weight was used to calculate BMI.

A total of four subjects were excluded from fetal data analyses. One normal weight comparison subject delivered at 35 weeks and 2 days gestational age; but the cardiac autonomic modulation data were included. One subject in the normal weight comparison group had treated thyroid disease and was found to be breech on day of testing. Because breech fetuses respond differently to sound stimulation (Van der Meulen, Davies & Kisilevsky, 2008), and are considered high-risk, both the maternal and fetal data for this subject were excluded. Two additional subjects were tested but not included in any data analyses: one normal weight comparison group subject with abnormally low amniotic fluid estimate and a growth restricted fetus at testing and one hypertensive subject due to experimenter error. Therefore, 61 pregnant women and their fetuses (n=20 hypertensive; n=20 overweight normotensive; n=21 normal weight comparison) were included in fetal data analyses.

Further, the maternal cardiac autonomic data in both the standing and supine position was excluded for 10 subjects: n = 2 for treated thyroid disease; n = 8 for recording equipment failure). The standing HRV data for four subjects and the supine HRV data for two subjects were excluded due to equipment failure.

Two hypertensives and one overweight subject were found to be on citalopram on the day of testing. Citalopram is rated a pregnancy risk category C (risk cannot be ruled out), but because guidelines state there is an apparently normal birth outcome (ACOG, 2008), these subjects were included in the data analyses. It was found on the day of testing that two overweight subjects had treated thyroid disease. The HRV data for these two subjects were excluded, but the fetal data for these subjects was ultimately included in data analyses. See Figure 2 for a consort diagram outlining participant exclusion from aspects of the study.

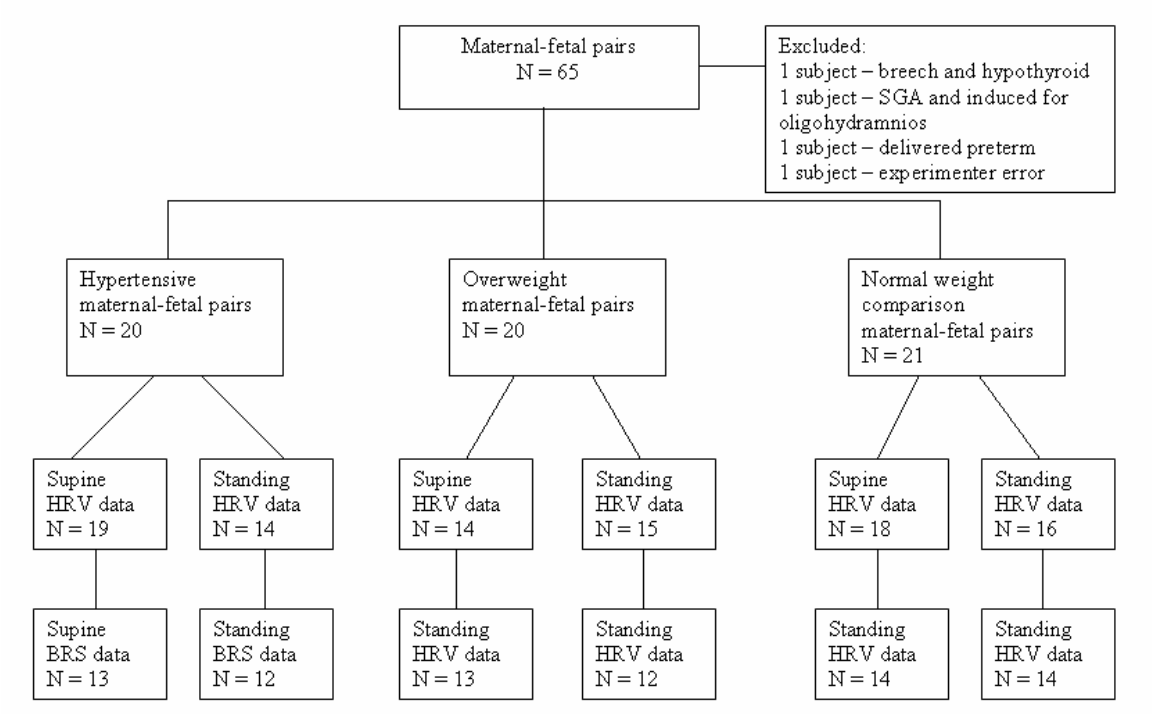

Figure 2. Consort diagram showing the flow of participant through the aspects of the study

Sample size was chosen from the literature, where groups of 10 fetuses compared to 100 have been shown to be reliable when stimulus and no-stimulus trials are compared (Kisilevsky, Muir & Low, 1989) and which are sufficient to demonstrate differences in maternal autonomic regulation (Swansburg et al., 2005). GA was set at near term as data from our laboratory have demonstrated that fetuses show a reliable response to the maternal voice at this time.

Testing took place in the Maternal-Fetal-Newborn Studies Laboratory located in the hospital, adjacent to the obstetrical outpatient and inpatient services. Ethics approval for the study was obtained from the Queen's University Health Sciences and Allied Teaching Hospitals Research Ethics Board prior to recruitment of subjects. Informed, written consent was obtained from each pregnant woman prior to testing (See Appendix B).

Equipment

A LifeSource One Step Auto-Inflation Blood Pressure Monitor Model UA-767 was used to measure BP on the left arm. A Finapres® 2300 digital automated blood pressure monitor was used to measure the spontaneous arterial blood pressure (ABP) by finger photoplethysmography based on unloaded artery principle for further baroreflex analyses. The reliability of this equipment in detecting changes in beat-to-beat BP changes has been established when compared to invasive measurements (Imholz et al., 1988; Jagomagi, Raamat & Talts, 2001).

The HRV data were collected using three standard surface latex-free electrocardiograph (ECG) electrodes to detect electrical activity of the heart. The electrodes were connected to a Spacelab 514 T cardiac monitor with a QRS detector to obtain ECG recordings of R-R intervals. The analog R-R interval output from the cardiac monitor was digitized by an analog-digital converter (QDS-16, Metrabyte), providing an R-R accuracy of 1 ms through a sampling rate of 1000 Hz (Yamamoto, Hughson & Peterson, 1991; Parlow et al., 1995). All digital R-R output data were stored on a personal computer (PC).

PRAAT computer software (version 4.4.27) running on a pc was used to record, manipulate, and play the voice stimuli. Voice stimuli were delivered through an Auratone speaker. Hewlett-Packard cardiotocograph (connected to a computer running custom software for data acquisition) with an event marker was used to record the FHR during the NST and sound stimulation; the onset and offset of each period of the auditory procedure was marked on a paper strip recording and a computer text file. A Siemens Sonoline SL ultrasound machine with built-in VHS was used to observe and video record fetal body and breathing movements and estimate amniotic fluid during the BPP and body movements during sound stimulation. The mother listened to soft jazz or guitar music through Panasonic noise cancellation headphones played on a Sony personal CD player during the voice trials. The A scale of a Bruel and Kjaer Sound Pressure Level (SPL) meter (model 2235) was used to measure the intensity of the sound stimuli in air at 10 cm.

Procedure

Following informed written consent, each maternal-fetal pair underwent a standardized procedure, lasting approximately 120 min. If the participants' height and weight (prepregnancy and weight on the day of testing) were not available from clinic records, self-reported data were obtained. Next, three blood pressure measurements (mmHg) were taken on the participant's left upper arm and recorded while the participant was sitting. The lower edge of the BP cuff was placed approximately 2.5 cm above the brachial artery; location of the artery was determined by palpation. Each participant was asked for demographic information, including maternal age, gestation, gravida, parity, smoking and education level (see appendix E for demographic data collection form). Next, the mother read a passage from a children's story, *Bambi* (Salten & Chambers, 1928), for approximately 2 min. Her reading was audio recorded.

The mother was placed in the left lateral semi-recumbent position on a hospital bed and three BP measurements (mmHg) again were taken on the left arm. The left lateral semi-recumbent position was used to prevent aortocaval compression syndrome (the compression of the maternal abdominal aorta and inferior vena cava by the uterus when a pregnant woman lies supine).

Next, maternal arterial beat-by-beat blood pressure was measured continuously via a finger cuff placed on the middle phalanx of the right middle finger connected to a transducer that was placed over the hand at heart level. The transducer was placed at heart level in order to ensure accurate BP readings. Hydrostatic pressure affects blood pressure, and can alter BP by 2 mmHg for every inch above or below heart level (e.g, Pickering et al., 2005). A cardiotocograph transducer was positioned on the maternal abdomen in order to measure spontaneous fetal heart rate simultaneously with maternal heart rate variability. Maternal and fetal heart rates and maternal heart rate variability and arterial blood pressure were then simultaneously recorded for 20 min. During this time, the mother was at rest but not sleeping, with minimal background noise/stimulation. The mother also was asked not to speak or move to reduce stimulation of the mother's sympathetic nervous system which would interfere with the heart rate variability measurement. Fetal heart rate activity was recorded in BPM on a paper strip and digitally in a computer text file in order to later measure FHR variability (Refer to Figure 3 for study design for fetal heart rate measures). Next, the mother was assisted into the standing position, the cardiotocograph was adjusted as necessary, and following a 3 min equilibration period, three BP measurements again were taken on the left arm, and the maternal HRV and beat-by-beat arterial BP and fetal heart rate were recorded for 5-10 min for a minimum of 512 maternal cardiac cycles (i.e., heart beats; Kamath, Fallen & McKelvie, 1991). Next, with the mother again in the left lateral recumbent position with her head elevated, the wand of a real-time ultrasound scanner was

held on the maternal abdomen for 20 consecutive minutes to project a cross-section or longitudinal view of the fetal body which may or may not have included fetal limbs. Spontaneous body movements were counted and breathing movements timed (cumulatively) simultaneously by two independent researchers using digital timers. The distance from the skin surface to the fetal head was measured with the ultrasound callipers, using a method similar to that used to estimate amniotic fluid volume in order to determine the distance of the sound source from the fetal head.

After the observations of spontaneous behaviour change, stimulation with the mother's voice occurred (Refer to Figure 4 for study design during the playing of the voices). FHR and body movements were recorded during the six minute auditory procedure: 2 min of no voice, followed by 2 min of the playing of the mother's voice recording (forwards or reverse; counterbalanced over subjects), followed by 2 min of no voice. The voice stimuli were delivered at an average of 95 dB SPL through a loud speaker held approximately 10 cm above the maternal abdomen. Sound intensity was measured at the maternal abdomen during the procedure to ensure the veracity of the intensity. Ambient noise level measured with all equipment running averaged 44 dB SPL. Following the 6 min auditory procedure there was a 20 min delay during which an estimate of amniotic fluid volume was obtained by measuring the largest pocket (vertical x horizontal) of fluid in each of the four quadrants of the maternal abdomen, and the 4 vertical measurements summed to provide an Amniotic Fluid Index. Manning's method (Manning, 1990) was used to calculate a biophysical profile score. This includes giving a score of 2 (presence) or 0 (absence) for each of: at least three body movements, 30 s of continuous breathing movements, good fetal tone (brisk extension of a fetal limb followed by return to flexion), and at least one, 2 cm X 2 cm pocket of amniotic fluid; with a score of 8 being normal, and a score of 4 or less being abnormal. Finally, the opposite recording was delivered using the same protocol.

Following birth, delivery outcome measures routinely collected (e.g., birth weight, gestational age, head circumference, APGAR scores and cord blood gases) and newborn/obstetrical complications (e.g., hypoxia, resuscitation) while in hospital were obtained from the maternal and newborn medical records.

Maternal Groups	**Obstetrical test**						
	Supine Maternal HRV/NST (20 minutes)		Standing Maternal HRV/NST (10 minutes)		BPP (20 minute)		
	Maternal HRV	FHR	Maternal HRV	FHR	Body Movement	Breathing Movement	AFI
Hypertensive (n=20)							
Overweight (n=20)							
Normal weight normotensive (n=21)							

Figure 3: Study design: maternal HRV and fetal spontaneous behaviour

Maternal Group	Voice processing procedure			Delay	Repeat
	No-sound, pre-voice baseline Period	Voice Period Mother's voice forward or backward (counterbalanced over subjects)	No-sound post-voice period		3 periods Repeated with alternate voice direction
	2 min	2 min	2 min	20 min	6 min
Hypertensive n=20					
Overweight n= 20					
Normal weight comparison n=20 or 21					

Figure 4: Study design: presentation of recording of mother reading a passage

Data Reduction of Maternal Cardiac Measures

For short-term HRV data recordings, the power spectral analysis method was used (TFENSCAPE, 1996). Beat-to-beat heart rate was converted to an interval tachogram representing R-R intervals presented as a function of time. The tachogram was edited (see appendix C) and converted via fast Fourier transformation to a frequency spectrum which separates signals into high and low frequency power peaks. The PNS indicator was calculated from the ratio of high frequency to total power (HF/TP) and the SNS indicator was derived from the ratio of low to high frequency power (LF/HF; TFNESCAPE, 1996; Yamamoto & Hughson, 1991). Analysis of spontaneous baroreflex sensitivity involves the identification and measurement of a change in systolic arterial BP followed by a change in R-R interval in the same direction for three or more beats. A computer software program was used to accomplish this (See appendix D for editing baroreflex sensitivity data; Blaber, Yamamoto & Hughson, 1995).

Data Analysis Strategy

Reliability for spontaneous fetal behaviour measures was determined for the number of fetal body movements and amount of fetal breathing by two trained research personnel who independently scored all participants on-line. Correlation between the two researchers was high for body movement, $r = 0.97$ ($p<0.01$) and for amount of breathing, $r = 0.90$ ($p<0.01$). Therefore, the data from scorer #1 (The person holding the ultrasound wand) was used for data analyses. Reliability was determined for FHR accelerations and decelerations by two trained research personnel who independently scored 12 FHR tracing strips. Correlation between the two researchers was high for both the supine, $r \geq 0.934$ ($p = .000$) and standing, $r \geq 0.802$ ($p < .009$) positions. Only the data from one scorer (JV) was used for analyses.

Data were analyzed using SPSS statistical software package with level of significance set at 0.05; Greenhouse-Geisser adjusted degrees of freedom were used for repeated measures analyses. Separate Chi-squared (frequency data) and one-way analysis of variance (ANOVA; interval data) tests were performed to determine differences in maternal demographic data among groups (See Figure 3). The number of body movements scored via ultrasound during the BPP were analyzed using Chi-squared tests. Between factors were maternal diagnostic group (hypertensive, overweight, normal weight/normotensive). The dependent variables were AFI, amount of breathing (s), delivery outcome information and the number of fetal heart rate accelerations and decelerations ($\geq$ 10 bpm and $\geq$ 15 bpm) during the NST and while the mother was in the supine and the standing positions.

Spectral analysis tabulated maternal HRV in respect to heart rate oscillations and a 1-way ANOVA was used to compare the peak high frequency, low frequency and total powers (ms^2), as well as the PNS and SNS indicators between the three maternal groups (hypertensive, overweight, normal weight normotensive) in the supine and standing positions separately in order

to examine the effect of diagnostic group on these measures. Spectral analysis tabulated maternal HRV in respect to heart rate oscillations and a 1 Between (Position – 2 levels), 1 Within (Group – 3 levels) ANOVA was used to compare the peak high frequency, low frequency and total powers (ms^2), as well as the PNS and SNS indicators between the three maternal groups (hypertensive, overweight, normal weight normotensive) in the supine and standing positions separately in order to examine the different responses to posture change. The sequence method was used to determine the spontaneous baroreflex slope (ms/mmHg; see appendix D). A 1 Between (Group – 3 levels), 1 Within (Position – 2 levels) ANOVA was used to compare the mean slopes of the three groups, as well as the number of FHR accelerations and decelerations (≥ 10 bpm and ≥ 15 bpm) during the supine and standing NST.

A 1 Between, 2 Within ANOVA was performed with Maternal diagnostic group (hypertensive, overweight, normal weight comparison) and stimulus (forwards vs backwards, first presentation) as between factors and Time (1-90 s) and Period of stimulation (prevoice, voice, postvoice) as within factors to examine differences in stimulus-induced fetal behaviours between the three groups over time. Relationships among maternal cardiac variables and fetal spontaneous behaviour were explored using Pearson r product moment correlations.

CHAPTER 4
Results

Maternal and Obstetrical Measures

A one-way ANOVA was used to examine the demographic and birth outcome data over the three groups. As can be seen in Table 1, as planned, the hypertensive and overweight groups compared to the normal weight comparison group had higher average prepregnancy BMIs [M (± SD) = 26.7 (6.1) $kg \cdot m^{-2}$ and 28.9 (3.1) $kg \cdot m^{-2}$ vs. 21.5 (2.2) $kg \cdot m^{-2}$, respectively] and BMIs at testing [M (± SD) = 33.5 (5.4) $kg \cdot m^{-2}$ and 34.8 (3.1) $kg \cdot m^{-2}$ vs. 26.7 (2.1) $kg \cdot m^{-2}$, respectively]. No differences were found between groups regarding maternal age [aggregate M (± SD) = 28.2 (3.9) years], or the number of pregnancies [aggregate M (± SD) = 1.6 (0.9)], or previous births [aggregate M (± SD) = 0.3 (0.5)]. However, fetuses in the hypertensive group were approximately a week older on average at time of testing, than the overweight and normal weight comparison groups (M (± SD) = 37.3 (1.3) weeks vs. 36.0 (0.8) and 36.4 (1.2) weeks].

When the one way ANOVA was repeated for the systolic and diastolic BPs for each position separately (see Table 2) with gestational age used as a covariate, differences were found among the groups. As can be seen in Table 2, there were differences among all three groups in average systolic BP in the sitting position [$F(2, 60) = 43.625$, $p < .001$] and the average diastolic BP in the supine position [$F(2, 58) = 22.407$ $p < .001$]. There were differences found between the hypertensive group and the overweight and normal weight comparison groups in the mean systolic BP in the supine [$F(2, 58) = 23.764$, $p < .01$] and standing [$F(2, 58) = 34.623$, $p < .001$] positions, and in the diastolic BP in the sitting [$F(2, 60) = 29.111$, $p < .001$] and standing [$F(2, 58) = 21.995$, $p < .001$] positions.

A one between (Group – 3 levels) one within (Position – 3 levels) ANOVA was performed to examine the effect of maternal posture on systolic and diastolic BP. As can be seen in Figure 5, there was a main effect of Group [$F(2, 55) = 25.722$, $p < .001$], with the highest systolic BPs found in the hypertensive group in all positions and a quadratic Position X Group interaction [$F(2, 55) = 3.437$, $p < .05$], with the highest systolic BP found in the sitting position in the hypertensive group. As seen in Figure 6, again there was a main effect of Group [$F(2, 55) = 20.389$, $p < .001$] with the highest diastolic BP found in the hypertensive group in all positions. No other effects were found.

Table 1: Means (± SD) and percentages for the maternal demographic and obstetrical characteristics for the hypertensive, overweight, and normotensive-normal weight groups Separately

Measure	Diagnostic Group			
	Hypertensive (n = 20) M (± SD)	Overweight (n = 20) M (± SD)	Normal weight comparison (n = 21) M (± SD)	*p*
Maternal age (years)	29.9 (3.5)	27.5 (4.4)	27.6 (3.5)	
GA at testing[2] (weeks)	37.3 (1.3)	36.0 (0.8)	36.4 (1.2)	< .01
Prepregnancy BMI[1] (kg/m^2)	26.71 (6.1)	28.9 (3.1)	21.5 (2.2)	< .001
BMI at testing[2] (kg/m^2)	33.5 (5.4)	34.8 (3.1)	26.7 (2.1)	< .001
	%	%	%	
Nulliparas	70.0	75.0	76.2	
Nulligravids	50.0	65.0	61.9	
Educational Level (% with at least secondary school diploma)	100	95	95.2	

Note: GA = gestational age; BMI = body mass index; BP = blood pressure; [1] significant difference between normal weight comparison and other two groups; [2] significant difference between hypertensive and other two groups Note: prepregnancy BMI or BMI at testing was unavailable for two of the subjects and therefore, not used in analysis.

Table 2: Means (± SD) and percentages for the maternal BPs for the hypertensive, overweight, and normotensive-normal weight groups separately

Measure	Diagnostic Group			
	Hypertensive (n = 20) M (± SD)	Overweight (n = 20) M (± SD)	Normal (n = 21) M (± SD)	*p*
Systolic BP sitting [3] (mm Hg)	136.0 (9.7)	117.8 (8.4)	110.8 (8.5)	> .001
Diastolic BP sitting [2] (mm Hg)	87.0 (8.5)	74.9 (5.5)	71.0 (6.7)	> .001
Systolic BP standing [2] (mm Hg)	133.3 (9.6)	116.7 (7.6)	111.1 (9.2)	> .001
Diastolic BP standing [2] (mm Hg)	86.2 (9.7)	72.9 (6.8)	71.5 (6.4)	> .001
Systolic BP supine [2] (mm Hg)	129.5 (10.4)	113.8 (9.5)	109.4 (8.5)	> .001
Diastolic BP supine[3] (mm Hg)	82.5 (8.2)	72.5 (7.4)	66.9 (6.3)	> .001

Note: [2] significant difference between hypertensive and other two groups; [3] significant difference between all three groups. Note: Supine BP data was unavailable for two of the included subjects, and therefore, not used in analysis.

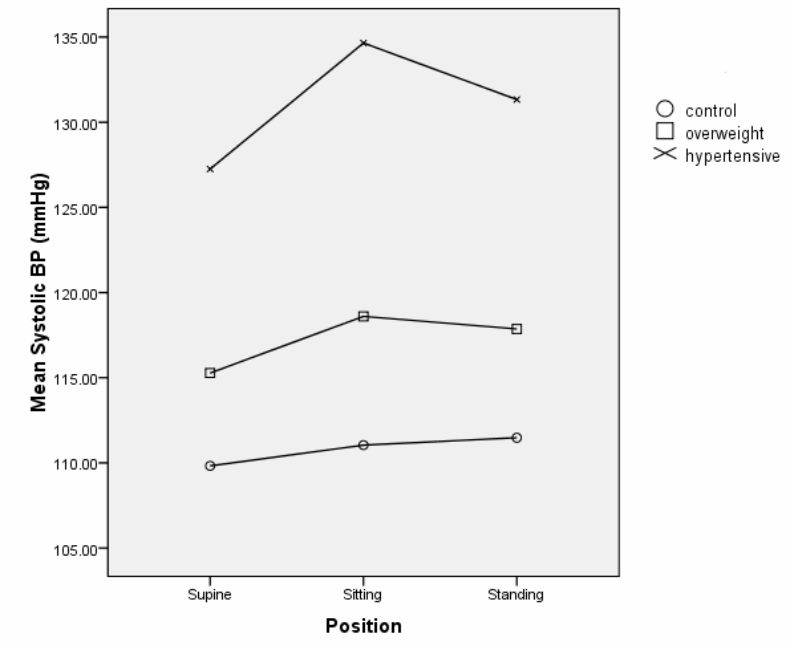

Figure 5: Mean systolic BP in the supine, sitting and standing position for each diagnostic group separately.

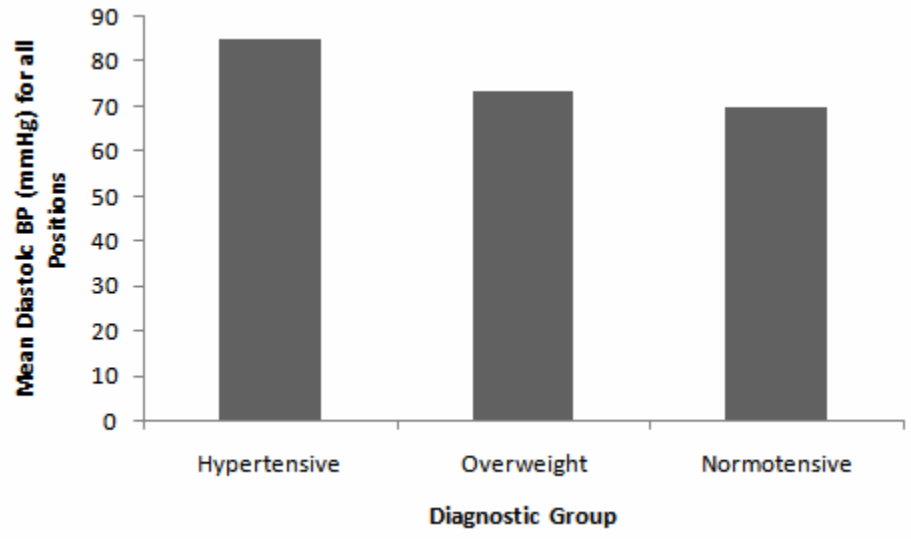

Figure 6: Mean diastolic BP in the supine, sitting and standing positions combined for each diagnostic group separately

Fetal Delivery Outcome Measures

A one way ANOVA with one between factor (Group – 3 levels) or X^2 tests were used to examine delivery outcome measures. No differences in delivery outcome measures were found between fetuses in the three groups. Means (± SD) and percentages for all infants are illustrated in Table 3. Three of the fetuses in the hypertensive group were born macrosomic; one of the fetuses in the overweight group was growth restricted. Therefore, two comparisons were done over the three groups to determine if the macrosomia or growth restriction affected birth weights. One analysis included all of the fetuses and the second analysis excluded the data for these four fetuses. The results were the same for both analyses; there were no differences across groups in birth weight.

Table 3. Means (± SD) and percentages of the newborn delivery outcome measures for each diagnostic group separately.

Measure	Diagnostic Group			
	Hypertensive (n = 20) M (± SD)	Overweight (n = 19) M (± SD)	Control (n = 19) M (± SD)	*P*
GA at birth	40.0 (1.1)	39.9 (1.2)	40.3 (1.2)	Ns
Birth weight (g)	3798.0 (648.0)	3573.2 (354.6)	3624.4 (418.8)	Ns
1-min APGAR score	7.3 (2.7)	7.4 (1.9)	7.9 (1.9)	Ns
5-min APGAR score	8.8 (0.7)	8.7 (0.6)	8.9 (0.6)	Ns
Caesarean section delivery (%)	25.0	42.1	15.0	Ns

Note: GA = gestational age. Comprehensive birth data were unavailable for three subjects, however, normal outcome was assured; APGAR scores were unavailable for 6 included subjects, and therefore not included in analyses.

Maternal Heart Rate Variability and Spontaneous Baroreflex Measures

Because the BRS and/or HRV data of the hypothyroid subject for which analyzable maternal autonomic data were available were greater than 2 SD from the mean values for the rest of the group, these data were excluded from analyses of maternal cardiac autonomic function. Repeated measures ANOVA was used to examine the effects of position on maternal HRV and BRS measures for each group. Because there was a difference in gestation between the diagnostic groups at the time of testing, gestation was used as a covariate for all analyses.

Effects of Diagnostic Group on Maternal HRV and Spontaneous Baroreflex Measures

As can be seen in Table 4 which shows the mean heart rate variability measures for each position and diagnostic group, no differences in heart rate variability measures were found between the three diagnostic groups. However, as can be seen in Table 5, as expected, a difference in supine systolic arterial BP was found, with the hypertensive group having a higher systolic BP than the overweight and normal weight comparison groups. No other differences in maternal baroreflex measures were found.

Table 4: Means (±SD) of the log transformed heart rate variability measures for each posture and group separately.

Variables	Hypertensive Group		Overweight Group		Control Group		*p*
	Supine (n = 19)	Standing (n = 14)	Supine (n = 14)	Standing (n = 15)	Supine (n = 18)	Standing (n = 16)	
HF Power (ms^2/Hz)	1.50 (.67)	1.51 (.57)	1.77 (.80)	1.53 (.48)	2.01 (.44)	1.65 (.39)	ns
LF Power (ms^2/Hz)	1.84 (.48)	1.89 (.42)	1.92 (.45)	1.88 (.38)	2.04 (.33)	2.08 (.31)	ns
Total Power (ms^2/Hz)	2.47 (.48)	2.67 (.42)	2.65 (.46)	2.60 (.34)	2.74 (.34)	2.78 (.27)	ns
SNS Indicator (LF/HF)	.27 (.46)	0.38 (.35)	.15 (.41)	.35 (.33)	.04 (.32)	0.43 (.28)	ns
PNS Indicator (HF/TP)	-.96 (.24)	-1.16 (.27)	-.88 (.36)	-1.07 (.38)	0.79 (.30)	-1.14 (.40)	ns

Note: Supine HRV data were analyzed for 47 subjects. Standing HRV data were analyzed for 45 subjects.

Table 5: Means (±SD) of baroreflex measures for each position and group separately.

Variables	Hypertensive Group		Overweight Group		Control Group		*P*
	Supine (n = 13)	Standing (n = 12)	Supine (n = 13)	Standing (n = 12)	Supine (n = 14)	Standing (n = 14)	
Baroreflex Slope (ms/mmHg)	7.2 (7.4)	5.3 (3.4)	9.5 (7.8)	6.0 (3.5)	9.1 (4.8)	5.7 (2.9)	
Beat-by-beat Systolic Arterial BP (mmHg)	119.6 (15.0)[2]	94.6 (34.8)	94.2 (26.9)[2]	85.1 (24.7)	100.4 (16.9)[2]	110.1 (37.2)	<.01
R-R interval (ms)	698.3 (96.8)	637.9 (71.4)	722.0 (97.5)	605.0 (59.6)	782.8 (95.2)	648.5 (80.9)	

Note: [2] = difference between hypertensive and other two groups. Supine baroreflex data were analyzed for 44 subjects. Standing baroreflex data were analyzed for 38 subjects

Effects of Position on Maternal Baroreflex Measures

A 1 Between (Group – 3 levels), 1 Within (Position – 2 levels) ANOVA was used to analyze the effects of maternal position on maternal baroreflex measures. A linear effect of Position [$F(1,32) = 6.287$; $p < .05$] was found for the mean baroreflex slope. As can be seen in Figure 7, the maternal baroreflex slope decreased in the standing compared to the supine position. No Position X Group interaction was found for the baroreflex slope. No other effects were found.

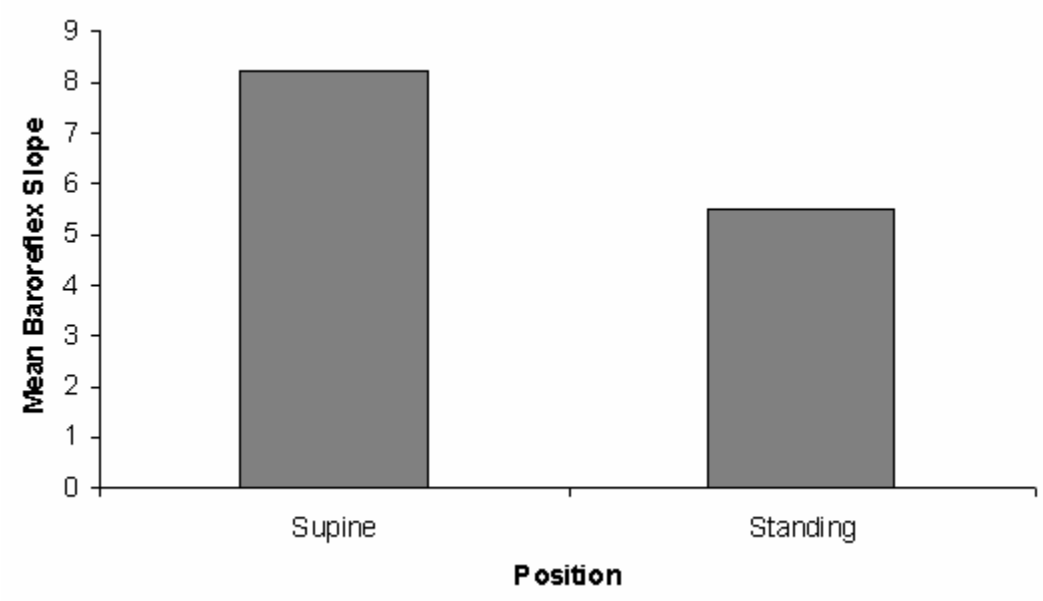

Figure 7: Mean baroreflex slope in the supine and standing position for the diagnostic groups combined.

Effects of Position on Maternal Heart Rate Variability Measures

A 1 Between (Group – 3 levels), 1 Within (Position – 2 levels) ANOVA was used to analyze the effects of maternal position on maternal HRV and baroreflex measures. A main effect of Position [$F(1,39) = 4.509$; $p < .05$] on the HF power was found. As can be seen in Figure 8, the HF power decreased in the standing compared to supine position. A main effect of Position [$F(1,39) = 5.176$; $p < .05$] also was found for the PNS indicator. As can be seen in Figure 9, a decreased PNS indicator was found while the mother was standing for all three groups. No Position X Group interaction was found for any of the HRV measures. No other effects were found for the other HRV measures.

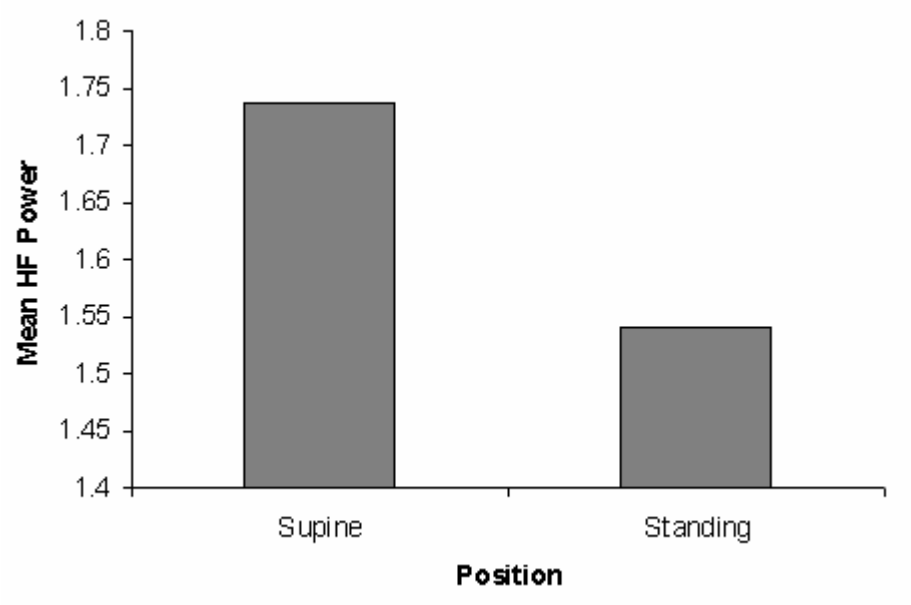

Figure 8: Mean HF power in the supine and standing position for the diagnostic groups combined.

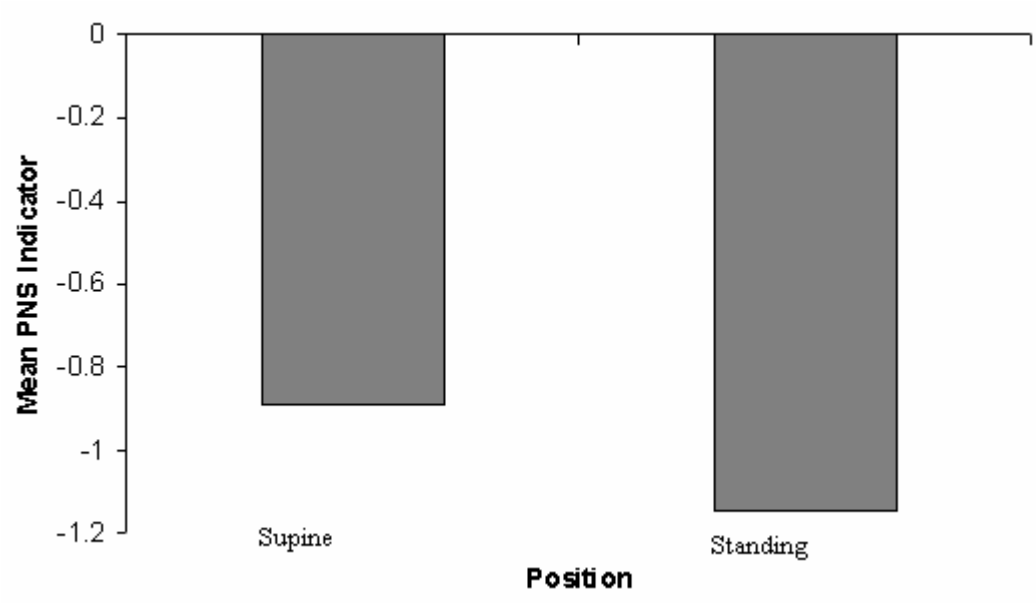

Figure 9: Mean PNS indicator in the supine and standing position for the diagnostic groups combined.

Influence of BMI

Because BMI differed between the diagnostic groups, the effect of BMI on the HRV and spontaneous baroreflex measures was examined for each group separately. No effect of prepregnancy BMI or BMI at time of testing was found for any of the maternal cardiac autonomic functions or response to maternal position change for any of the diagnostic groups.

Spontaneous Fetal Cardiac and Movement Behaviour

A 1-way ANOVA with 1 Between factor (Group – 3 levels) was used to examine fetal spontaneous behaviours to determine differences among groups. As can be seen in Table 6, no differences in spontaneous fetal behaviour were found among the three groups. However, the average number of FHR accelerations ≥ 15 bpm in a 20 min period approached significance at the .05 level; fetuses of the normotensive normal weight mothers demonstrated an average of 2 more accelerations ≥ 15 bpm than those in the hypertensive group.

Table 6: Means (± SD) of the spontaneous fetal behaviours for each diagnostic group separately.

Measure	Diagnostic Group			*p*
	Hypertensive M (± SD)	Overweight M (± SD)	Control M (± SD)	
# FHR accelerations ≥ 10 BPM	6.4 (3.2)	7.5 (4.4)	7.7 (2.8)	
# FHR accelerations ≥ 15 BPM	4.1 (2.3)	5.2 (3.0)	6.1 (2.5)	.055
# FHR decelerations ≥ 10 BPM	0.8 (1.0)	0.9 (1.2)	1.1 (0.9)	
# FHR decelerations ≥ 15 BPM	0.3 (0.6)	0.3 (0.7)	0.4 (0.7)	
AFI	128.5 (46.9)	129.5 (31.3)	120.3 (25.6)	
# body movements BPP	10.1 (4.2)	8.7 (5.0)	9.0 (6.0)	
Amount of cumulative breathing (s)	633.4 (330.8)	699.1 (390.1)	643.8 (280.9)	
BPP score	7.78 (0.6)	7.79 (0.6)	7.33 (1.3)	
Distance from maternal skin surface to fetal head (cm)	3.2 (1.3)	2.8 (1.0)	3.2 (1.1)	

Note: BPP = Biophysical profile; AFI = amniotic fluid index. Supine FHR data was analyzed for all 61 included subjects. Standing FHR data was analyzed for 52 subjects.

Because spontaneous FHR was recorded with the mother in the standing position for only 5 min, the spontaneous FHR collected for 20 min while the mother was in the supine position was divided by 4 to estimate the average number of FHR accelerations in 5 min so that the two measures were comparable time periods for analyses. Subsequently, a repeated measures ANOVA with 1 between factor (Group – 3 levels) and 1 within factor (Position – 2 levels) was used to compare the average supine data to 5 min of FHR data while the mother was in the supine

and standing position across diagnostic groups. Gestational age at testing was used as a covariate for all analyses. As can be seen in Figure 10, a main effect of Position [F (1,48) = 5.070, $p < .05$], was qualified by a Position X Group [F (2,48) = 3.279, $p < .05$] interaction on the number of FHR accelerations ≥ 15 bpm. Fetuses of hypertensive mothers had fewer mean number of FHR accelerations ≥ 15 bpm while the mother was supine compared to standing whereas fetuses of women in the normal weight comparison group experienced more accelerations when supine compared to standing. The number of FHR accelerations were the same in the supine and standing positions for the overweight group.

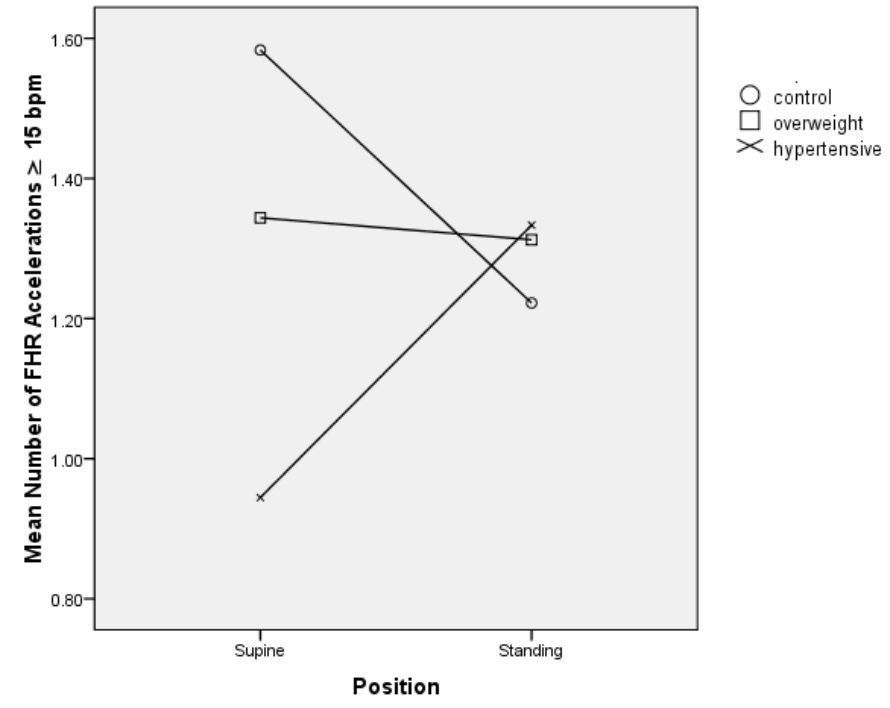

Figure 10: Mean number of spontaneous FHR accelerations ≥ 15 bpm for each diagnostic group separately in the supine and standing postures.

Relationship between Spontaneous Fetal Behaviours and Maternal Cardiac Autonomic Function

Pearson correlations were used to examine relationships between maternal cardiac autonomic variables and spontaneous fetal behaviour. Refer to Appendix G for the correlation tables. For simplicity, only significant correlations are displayed in the tables.

Spontaneous FHR. In the supine position, examination of the relationships between maternal autonomic measures (low frequency power; high frequency power; total power; PNS indicator; SNS indicator; systolic arterial BP; baroreflex slope; R-R interval) and the number of FHR accelerations (≥ 10 bpm; ≥ 15 bpm) and decelerations (≥ 10 bpm; ≥ 15 bpm) revealed a positive correlation between maternal fingercuff arterial systolic BP and the number of FHR decelerations ≥ 15 in the Overweight group ($r = .621$, $p < .05$).

In the standing position, examination of the relationships between maternal autonomic measures and the number of FHR accelerations and decelerations revealed a positive correlation between the standing fingercuff arterial systolic BP and the number of FHR accelerations ≥ 15 ($r = .693$, $p < .05$) in the normal weight comparison group. In the Hypertensive group, a positive relationship between the maternal systolic arterial BP and the number of FHR decelerations ≥ 10 was found ($r = .702$, $p < .05$).

Spontaneous Fetal Body Movements. When the relationship between maternal autonomic variables and spontaneous fetal body movements were examined, a negative relationship between the maternal supine LF power in the normal weight comparison group and the number of fetal body movements observed during the BPP was found ($r = -0.564$, $p < .05$). Also, a negative relationship between the maternal standing LF power in the normal weight comparison group and the number of spontaneous fetal body movements was found ($r = .585$, $p < .05$).

Spontaneous Fetal Breathing Movement. When the relationship between the maternal autonomic variables and the cumulative amount of spontaneous fetal breathing movements (s)

were examined, negative relationships were found between fetal breathing and 1) maternal supine HF power (r = -0.611, $p < .05$); 2) maternal supine PNS indicator (r = -0.695, $p < .05$); 3) maternal supine SNS indicator (r = -0.625, $p < .05$). A positive relationship was found between the maternal standing SNS indicator and the spontaneous fetal breathing movements in the Overweight group (r = .629, $p < .05$).

Voice Processing

For each voice presentation, a 1-between (Group – 3 levels), 2-within (Voice condition – 2 levels; Time – 30 or 90 s) ANOVA was performed for the pre-voice, voice, and post-voice periods separately. Because there were not enough term fetuses in each diagnostic group to analyze by gestational age classification, gestational age was used as a covariate in all voice processing analyses. Because no voice order presentation effect was found [forwards voice: F (119, 7140) = 0.617, $p = 0.746$; reverse voice: F (119, 6664) = 1.099, $p = .363$], FHR and body movements from the first and second presentation of the voice forward and backward were combined for analyses.

Mother's Voice Played Forward

Before/after voice onset. A 1 between (Group - 3 levels), 2 within (Before/After voice onset –2 levels; Time, 30 s) was used to examine the 30 s immediately prior to and following onset of the mother's voice; no significant differences were found. The 1 between, 2 within ANOVA was repeated for the 90 s prior to and following voice onset. An effect of Before/After X Group [F (2, 57) = 3.801, $p = .028$], Before/After X Time [F (6.773, 386.079) = 3.771, $p = .001$], and a Before/After X Time X Group [F (178, 386.079) = 1.871, $p = .030$] interactions were found for the 90 s prior to and following voice onset. Because this omnibus ANOVA showed a triple interaction, a 1 between (Group – 3 levels), 1 within (Time – 90 levels) ANOVA was used to analyze the prevoice and voice periods separately in order to further explore the

differences. As can be seen in Figure 11, a main effect of Group was marginally significant [F (2, 52) = 3.123, p = 0.052] for the prevoice period, indicating a difference in average baseline FHR prior to playing the mother's voice. Because of the differences found in the prevoice period, when the 1 between (Group – 3 levels), 1 within (Time – 90 levels) ANOVA was used to analyze the voice period, the mean FHR in the 90 s period prior to voice onset was used as a covariate. A linear effect of Time [F (1, 56) = 6.784, p <.05] was found which was further qualified by a cubic Time X Group interaction [F (2, 56) = 4.165, p <.05]. As can be seen in Figure 12, fetuses in the hypertensive and normal weight comparison groups showed a decrease in FHR beginning approximately 45 s following onset of the mother's voice. In contrast, fetuses in the overweight group showed a FHR increase.

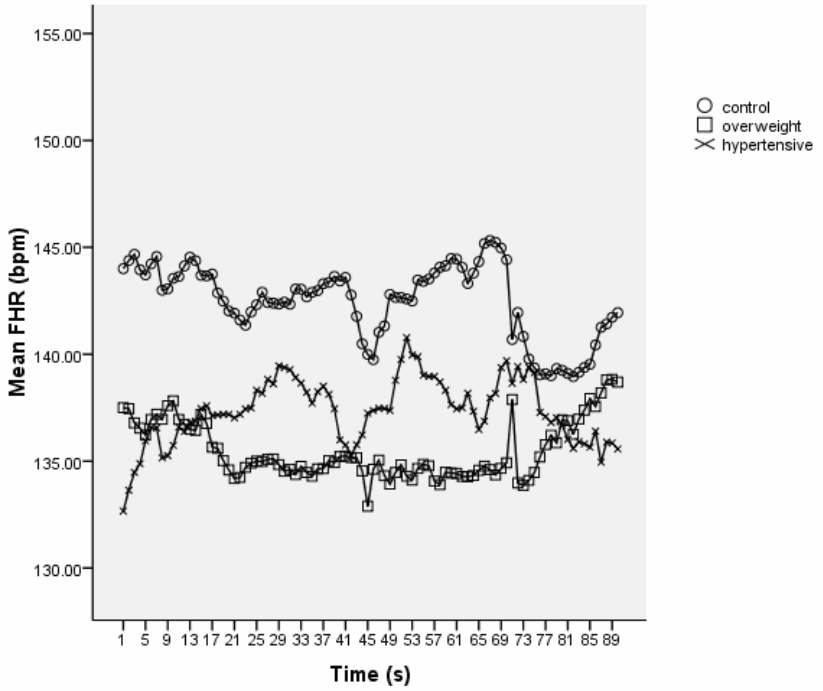

Figure 11: Mean FHR in the 90 s immediately prior to onset of the mother's voice for each diagnostic group separately.

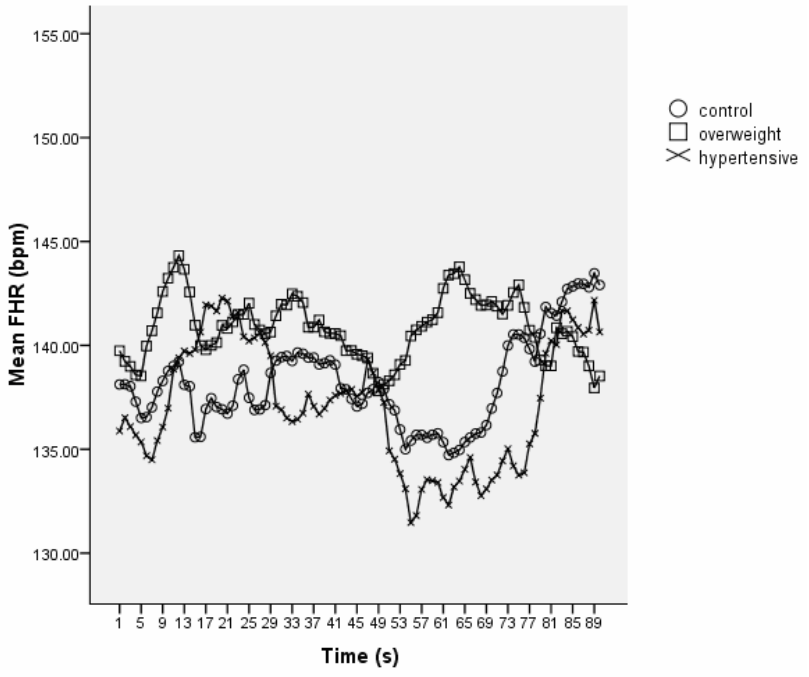

Figure 12: Mean FHR during the 90s period following the onset of the mother's voice for each diagnostic group separately.

Before/after voice offset. When the 1 Between, 2 Within ANOVA was repeated for the 30 s surrounding voice offset, no significant differences were found. When the 1 Between, 2 Within ANOVA was repeated for the 90 s surrounding voice offset, a main effect of Group [$F (2, 56) = 3.470$, $p < .05$] and a Time X Group [$F (178, 4984) = 1.642$, $p = 0.073$] interaction were found. When the 1 Between (Group – 3 levels), 1 Within (Time – 30 s) ANOVA was used to analyze the 30 s immediately prior to offset of the mother's voice played forward, no differences were found. When the 1 Between (Group – 3 levels), 1 Within (Time – 90 s) ANOVA was repeated for the 90 s immediately prior to offset of the mother's voice played forward, a main effect of Time [$F (5.937, 302.790) = 3.455$, $p = 0.000$] was found. When the 1 Between (Group – 3 levels), 1 Within (Time – 30 s) ANOVA was used to analyze the 30 s immediately following voice offset, a main effect of Group [$F (2, 57) = 3.933$, $p < 0.05$] was found. When the 1 Between, 1 Within

ANOVA was repeated for the 90 s immediately following offset of the mother's voice played forward, a Time X Group interaction approached significance [F (13.189, 369.288) = 1.672, p = .064] and a main effect of Group [F (2, 56) = 3.981, $p < .05$] was found. As can be seen in Figure 13, fetuses in the normal weight comparison group had an increased FHR at the end of the voice period which continued for approximately 50 s following voice offset, whereas the FHR of fetuses in the overweight and hypertensive groups appeared to return to baseline.

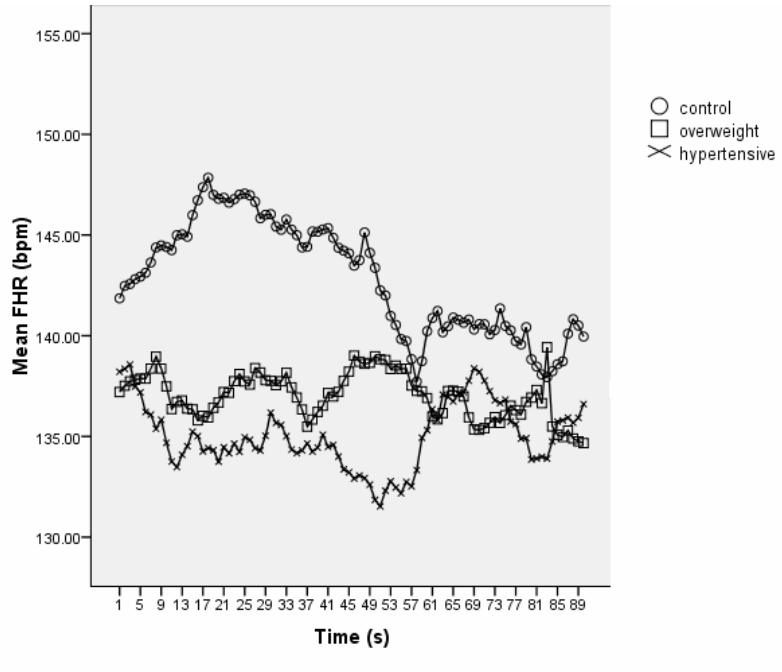

Figure 13: Mean FHR during the 90 s immediately following offset of the mother's voice for each group separately.

Mother's Voice Played Backward

Before/after voice onset. A 1 Between (Group - 3 levels), 2 Within (Before/After voice onset – two levels; Time, 30 s) was used to examine the 30 s immediately prior to and following onset of the reverse voice. A Before/After X Time X Group interaction [F (8.208, 217.522) =

1.966, $p = .050$] was found. Subsequently, each voice period was analyzed separately to sort out the effects. A 1 Between (Group – 3 levels), 1 Within (Time – 30 s) ANOVA was used to analyze the 30 s period immediately prior to the onset of the mother's voice played backward. No effects were found. A 1 Between (Group – 3 levels), 1 Within (Time – 30 levels) ANOVA was repeated for the 30s immediately following onset of the mother's voice played in reverse. No differences were found in the 30 s immediately following onset of the mother's voice played backward.

When the 1 between 2 within ANOVA was repeated for the 90 s surrounding onset of the reverse voice, a main Before/After X Time X Group interaction [F (13.113, 327.822) = 2.665, $p = .001$] was found for the 90 s prior to and following onset of the reverse voice. Because this omnibus ANOVA showed a triple interaction, each voice period was analyzed separately to examine the effects. A 1 Between (Group – 3 levels), 1 Within (Time – 90 s) ANOVA was used to analyze the 90 s period immediately prior to the onset of the mother's voice played backward. No effects were found. A 1 Between (Group – 3 levels), 1 Within (Time – 90 levels) ANOVA was repeated for the 90s immediately following onset of the mother's voice played in reverse. A linear Time by Group interaction [F (2, 54) = 5.492, $p < .01$] was found. As can be seen in Figure 14, fetuses in the hypertensive group showed a linear increase in FHR lasting the 90 s period following onset of the mother's voice played backward. Fetuses in the overweight and comparison groups showed no change in FHR.

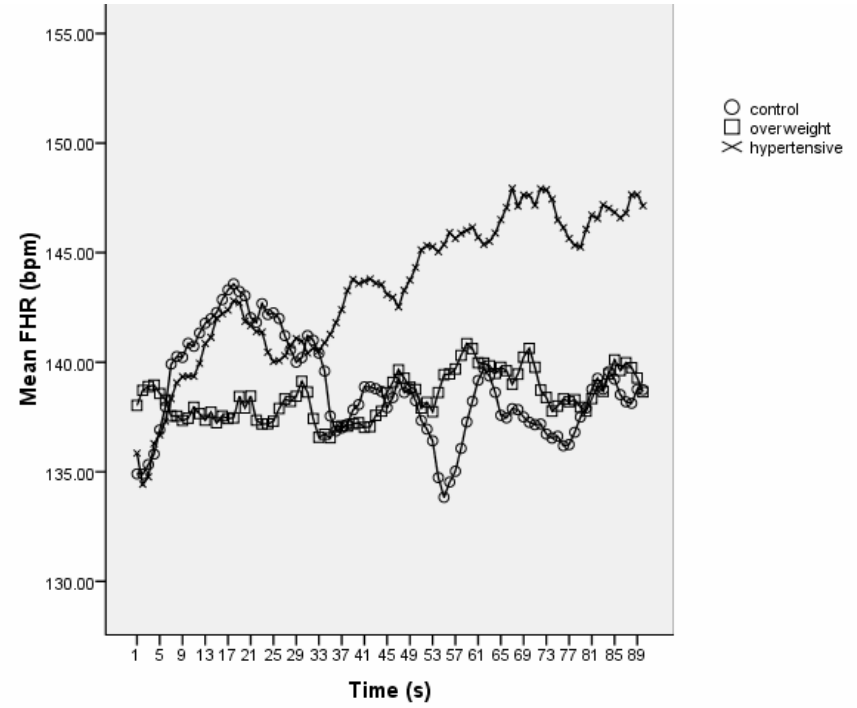

Figure 14: Mean FHR during the 90 s immediately following onset of the mother's voice played backward for each group separately

Before/after voice offset. When the 1 Between (Group – 3 levels), 2 Within (Before/After voice offset – 2 levels; Time, 30 levels) ANOVA was repeated for 30 s prior to and following voice offset, no effects were found. When the 1 Between (Group – 3 levels), 2 Within (Before/After voice offset – 2 levels; Time, 90 levels) was repeated for the 90 s prior to and following offset of the reverse voice, a main effect of Before/After voice offset [$F (1, 54) = 10.425$, $p < .01$] and a Before/After voice offset X Time [$F (6.445, 4806) = 2.135$, $p < .05$] was found. Also, a Before/After voice offset X Group interaction was found [$F (2, 54) = 5.033$, $p < .01$], along with a Before/After voice offset X Time X Group interaction [$F (12.890, 4806) = 2.130$, $p < .05$]. Because the omnibus ANOVA showed a triple interaction, the 90 s periods prior to and following offset of the mother's voice played backward were analyzed separately. A 1

Between (Group – 3 levels), 1 Within (Time, 90 s) ANOVA was used to analyze the 30 s immediately prior to offset of the mother's voice played backward; no differences were found. When the 1 Between (Group – 3 levels) 1 Within (Time – 90 s) ANOVA was used to analyze the 90 s immediately following offset of the mother's voice played backward, a quadratic effect of Time [$F (1, 56) = 6.436$, $p < .05$] was found.

Fetal Body Movements

To determine whether there were differences in fetal body movements among groups over time, an ANOVA with 1 between factor (Group - 3 levels) and 1 within factor (Time - 4, 30 s blocks) was used to examine movements in the pre-voice, voice, and post-voice periods separately. No differences were found for the number of fetal body movements for any of the periods. However as can be seen in Figure 15, when the duration (s) of fetal body movement was examined, a main effect of Time [$F (2.511, 130.589) = 2.982$, $p = .042$] was found for the 2 min following offset of the reverse voice.

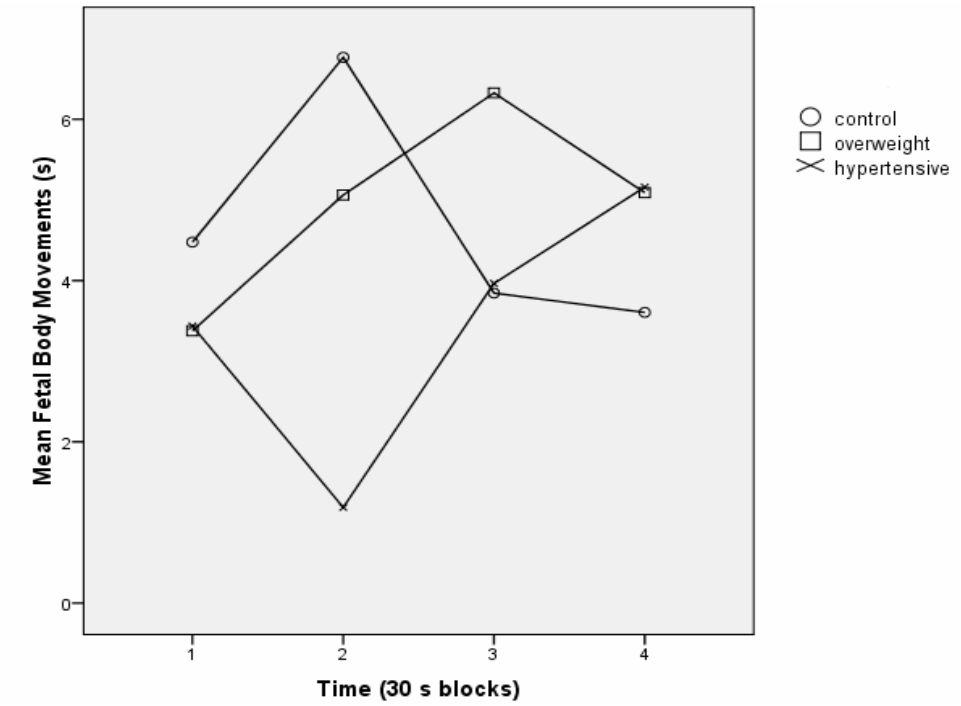

Figure 15: Duration (s) of fetal body movements in 30 s blocks following the offset of the reverse voice.

CHAPTER 5

Discussion

The purpose of this study was to characterize maternal heart rate variability as well as fetal spontaneous and auditory elicited behaviour, and the relationship between maternal and fetal cardiac measures in pregnancies complicated by hypertension and excess body weight compared to a normotensive, normal body weight comparison group. As expected, women in the hypertensive group had greater mean systolic and diastolic BPs than did women in the overweight and normal weight comparison groups. The highest systolic and diastolic BPs were found while the mother was sitting for each of the three groups. Fetuses of hypertensive pregnant women appear to respond differently to maternal position change than do fetuses of overweight and normal weight comparison pregnant women. They showed a greater number of FHR accelerations ≥ 15 bpm while their mother was standing compared to supine while fetuses of normal weight women showed fewer FHR accelerations. Fetuses in the overweight group showed no changes in response to position. Fetuses in the hypertensive and normal weight comparison groups showed a decrease in FHR in response to their mother's voice played forward, whereas fetuses in the overweight group showed a FHR increase. Fetuses in the hypertensive group showed a linear increase in FHR in response to the their mother's voice played backward lasting the entire voice period, whereas fetuses in the normal weight and overweight groups showed no FHR change.

Fetuses in the normal weight comparison groups demonstrated fewer FHR accelerations while their mother was in the standing compared to supine position. This is in contrast to findings by Van Katwijk and Wladimiroff (1991), who found no positional differences in FHR in uneventful pregnancies. However, fetuses of hypertensive mothers demonstrated an increased

number of FHR accelerations ≥ 15 when the mother changed position from supine to standing. Fetuses in the normal weight comparison group demonstrated a decreased number of FHR accelerations ≥ 15 between the two positions. Fetuses of overweight mothers showed no differences in the number of FHR accelerations ≥ 15 between the two positions. Examining the effect of maternal position (supine vs. left lateral recumbent) on FHR in uneventful pregnancies, Tamás and colleagues (2007)) found relationships between maternal and fetal hemodynamic measures. Pregnant women with hypertension have demonstrated a differential response to postural change (left lateral recumbent to standing; Dyer, Anthony, Ledeboer & James, 2004). Perhaps the differential maternal response to postural change in hypertension exerts an effect on fetal response to postural change.

The reason for this is a matter of speculation; however, given the correlation between maternal BP group and spontaneous fetal behaviours, it is possible that maternal factors influence spontaneous fetal behaviours. Because fetuses in each diagnostic group responded differently to position change, and fetuses in the hypertensive group actually had fewer FHR accelerations ≥ 15 bpm compared to the normal weight normotensive diagnostic group, these differences could possibly reflect placental differences from the norm, or potentially reflect differences in maternal catecholamine levels between diagnostic groups. Zhang, Zhao and Yin (2003) have demonstrated that hypertensive women have greater levels of serum norepinephrine and dopamine than do normotensive pregnant women, and the umbilical artery levels of epinephrine and norepinephrine were greater than the maternal serum levels in both populations. Dopamine and norepinephrine may act on the sympathetic nervous system, producing effects such as increased heart rate and blood pressure in healthy adults; it is possible that these catacholamines also affect the autonomic function of fetuses. Furthermore, it has been demonstrated that serum catecholamines can affect fetal behaviour. For example, in a controlled study, antenatal administration of synthetic

glucocorticoids (i.e., betamethasone) to enhance fetal lung maturation has been associated with transient reductions in FHR variation, breathing, and body movements two days after the first dose (Derks, Mulder & Visser, 1995). However, subsequent research has demonstrated that these fetal behaviours are reduced in the afternoon and evening but not the morning, suggesting that administration of glucocorticoids suppresses the diurnal rhythms of fetal behaviours (Koenen, Mulder, Wijnberger & Visser, 2005). Thus, it could be that maternal catecholamines affect spontaneous fetal behaviour in pregnancies complicated by maternal hypertension.

As was expected, the women experiencing pregnancies complicated by hypertension had higher average systolic and diastolic blood pressures compared to the women experiencing a normotensive pregnancy. Although the women in the hypertensive group met the diagnostic criteria for hypertension in pregnancy in clinic, their average BP (136/87 in the sitting position) at time of testing did not meet the definition of gestational hypertension. The reason for this is a matter of speculation. However, few of the women with hypertension had both a systolic and a diastolic BP that met the $\geq$ 140/90 criteria for hypertension. The majority had either a high systolic reading with a normal diastolic BP, or a normal systolic BP with a hypertensive diastolic BP. Still others, though meeting the diagnostic criteria in clinic, were not hypertensive at time of testing. This could reflect the mild nature of the hypertension and account for the good outcome of both the mothers and newborns at delivery.

While obesity is a risk factor for hypertension, hypertension can occur in the absence of obesity, and there were six hypertensive subjects in this study whose prepregnancy BMI fell under the "normal weight" classification. Though excess body weight is a risk factor for the development of hypertension, other factors, such as genetics and activity level contribute to an individual's risk of developing hypertension. This may explain why the overweight and hypertensive groups had similar BMI's both prior to pregnancy and at time of testing. Not all

overweight pregnant women develop hypertension. Furthermore, the 30% of the hypertensive sample being a normal weight could explain why differences among the three groups were few.

As expected, the mean finger cuff arterial systolic BP was lower than the mean brachial systolic BP. Pressure gradients along the arterial system causes finger pressure to be below mean brachial pressure; as a result, finger arterial systolic BP is on average 7-8 mmHg lower than brachial systolic BP (Smith, Wesseling & de Wit, 1985). Furthermore, the Finapres is understood to track changes in arterial BP, rather than the actual BP value (Parlow, 1993).

Interestingly, the mean systolic blood pressure in the sitting position and the diastolic blood pressure in the supine position of the women in the overweight/obese diagnostic group were significantly higher than those of the normal weight group, and approached the definition of "prehypertension". Prehypertension is defined as a systolic BP of 120 to 139 mmHg or a diastolic BP between 80 and 89 mmHg (Miller & Jehn, 2004). This supports findings by Gilmour (2004), who found a positive relation between maternal weight and maternal systolic and diastolic BPs. However, this observed difference in BP between the overweight and normal weight group was not found in all three positions, suggesting a possible differential response to position change in the overweight compared to normal weight populations. The finding here is consistent with Kim and colleagues (2005) who found that in the non-pregnant population, obese subjects showed differences in HRV at rest compared to normal weight subjects; however these differences were not apparent in the standing position. Furthermore, a negative relationship between BMI and mental stress has been described (Laederach-Hoffman, Mussgay & Ruddel, 2000). This is suggestive of different autonomic response to mental and/or physical stress in the non-pregnant obese population which may extend to the pregnant obese population. While mental stress was not examined in this study, the autonomic response to mental stress in the obese pregnant

population could be examined to determine differences when compared to normal weight pregnant subjects.

One of the shortcomings of the present study which may have resulted in variability in BP readings was the size of the BP cuff. The Society of Obstetricians and Gynaecologists of Canada (SOGC, 2008) recommend using a BP cuff with a length 1.5 times the circumference of the arm. However, only one cuff was used in this study and the study by Gilmour (2004) and the cuff was most likely too small for some of the obese subjects. A small cuff may give a falsely high reading. The mean arterial systolic BP of the obese women was actually the lowest arterial SBP in the beat-by-beat baroreflex measures, supporting the postulation that the higher BP in the overweight compared to normal weight diagnostic group may be related to cuff size rather than to elevated BP. Of course, this issue could be untangled in a future study accommodating cuff size to arm circumference. It is important to note that for the hypertensive group, diagnosis was based on two BP measurements obtained by clinicians in the antenatal clinic and not by BP measurements obtained at time of testing. Thus, cuff size, which may have affected BP readings during subject testing, did not influence diagnosis.

Though standing is the expected position with the highest BP readings in the non-pregnant populations, for all 3 pregnancy groups, in this study the highest mean systolic BP was found in the sitting position (See Figure 4). This could be a result of the sitting BP being taken shortly after the participant's arrival at the laboratory without sufficient time for relaxation prior to the measurement. In contrast, the standing BP was taken following 20 min of rest in a semi-recumbent position. Furthermore, the reduced heart rate "recovery" in response to position change observed in pregnancy, indicating a diminished baroreflex-induced slowing of heart rate (Ekholm, Piha, Antilla & Erkkola, 1994) also could account for the decreased BP observed in the standing position; perhaps the BP had not returned to equilibrium prior to the BP measurements.

In order to further understand this phenomenon, HRV and baroreflex sensitivity measures while participants are sitting could be examined in the pregnant population.

No effects of weight group (overweight vs. normal weight) on any of the HRV or BRS measures were found in this study. This supports the results of Schmidt-Stutzman (2005), who found evidence of lower sympathetic tone (a greater decrease in low frequency power) in normal weight pregnant women compared to obese pregnant women during exercise at 36 weeks GA, but no differences between weight groups while the subjects were at rest. In contrast, Swansburg (2005) who studied preeclamptic women found a correlation between delivery BMI and HRV measures for both the preeclamptic and normotensive groups; delivery BMI had an influence on the standing total power measure. Delivery BMI also correlated with systolic arterial finger-cuff BP and RR interval in the supine position. Thus it could be that differences in weight groups are only revealed when hypertension is more severe (i.e., preeclampsia vs. mild gestational hypertension). Or perhaps the differences in less severe disease are milder and require a larger sample size to be detected. Furthermore, contrary to expectations, 6 of the 21 hypertensive subjects were classified as normal weight (according to BMI) prior to pregnancy. In contrast to observations by Levario-Carrillo and colleagues (2006), the subjects who developed hypertension did not gain more weight in pregnancy than the subjects who did not. However, despite the normal prepregnancy BMI of these six subjects, the mean prepregnancy and testing BMI of the hypertensive subjects was not significantly different from those of the overweight normotensive groups. These measures were greater than those of the comparison group. In the non-pregnant population, differences have been observed between normal-weight and obesity-related hypertension. In contrast to hypertension in the presence of obesity, which is characterized by increased cardiac output (Licata et al., 1990), hypertension in the absence of obesity is characterized by increased arterial stiffness and systemic vascular resistance (Weber, Neutel &

Smith, 2001) as well as increased sympathetic activity to the heart (Lambert et al., 2007). Perhaps the different physiological characteristics of the two subgroups, along with small sample size prevented any differences in the hypertensive group from becoming apparent. Future studies should examine each subgroup separately and employ a larger sample size in order to better examine any differences between diagnostic groups.

Interestingly, few differences between the hypertensive and normotensive (overweight and normal weight) groups were found for the maternal cardiac autonomic measures when gestation was controlled statistically. This supports results from Voss and colleagues (2000), who found no effect of gestational age on maternal HRV or baroreflex measures.

Contrary to Lee (2003), who found no differences in supine spontaneous baroreflex measures, here it was found that hypertensive women had a higher supine arterial systolic BP than normotensive women (both overweight and normal weight). The reason for this is a matter of speculation; however, in the nonpregnant population, it is understood that the pathophysiology behind hypertension in the presence of obesity differs from hypertension in nonobese individuals (e.g., Lambert et al., 2006; Esler et al., 1988). Furthermore, Faber and colleagues (2004), found differences in HRV and baroreflex parameters between pregnant women with preeclampsia, chronic hypertension and women with gestational hypertension. Given that 6/21 hypertensive subjects in this study were normal weight prior to pregnancy, and at least one subject had chronic hypertension (and 4 went on to develop preeclampsia), it could be that our data are confounded by subsamples of hypertensive groups with different mechanisms responsible for the hypertension. This also could explain the relatively few correlations found between maternal HRV and baroreflex measures and fetal spontaneous behaviour. Furthermore, as the autonomics data were lost for several subjects, it was difficult to fully determine any differences between the groups. More definitive results may have been found with a more complete sample.

Information about maternal activity level was not collected for the purpose of this study. Activity level could affect BP and maternal cardiac autonomic factors, particularly in overweight subjects, which could account for the few differences in maternal cardiac autonomic factors found between the three groups in this study. As early as 1970, researchers suggested a possible interaction between physical activity, fatness and cardiovascular risk (Paffenbarger, Laughlin, Gima & Black, 1970). Another study of female US nurses found decreased risk of death from cardiovascular disease with increased number of hours of self-reported physical activity within BMI classes (Hu et al., 2004). While activity level throughout pregnancy would be useful information to collect, there is the problem of recall bias given that we would be collecting it at the end of the pregnancy. Differing activity levels over pregnancy could account for the lack of differences in maternal cardiac measures between groups in this study, and explain the conflicting results in other studies examining HRV and BRS in obesity.

BMI was used as an indicator of body fat in this study. However, while BMI takes into account one's height, it fails to take into account relative muscle mass or body frame (i.e., people who are naturally very lean, or those with a muscular body build). Furthermore, BMI does not give an indication of the distribution of body fat; and research has shown that excess abdominal fat is associated with increased health risk (Health Canada, 2004). Waist circumference is a stronger independent indicator of health risk; however, waist circumference cannot be used as a measure of body fat in pregnant women. Clearly, a more definitive means of determining maternal weight classification (e.g. water displacement) during pregnancy would be an asset.

Another limitation of this study was in the use of two methods of subject recruitment; from the OB clinic and word of mouth. Due to the inability to control for confounding variables such as maternal disease left unreported by subjects. This resulted in some subjects being tested who did not meet the inclusion criteria. Clearly, for this type of study, word-of-mouth recruiting

was problematic and should not be employed. Again, it is important to note that no hypertensive subjects were recruited through word of mouth.

No differences in birthweight were found between the three groups. Contrary to expectations, three macrosomic newborns were born to hypertensive mothers. Conversely, one of the infants born to an obese mother was small for gestational age. When the data were re-analysed excluding these four infants there remained no difference in birthweight between the three groups. Two of the three macrosomic infants were born to hypertensive mothers who also were obese or overweight; perhaps the overabundance of nutrients in today's society might mitigate the effects of placental insufficiency in some cases of hypertension.

As found in previous studies (e.g., Lee et al, 2007; Gilmour, 2004), no significant differences in spontaneous behaviours were found between fetuses of hypertensive, overweight, and normal weight comparison mothers. However, contrary to some studies (Warner et al., 2001; Gilmour, 2004), but similar to Lee and colleagues (2007), no differences between the groups were found in regards to amniotic fluid index. The differences among the studies may be a result of the small sample sizes, leading to spurious findings or revealing differences of low magnitude. Furthermore, unlike the study by Warner and colleagues (2001), no severe pre- or post-natal complications were noted in hospital records for the hypertensive group. In contrast to the study by Gilmour (2004), one of the fetuses in the overweight group in this study was admitted to the NICU for severe postnatal complications.

At time of testing, fetuses in the overweight diagnostic group were younger than the fetuses in the hypertensive diagnostic group. Fetuses in the normal weight comparison group had a mean GA which was not significantly different from the GA of the other two groups. The mean GA of the control and overweight groups fell under the "preterm" category (35-37 weeks) and the mean GA of the fetuses in the hypertensive group would be classified as "term" (>37 weeks).

Because it has been established that fetuses in different age groups demonstrate different responses to acoustic stimulation (Kisilevsky, Muir & Low, 1999; Kisilevsky & Hains, 2005), more definitive differences may have been observed had the GA of the fetuses been controlled. Differences in GA could mask some of the differential response to acoustic stimulation.

Fetuses in the overweight group demonstrated a mature (term) response to their mother's voice when it was played forward. In contrast to fetuses in the hypertensive and normal weight comparison groups who showed a decrease in mean FHR approximately 45 s following onset of the mother's voice, fetuses of overweight women showed a mean FHR increase. The reasoning behind this is a matter of speculation. However, as previously stated, the fetal sound environment is affected by maternal fluids and tissues (eg., Querleu et al., 1988). Perhaps the increased maternal tissue found in the overweight state accounts for the differential behaviour observed in the overweight group in response to the mother's voice. Furthermore, perhaps the hypoxia associated with hypertensive pregnancies (Brown, 1995; Sapunar, 1996) could account for the immature response of fetuses in the hypertensive group to their mother's voice. Alternatively, given the difference in mean FHR over time among the groups during the pre-voice period, this perceived difference in fetal response to sound stimulus could potentially be a result of FHR variability/baseline changes as opposed to a response to the stimulus.

Interestingly, fetuses in the hypertensive group showed an increased FHR in response to the mother's voice played backward, whereas fetuses in the overweight and normal weight comparison groups showed no response. However, given that the FHR response of fetuses in the hypertensive group was immediate, this could potentially reflect a non-discriminatory response to a sound stimulus rather than higher-order language processing. If so, this non-discriminatory response might reflect differential cognitive maturation rather than simply a higher stimulus threshold in fetuses of hypertensive mothers.

Four of the 21 hypertensive subjects subsequently developed preeclampsia after testing. Because unpublished data from the Kisilevsky laboratory has found no difference in spontaneous or sensory-elicited fetal behaviour between fetuses of preeclamptic and hypertensive women, these fetuses were included in data analysis. When these four subjects were examined separately to determine whether they were within 1 SD of the mean for the hypertensive group, no consistent differences were found; though there were differences in FHR accelerations/decelerations, No two preeclamptic subjects had the same deviation from the mean.

In keeping with another study in the Kisilevsky laboratory (Gilmour, 2004), fetuses of overweight mothers demonstrated a greater FHR increase throughout most of the voice period, fetuses in the overweight group in this study showed a decrease in heart rate to the mother's voice played forward beginning about 45 s following onset. A FHR decrease followed by a FHR increase would be expected similar to that shown by the normal weight comparison group. However, in another study in the Kisilevsky laboratory (Schmidt-Stutzman, 2005) which employed a smaller sample size, fetuses of overweight women enrolled in an exercise program also demonstrated a FHR increase in response to maternal voice. However, fetuses of overweight sedentary women demonstrated no increase in FHR in response to their mother's voice. The smaller sample size in the Schmidt-Stutzman study could account for the inconsistent results.

Contrary to expectations, no difference in distance from the maternal skin surface to the fetal head was found between the three diagnostic groups. Most likely, this is due to the measurement having been taken near the symphysis pubis, a location of relatively little subcutaneous fat, and under the pannus (if applicable) of overweight subjects, thereby mitigating any difference in body fat that may have been found in other body locations.

Few correlations between maternal cardiac autonomic variables and spontaneous fetal behaviour measures were found. Furthermore, no pattern was found for these correlations, and

given that the maximum number of correlations found for each group/position was 3 (and given with an α level of .05, 2.5/50 significant correlations could be expected by chance), these correlations may be spurious. Further investigation with a larger sample size is warranted in order to further explore any correlations between maternal cardiac autonomic function and fetal behaviour.

The diagnostic criteria for hypertension in pregnancy were changed during the course of this study. At the onset of the study, the diagnosis of gestational hypertension was made using the criteria in existence at the time (ACOG, 2001): either two systolic readings ≥ 140 mmHg, or two diastolic readings ≥ 90 mmHg taken at least six hours apart. Following 7 months of data collection, in March 2008, new criteria were adopted (SOGC, 2008): a diastolic BP ≥ 90 mmHg based on the average of at least two measurements taken on the same arm. Women with a systolic BP 140-160 mmHg are no longer classified as hypertensive. Rather, the guidelines recommend these individuals be closely monitored for the development of elevated diastolic BP. Severe hypertension is now defined as a systolic BP ≥ 160 mmHg or diastolic BP ≥ 110 mmHg, with the recommendation that women with systolic BP between 140 and 160 mmHg be monitored for the development of diastolic hypertension. The new criteria were based on evidence such as that provided by Peek and colleagues (1996), who demonstrated that a diastolic BP is a more reliable measure of hypertension. It is less variable and a better predictor of negative outcome than systolic blood pressure; it is generally accepted that diastolic BP and proteinuria, alone and in combination, predict fetal outcomes (Friedman & Neff, 1976; Peek et al., 1996; SOGC, 2008). Most of the hypertensive subjects in this study had high systolic BP. Only 11 subjects would be diagnosed as hypertensive using these new criteria However, there were insufficient subjects to analytically explore potential differences based on diagnostic criteria.

Summary

In summary, differential FHR response to maternal position change and auditory processing were observed in the three diagnostic groups. Contrary to expectation, three of the women in the hypertensive group delivered a macrosomic infant, and one of the overweight women delivered a growth restricted infant. No differences were found between groups in the response to position change for any of the maternal cardiac autonomic measures. However, the HF power, PNS indicator and baroreflex slope decreased from supine to standing for all three diagnostic groups.

Future Directions

To further investigate the relationship between maternal cardiac autonomic function and spontaneous and auditory elicited fetal behaviours in pregnancies complicated by hypertension and maternal overweight, more stringent inclusion and exclusion criteria should be used to provide a more homogenous sample. Effects of severity of hypertension on maternal cardiac autonomic function and fetal behaviour could be studied by examining women with mild compared to severe hypertension, or overweight women with hypertension compared to normal weight women with hypertension. Furthermore, sample size should be increased to allow for examination of auditory processing as a function of GA and maternal cardiac autonomic function as a function of BMI.

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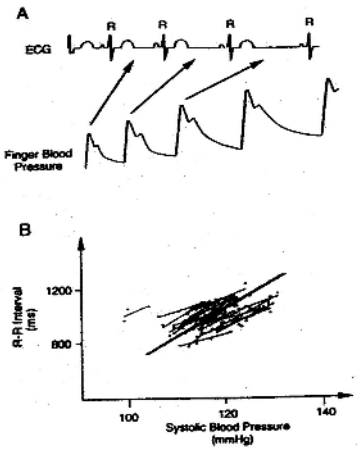
APPENDIX A

Spontaneous Baroreflex Sensitivity

Baroreflex Slope



- A: Systolic BP increase followed by R-R interval increase
- B: Slopes of relation between systolic BP & R-R interval

(Parlow, 1993).

A) Identification of baroreflex sequence: 3 cardiac cycles demonstrating a lengthening of R-R intervals following a rise in systolic BP.
B) Index of spontaneous baroreflex sensitivity: the average slope of the R-R interval-systolic BP relationship determined from the plots of all baroreflex sequences.

APPENDIX B

Information Sheet and Consent Form

Study of Maternal Heart Rate Variability and Fetal Behavior in Women of Varying Weight Classifications and Women with High Blood Pressure

Queen's University School of Nursing and
Department of Obstetrics/Gynaecology

Research Information and Consent Form

Explanation of the Study

You are invited to participate in a study of the relationship between mothers' heart rate changes and fetal behaviour (heart rate, body and breathing movements) and the effect of sound on behaviour. The immediate purpose of the study is to learn more about changes in mothers' heart rate and changes in behaviour of babies in relation to their mother's weight and blood pressure. The long term goal of this work is to develop a better test of the health of babies before birth.

The study of your unborn baby includes four parts and **takes about 90 min.** Before we start the study, we will ask you to tape record a passage (e.g. reading 2 minutes of Bambi) and we will measure your height, weight and blood pressure. Then, in the first part of the study, the unborn baby's **heart rate** will be recorded for 20 min using a fetal heart rate monitor. At the same time, your heart rate and blood pressure will be recorded using three electrodes (non-latex stickers with a special sensor) on your chest area and a finger probe on your middle finger while you are lying on your left side. You will be helped to stand, and your heart rate and blood pressure, and the baby's heart rate will be measured for 10 minutes.

The third part includes about a 30 min **ultrasound scan** during which his/her body movements will be counted, the amount of breathing timed, and the amount of fluid measured.

The fourth part includes about a 25 min **sound** sensitivity test. For the sound test, the 2-minute tape recording of Bambi (which you read at the onset of the study) will be played to your baby through a loud speaker held above your abdomen. About 10 min after we play your voice, we will play a 2-minute tape recording of a noise. The fetal heart rate and body movements will be recorded before, during, and after the sounds using ultrasound monitors. Also the unborn baby will be videotaped during the study.

Benefits and Risks

There are no known risks or benefits. The sound and ultrasound monitor used have no known effects on babies or mothers. The ultrasound is the same as that now used for other tests in pregnancy. The sounds are sounds that occur in the environment.

Freedom to Withdraw

Participation in this study is voluntary and there is no compensation. You may withdraw from this study at any time, for any reason and your withdrawal will not affect your present or future medical care at Kingston General Hospital.

Consent

I agree to participate and I give permission for my baby to participate in this study, having understood the explanation and having had all of my questions answered to my satisfaction. I understand that I may withdraw on request at any time for any reason. I also realize that the study will not directly benefit my baby or me and whether or not I participate has no relation to my health care. Furthermore, I agree that information gathered during this study may be shared with my medical caregivers, if requested or if the study team considers that sharing such information might be of benefit to my baby or myself.

In addition to the records obtained by the investigators for this study, I give permission for the investigators to use clinical records obtained during other assessments of this baby before and after birth including, for example, ultrasound examinations, fetal heart rate records, nursery and maternal hospital records. Confidentiality of my participation and my baby's participation will be maintained except that, as noted above, information may be shared with my medical caregivers. The information concerning my baby as well as the videotapes may be used for

research and educational purposes, including publication, with no disclosure of my or his/her identity.

Finally, I give permission for the audiotape made of my voice to be used in other similar studies.

If, as a study participant, you have any questions or concerns about the research, you should feel free to discuss them at any time with the Student Investigator, Jennifer Van der Meulen (613-531-0903), or with the Thesis Supervisor, Dr. Barbara Kisilevsky at Queen's University, School of Nursing (613-545-6000, ext 74766), the Director of the School of Nursing, Dr. Cynthia Baker (613-533-2669), or the Chair of the Research Ethics Board, Dr. A. Clark (533-6081).

Name (Printed) _____

Signature_____Date_____

Witness_____

I have carefully explained the nature of this research study to the participant. I certify that, to the best of my knowledge, the person understands clearly the nature of the study and their participation.

Signature_____

NOTE:

1) **Our observations of your unborn baby during this study will not tell us whether or not she/he is healthy.**

2) **During this study, we will not determine the sex of your unborn baby.**

3) **The observations being carried out during this study are for research purposes and a physician will not read the heart rate strip recording or review the videotapes ultrasound scan.**

APPENDIX C
Editing Heart Rate Variability

Hughson and Yamamoto's general spectral analysis (GSA) program was used to convert the raw data file containing the beat-by-beat heart rate measurements into R-R interval data and saved under a different file extension (.rr). Next, the R-R interval data was entered into the Hughson and Yamamoto GSA040 program to give an R-R interval time series graph which was saved under a different extension (.gs). At this stage, it was possible to edit the data. The time series graph plotted the time in min on the X axis and the R-R intervals in ms on the Y axis. A toggle, located on the 0 time mark was moved across the data points using the left and right arrow keys. The shift key was used along with the arrow keys in order to speed up the movement of the toggle.

The objective of the editing process in this study was to delete obvious outliers in the time series data. R-R interval data points with greater than 30% difference from the previous data point were considered outlier (Kamath & Fallen, 1995). The deletion of an R-R interval was accomplished by pressing the enter key while the toggle was on the outlier point. The same was done for the point which preceded it. Pressing the delete key deleted the line connecting these two points, as well as the point considered to be the outlier.

Upon completion of editing, the program generated o second time series plot which could not be edited. Fast Fourier transformation then converted the time series data into a frequency distribution table. The frequency table displays power in ms^2/Hz on the Y axis and frequency in Hz on the X axis.

APPENDIX D

Editing Baroreflex Sensitivity Data

Raw data was collected as beat-by-beat heart rate and arterial blood pressure measurements, and heart rate data was converted into R-R intervals and saved under a different file extension (.rr). The converted data file was entered into the spontaneous baroreflex program developed by Andrew Blaber of Cambridge, Ontario, Canada and the summary data generated by this program as described below was saved to a different file extension (.SBR). This program detects spontaneous sequences of three or more heart beats in which systolic BP and R-R interval simultaneously change in the same direction. It then uses linear regression to calculate the slope of each sequence. Editing for outliers or artifacts was accomplished automatically by using the "fl" command-line parameter when executing the command for each RR file.

APPENDIX E

Demographic Information Forms

Study ID: _____

HOAP Study: Demographics of Mother

Date of Testing _____ Time of Testing _____

Mother's First Name and last initial _____

Mother's Date of Birth _____ Age _____

Height: _____ Weight: Pre-pregnancy _____ Current: _____ BMI: _____

Education (last year completed) _____

Phone # _____

Family physician _____ Obstetrician _____

G____T____P____A____L____ EDB _____ GA _____

Smoker: No _____ Yes _____ Amount per day _____

Blood pressure: Supine _____ _____ _____

Blood pressure: Sitting _____ _____ _____

Blood pressure: Stand _____ _____ _____

Medications_____

Other pertinent information: _____

Date of Testing_____ Time of Testing_____ Study ID: _____

NON STRESS TEST

Clinical Criteria:

1. Number of FHR accelerations > 10 bpm _____
2. Number of FHR accelerations > 15 bpm _____
3. Number of FHR decelerations > 10 bpm _____
4. Number of FHR decelerations > 15 bpm _____

Reactive? Yes No

BIOPHYSICAL PROFILE

Fetal Breathing (s) Recorder # 1: _____ Initials: _____

Fetal Breathing (s) Recorder # 2: _____ Initials: _____

Fetal Body Movements (count) Recorder # 1: _____ Initials: _____

Recorder # 2: _____ Initials: _____

RUQ: _____ LUQ: _____

RLQ: _____ LLQ: _____

AFI _____

BPP score:

Fetal breathing movements (30 consecutive seconds) ____/2

Fetal body movements x 3 ____/2

Fetal tone (brisk extension and return to flexion) ____/2

Amniotic fluid pocket 2cm x 2cm ____/2

Fetal Position _____ Placental Location _____

Membranes: Intact Ruptured

Comments: _____

Study ID:_____

HOAP Study: DEMOGRAPHICS OF BABY

Baby's Name (first, middle initial) _____ Gender: M F

Birth date _____ Gestational age_____

Length of labour _____ Type of Birth: _____

Complications during labour & birth: _____

_____

Head circumference _____cm Length _____cm

Chest circumference _____cm Abdominal circum. _____cm

Birth weight _____g Percentile_____%

APGAR score: 1 min _____ 5 min _____ 10 min _____

Cord Gases	Artery	Vein
	Base Excess_____	Base Excess_____
	pH_____	pH_____

Length of hospital stay _____

Comments: _____

APPENDIX F

ANOVA Summary Tables

1-way ANOVA for Demographic and Obstetrical Maternal Characteristics

		SS	df	MS	F	P
GA testing	Between Groups	17.083	2	8.542	6.929	.000*
	Within Groups	71.500	58	1.233		
	Total	88.583	60			
Maternal age	Between Groups	76.796	2	38.398	2.664	.000*
(years)	Within Groups	835.893	58	14.412		
	Total	912.689	60			
Prepreg BMI	Between Groups	592.421	2	296.210	17.433	.000*
	Within Groups	968.505	57	16.991		
	Total	1560.926	59			
BMI at	Between Groups	770.331	2	385.165	26.961	.000*
testing	Within Groups	814.313	57	14.286		
	Total	1584.644	59			

Note: YEARS = Maternal age in years; GA = gestational age; BMI = body mass index

1-way ANOVA for Delivery Outcome Measures

Source		SS	df	MS	F	P
GA delivery	Between Groups	1.428	2	.714	.532	.590
	Within Groups	75.080	56	1.341		
	Total	76.508	58			
1 min APGAR	Between Groups	4.573	2	2.287	.459	.635
	Within Groups	259.136	52	4.983		
	Total	263.709	54			
5 min APGAR	Between Groups	.498	2	.249	.637	.533
	Within Groups	20.302	52	.390		
	Total	20.800	54			
BW	Between Groups	546365.647	2	273182.824	1.121	.333
	Within Groups	1.34E7	55	243645.831		
	Total	1.395E7	57			

Note: BW = birth weight

Effects of Maternal Position on Systolic BP

Within-Subjects

Source	Type III Sum of Squares	df	Mean Square	F	Sig.
position	61.284	1.982	30.924	1.546	.218
position * GAtesteddays	52.135	1.982	26.308	1.316	.272
position * Group	162.143	3.963	40.909	2.046	.094
Error(position)	2179.606	108.996	19.997		

Between-Subjects

Source	Type III Sum of Squares	df	Mean Square	F	Sig.
Intercept	337.505	1	337.505	1.679	.200
GAtesteddays	750.942	1	750.942	3.735	.058
Group	10342.300	2	5171.150	25.722	.000
Error	11057.382	55	201.043		

Effects of Maternal Position on Diastolic BP

Within-Subjects

Source	Type III Sum of Squares	df	Mean Square	F	Sig.
position	27.055	1.991	13.591	.775	.463
position * GAtesteddays	23.489	1.991	11.800	.673	.512
position * Group	105.591	3.981	26.522	1.512	.204
Error(position)	1919.927	109.485	17.536		

Between-Subjects

Source	Type III Sum of Squares	df	Mean Square	F	Sig.
Intercept	266.187	1	266.187	2.033	.160
GAtesteddays	163.819	1	163.819	1.251	.268
Group	5338.310	2	2669.155	20.389	.000
Error	7200.196	55	130.913		

1-way ANOVA for Maternal BP in the Supine, Sitting and Standing Positions Separately

		SS	df	MS	F	P
Sitting	Between Groups	6853.778	2	3426.889	43.625	.000*
SBP	Within Groups	4556.091	58	78.553		
	Total	11409.869	60			
Sitting	Between Groups	2854.938	2	1427.469	29.111	.000*
DBP	Within Groups	2844.095	58	49.036		
	Total	5699.034	60			
Stand	Between Groups	5406.795	2	2703.398	21.995	.000*
SBP	Within Groups	4528.724	58	78.081		
	Total	9935.519	60			
Stand	Between Groups	2632.190	2	1316.095	21.995	.000*
DBP	Within Groups	3470.479	58	59.836		
	Total	6102.669	60			
Supine	Between Groups	2402.560	2	1201.280	23.764	.000*
SBP	Within Groups	3002.326	56	88.982		
	Total	5404.886	58			
Supine	Between Groups	2402.560	2	1201.280	22.407	.000*
DBP	Within Groups		56	53.613		
	Total		58			

Note: Dia = Diastolic BP; Sys = Systolic BP

1-way ANOVA for Supine Maternal HRV Measures

		SS	df	MS	F	P
Supine LF Power	Between Groups	.341	2	.170	.978	.384
	Within Groups	7.668	44	.174		
	Total	8.008	46			
Supine HF Power	Between Groups	2.047	2	1.023	2.538	.091
	Within Groups	17.738	44	.403		
	Total	19.784	46			
Supine Total	Between Groups	.631	2	.315	1.743	.187
Power	Within Groups	7.959	44	.181		
	Total	8.590	46			
Supine SNS	Between Groups	.431	2	.216	1.406	.256
indicator	Within Groups	6.749	44	.153		
	Total	7.180	46			
Supine PNS	Between Groups	.241	2	.120	1.304	.282
indicator	Within Groups	4.059	44	.092		
	Total	4.300	46			

1-way ANOVA for Standing Maternal HRV Measures

		SS	df	MS	F	P
Standing LF Power	Between Groups	.375	2	.188	1.349	.271
	Within Groups	5.842	42	.139		
	Total	6.217	44			
Standing HF Power	Between Groups	.169	2	.085	.366	.695
	Within Groups	9.691	42	.231		
	Total	9.860	44			
Standing Total	Between Groups	.263	2	.131	1.098	.343
Power	Within Groups	5.025	42	.129		
	Total	5.287	44			
Standing SNS	Between Groups	.062	2	.031	.238	.789
indicator	Within Groups	5.439	42	.129		
	Total	5.500	44			
Standing PNS	Between Groups	.049	2	.024	.238	.789
indicator	Within Groups	4.294	42	.102		
	Total	4.343	44			

1-way ANOVA for Maternal Baroreflex Measures

		SS	df	MS	F	P
Supine RR	Between Groups	4627.128	2	29944.595	3.225	.050*
Interval	Within Groups	380722.860	41	9285.923		
	Total	440612.049	43			
Supine	Between Groups	4627.128	2	2313.564	5.838	.006*
Arterial	Within Groups	16246.749	41	396.262		
BP	Total	20873.877	43			
Supine	Between Groups	41.335	2	20.668	.474	.626
Slope	Within Groups	1787.418	41	43.596		
	Total	1828.754	43			
Standing	Between Groups	12961.152	2	6480.576	1.259	.297
RR	Within Groups	180205.806	35	5148.737		
Interval	Total	193166.959	37			
Standing	Between Groups	3925.632	2	1962.816	1.806	.179
Arterial	Within Groups	38042.484	35	1086.928		
BP	Total	41968.116	37			
Standing	Between Groups	3.131	2	1.565	.147	.863
Slope	Within Groups	371.652	35	10.619		
	Total	374.782	37			

Effect of Maternal Position on Baroreflex Slope

Within-Subjects

Source	Type III Sum of Squares	df	Mean Square	F	Sig.
position	67.503	1.000	67.503	6.287	.017
position * GAtesteddays	62.293	1.000	62.293	5.802	.022
position * Group	35.062	2.000	17.531	1.633	.211
Error(position)	343.583	32.000	10.737		

Between-Subjects

Source	Type III Sum of Squares	df	Mean Square	F	Sig.
Intercept	58.452	1	58.452	1.424	.242
GAtesteddays	35.182	1	35.182	.857	.362
Group	24.814	2	12.407	.302	.741
Error	1313.829	32	41.057		

Effect of Maternal Position on Finger-Cuff Arterial Systolic BP

Within-Subjects

Source	Type III Sum of Squares	df	Mean Square	F	Sig.
position	234.835	1.000	234.835	.462	.502
position * GAtesteddays	278.542	1.000	278.542	.548	.465
position * Group	2519.951	2.000	1259.975	2.478	.100
Error(position)	16268.654	32.000	508.395		

Between-Subjects

Source	Type III Sum of Squares	df	Mean Square	F	Sig.
Intercept	11.708	1	11.708	.012	.912
GAtesteddays	818.255	1	818.255	.861	.361
Group	5634.399	2	2817.200	2.963	.066
Error	30425.029	32	950.782		

Effect of Maternal Position on RR interval

Within-Subjects

Source	Type III Sum of Squares	df	Mean Square	F	Sig.
position	2427.844	1.000	2427.844	1.522	.226
position * GAtesteddays	1297.234	1.000	1297.234	.813	.374
position * Group	3953.648	2.000	1976.824	1.239	.303
Error(position)	51046.572	32.000	1595.205		

Between-Subjects

Source	Type III Sum of Squares	df	Mean Square	F	Sig.
Intercept	40527.510	1	40527.510	2.947	.096
GAtesteddays	914.163	1	914.163	.066	.798
Group	22584.106	2	11292.053	.821	.449
Error	440075.289	32	13752.353		

Effect of Maternal Position on LF Power

Within-Subjects

Source	Type III Sum of Squares	df	Mean Square	F	Sig.
position	.072	1.000	.072	1.496	.229
position * GAtesteddays	.074	1.000	.074	1.540	.222
position * Group	.090	2.000	.045	.936	.401
Error(position)	1.880	39.000	.048		

Between-Subjects

Source	Type III Sum of Squares	df	Mean Square	F	Sig.
Intercept	.171	1	.171	.601	.443
GAtesteddays	.014	1	.014	.049	.826
Group	.502	2	.251	.882	.422
Error	11.092	39	.284		

Effect of Maternal Position on HF Power

Within-Subjects

Source	Type III Sum of Squares	df	Mean Square	F	Sig.
position	.485	1.000	.485	4.509	.040
position * GAtesteddays	.449	1.000	.449	4.176	.048
position * Group	.042	2.000	.021	.198	.822
Error(position)	4.193	39.000	.108		

Between-Subjects

Source	Type III Sum of Squares	df	Mean Square	F	Sig.
Intercept	.039	1	.039	.072	.790
GAtesteddays	.065	1	.065	.119	.732
Group	1.262	2	.631	1.160	.324
Error	21.220	39	.544		

Effect of Maternal Position on Total Power

Within-Subjects

Source	Type III Sum of Squares	df	Mean Square	F	Sig.
position	.032	1.000	.032	.517	.476
position * GAtesteddays	.036	1.000	.036	.582	.450
position * Group	.118	2.000	.059	.949	.396
Error(position)	2.433	39.000	.062		

Between-Subjects

Source	Type III Sum of Squares	df	Mean Square	F	Sig.
Intercept	.781	1	.781	3.009	.091
GAtesteddays	.024	1	.024	.091	.764
Group	.382	2	.191	.735	.486
Error	10.126	39	.260		

Effect of Maternal Position on SNS Indicator

Within-Subjects

Source	Type III Sum of Squares	df	Mean Square	F	Sig.
position	.147	1.000	.147	1.797	.188
position * GAtesteddays	.122	1.000	.122	1.494	.229
position * Group	.095	2.000	.048	.584	.562
Error(position)	3.185	39.000	.082		

Between-Subjects

Source	Type III Sum of Squares	df	Mean Square	F	Sig.
Intercept	.068	1	.068	.377	.543
GAtesteddays	.034	1	.034	.190	.666
Group	.131	2	.066	.366	.696
Error	7.002	39	.180		

Effect of Maternal Position on PNS Indicator

Within-Subjects

Source	Type III Sum of Squares	df	Mean Square	F	Sig.
position	.321	1.000	.321	5.176	.028
position * GAtesteddays	.284	1.000	.284	4.571	.039
position * Group	.025	2.000	.012	.199	.820
Error(position)	2.422	39.000	.062		

Between-Subjects

Source	Type III Sum of Squares	df	Mean Square	F	Sig.
Intercept	.404	1	.404	2.619	.114
GAtesteddays	.126	1	.126	.819	.371
Group	.185	2	.092	.600	.554
Error	6.011	39	.154		

1-way ANOVA for FHR Accelerations and Decelerations

		SS	df	MS	F	P
FHR accel	Between Groups	27.761	2	13.880	1.113	.335
≥ 10	Within Groups	723.321	58	12.471		
	Total	751.082	60			
FHR accel	Between Groups	40.957	2	20.479	3.058	.055
≥ 15	Within Groups	388.452	58	6.697		
	Total	429.410	60			
FHR decel	Between Groups	.707	2	.354	.327	.722
≥ 10	Within Groups	62.702	58	1.081		
	Total	63.410	60			
FHR decel	Between Groups	.350	2	.175	.439	.647
≥ 15	Within Groups	23.093	58	.398		
	Total	23.443	60			
Standing	Between Groups	2.736	2	.354	.327	.722
FHR accel	Within Groups	95.938	49	1.081		
≥ 10	Total	98.673	51			
Standing	Between Groups	.124	2	.175	.439	.647
FHR accel	Within Groups	58.549	49	.398		
≥ 15	Total	58.673	51			
Standing	Between Groups	.259	2	.129	.488	.617
FHR decel	Within Groups	12.972	49	.265		
≥ 10	Total	13.231	51			
Standing	Between Groups	.036	2	.018	.913	.408
FHR decel	Within Groups	.944	49	.020		
≥ 15	Total	.980	51			

Effect of Maternal Position on FHR Accelerations ≥ 10

Within-Subjects

Source	Type III Sum of Squares	df	Mean Square	F	Sig.
condition	3.724	1.000	3.724	3.335	.074
condition * GAtesteddays	3.456	1.000	3.456	3.095	.085
condition * Group	.693	2.000	.347	.310	.735
Error(condition)	53.606	48.000	1.117		

Between-Subjects

Source	Type III Sum of Squares	df	Mean Square	F	Sig.
Intercept	.073	1	.073	.045	.834
GAtesteddays	.790	1	.790	.485	.490
Group	6.173	2	3.086	1.893	.162
Error	78.282	48	1.631		

Effect of Maternal Position on FHR Accelerations ≥ 15

Within-Subjects

Source	Type III Sum of Squares	df	Mean Square	F	Sig.
condition	3.261	1.000	3.261	5.070	.029
condition * GAtesteddays	3.270	1.000	3.270	5.083	.029
condition * Group	4.218	2.000	2.109	3.279	.046
Error(condition)	30.875	48.000	.643		

Between-Subjects

Source	Type III Sum of Squares	df	Mean Square	F	Sig.
Intercept	.302	1	.302	.319	.575
GAtesteddays	.026	1	.026	.027	.870
Group	1.259	2	.629	.665	.519
Error	45.459	48	.947		

Effect of Maternal Position on FHR Decelerations ≥ 10

Within-Subjects

Source	Type III Sum of Squares	df	Mean Square	F	Sig.
condition	.007	1.000	.007	.051	.823
condition * GAtesteddays	.006	1.000	.006	.047	.829
condition * Group	.169	2.000	.084	.635	.534
Error(condition)	6.367	48.000	.133		

Between-Subjects

Source	Type III Sum of Squares	df	Mean Square	F	Sig.
Intercept	.001	1	.001	.004	.952
GAtesteddays	.002	1	.002	.009	.925
Group	.110	2	.055	.262	.771
Error	10.086	48	.210		

Effect of Maternal Position on FHR Decelerations ≥ 15

Within-Subjects

Source	Type III Sum of Squares	df	Mean Square	F	Sig.
condition	.071	1.000	.071	3.145	.083
condition * GAtesteddays	.066	1.000	.066	2.919	.094
condition * Group	.023	2.000	.011	.505	.607
Error(condition)	1.056	47.000	.022		

Between-Subjects

Source	Type III Sum of Squares	df	Mean Square	F	Sig.
Intercept	.016	1	.016	.775	.383
GAtesteddays	.021	1	.021	.974	.329
Group	.001	2	.000	.020	.980
Error	.990	47	.021		

1-way ANOVA for Spontaneous Fetal Behavioural Measures

		SS	df	MS	F	P
AFI	Between Groups	1037.383	2	518.692	.410	.666
	Within Groups	73362.617	58	1264.873		
	Total	74400.000				
Breathing movements (s)	Between Groups	45383.623	2	22691.812	.202	.818
	Within Groups	5946635.806	53	112200.676		
	Total	599.2019.429	55			
Distance to Fetal head	Between Groups	1.118	2	.559	.468	.629
	Within Groups	69.344	58	1.196		
	Total	70.462	60			

Note: AFI = Amniotic Fluid Index

Auditory – Induced FHR

Voice order effect

Within-Subjects

Source	Type III Sum of Squares	df	Mean Square	F	Sig.
time	13095.120	7.173	1825.660	2.021	.050
time * direction	3999.506	7.173	557.592	.617	.746
Error(time)	388837.130	430.369	903.497		

Between subject

Source	Type III Sum of Squares	df	Mean Square	F	Sig.
Intercept	1.432E8	1	1.432E8	19201.873	.000
direction	1139.230	1	1139.230	.153	.697
Error	447456.893	60	7457.615		

Mother's Voice forwards – 30 s

30 s Surrounding Onset of the Mother's Voice Forward

Within-Subjects

Source	Type III Sum of Squares	df	Mean Square	F	Sig.
condition	274.399	1.000	274.399	.305	.583
condition * GAtesteddays	297.812	1.000	297.812	.331	.567
condition * Group	3488.042	2.000	1744.021	1.938	.153
Error(condition)	51307.199	57.000	900.126		
time	1499.011	3.909	383.509	1.476	.211
time * GAtesteddays	1491.597	3.909	381.612	1.469	.214
time * Group	4476.994	7.817	572.700	2.204	.029
Error(time)	57883.128	222.794	259.805		
condition * time	1730.042	2.849	607.228	1.281	.283
condition * time * GAtesteddays	1690.123	2.849	593.217	1.252	.293
condition * time * Group	3757.907	5.698	659.495	1.392	.224
Error(condition*time)	76955.990	162.398	473.874		

Between-Subjects

Source	Type III Sum of Squares	df	Mean Square	F	Sig.
Intercept	67100.879	1	67100.879	16.667	.000
GAtesteddays	112.925	1	112.925	.028	.868
Group	13467.052	2	6733.526	1.672	.197
Error	229485.935	57	4026.069		

Last 30 s Prior to Mother's Voice Onset

Within-Subjects

Source	Type III Sum of Squares	df	Mean Square	F	Sig.
time	1735.824	2.433	713.496	1.393	.251
time * GAtesteddays	1673.483	2.433	687.872	1.343	.265
time * Group	5240.941	4.866	1077.123	2.103	.070
Error(time)	71023.020	138.672	512.166		

Between-Subjects

Source	Type III Sum of Squares	df	Mean Square	F	Sig.
Intercept	38622.600	1	38622.600	15.280	.000
GAtesteddays	457.625	1	457.625	.181	.672
Group	14841.327	2	7420.664	2.936	.061
Error	144078.635	57	2527.695		

First 30 s Following Onset of the Mother's Voice

Within-Subjects

Source	Type III Sum of Squares	df	Mean Square	F	Sig.
time	1339.906	3.780	354.461	1.240	.295
time * GAtesteddays	1721.466	3.780	455.399	1.593	.180
time * mumbaseFHR	1320.875	3.780	349.426	1.223	.303
time * Group	2780.876	7.560	367.829	1.287	.254
Error(time)	60500.086	211.687	285.800		

Between-Subjects

Source	Type III Sum of Squares	df	Mean Square	F	Sig.
Intercept	2161.609	1	2161.609	1.722	.195
GAtesteddays	.698	1	.698	.001	.981
mumbaseFHR	67060.228	1	67060.228	53.421	.000
Group	3150.299	2	1575.149	1.255	.293
Error	70298.001	56	1255.321		

30 s Surrounding Offset of the Mother's Voice Forward

Within-Subjects

Source	Type III Sum of Squares	df	Mean Square	F	Sig.
condition	.008	1.000	.008	.000	.998
condition * GAtesteddays	1.518	1.000	1.518	.001	.970
condition * Group	3095.859	2.000	1547.930	1.457	.242
Error(condition)	60575.449	57.000	1062.727		
time	1641.500	3.382	485.348	2.259	.075
time * GAtesteddays	1575.877	3.382	465.945	2.168	.085
time * Group	1582.691	6.764	233.980	1.089	.372
Error(time)	41425.824	192.780	214.886		
condition * time	503.838	3.421	147.261	.562	.664
condition * time * GAtesteddays	496.984	3.421	145.258	.554	.669
condition * time * Group	1755.140	6.843	256.494	.978	.447
Error(condition*time)	51126.334	195.020	262.160		

Between-Subjects

Source	Type III Sum of Squares	df	Mean Square	F	Sig.
Intercept	44919.437	1	44919.437	9.318	.003
GAtesteddays	1388.748	1	1388.748	.288	.594
Group	29259.004	2	14629.502	3.035	.056
Error	274793.408	57	4820.937		

30 s Immediately Prior to Offset of the Mother's Voice Forward

Within-Subjects

Source	Type III Sum of Squares	df	Mean Square	F	Sig.
Time	524.264	4.407	118.961	.706	.602
Time * meanmumFHR	1384.360	4.407	314.126	1.863	.111
Time * GAtesteddays	1353.558	4.407	307.137	1.822	.119
Time * Group	929.953	8.814	105.508	.626	.771
Error(Time)	37890.808	224.758	168.585		

Between-Subjects

Source	Type III Sum of Squares	df	Mean Square	F	Sig.
Intercept	6557.283	1	6557.283	2.602	.113
meanmumFHR	8719.384	1	8719.384	3.460	.069
GAtesteddays	1431.708	1	1431.708	.568	.454
Group	2454.233	2	1227.116	.487	.617
Error	128507.514	51	2519.755		

30 s Immediately Following Offset of the Mother's Voice

Within-Subjects

Source	Type III Sum of Squares	df	Mean Square	F	Sig.
time	868.412	2.622	331.148	.955	.407
time * GAtesteddays	852.651	2.622	325.138	.937	.415
time * Group	2347.334	5.245	447.550	1.290	.270
Error(time)	51855.936	149.478	346.913		

Between-Subjects

Source	Type III Sum of Squares	df	Mean Square	F	Sig.
Intercept	22478.822	1	22478.822	6.884	.011
GAtesteddays	741.046	1	741.046	.227	.636
Group	25684.825	2	12842.413	3.933	.025
Error	186122.719	57	3265.311		

Mother's Voice – 90 s

90 s Surrounding Onset of the Mother's Voice Forward

Within-Subjects

Source	Type III Sum of Squares	df	Mean Square	F	Sig.
condition	1783.038	1.000	1783.038	1.174	.283
condition * GAtesteddays	1837.291	1.000	1837.291	1.210	.276
condition * Group	11548.106	2.000	5774.053	3.801	.028
Error(condition)	86584.217	57.000	1519.021		
time	4461.876	6.337	704.149	1.010	.421
time * GAtesteddays	4432.917	6.337	699.579	1.003	.425
time * Group	6581.427	12.673	519.322	.745	.715
Error(time)	251889.252	361.183	697.400		
condition * time	15600.479	6.773	2303.227	3.771	.001
condition * time * GAtesteddays	15345.757	6.773	2265.620	3.710	.001
condition * time * Group	15479.172	13.547	1142.659	1.871	.030
Error(condition*time)	235786.163	386.079	610.720		

Between-Subjects

Source	Type III Sum of Squares	df	Mean Square	F	Sig.
Intercept	135305.148	1	135305.148	12.002	.001
GAtesteddays	3808.016	1	3808.016	.338	.563
Group	65129.709	2	32564.855	2.889	.064
Error	642568.647	57	11273.134		

90 s Following Onset of the Mother's Voice

Within-Subjects

Source	Type III Sum of Squares	df	Mean Square	F	Sig.
time	13309.284	6.790	1960.152	3.100	.004
time * GAtesteddays	10238.155	6.790	1507.846	2.385	.023
time * mumbaseFHR	12099.811	6.790	1782.025	2.819	.008
time * Group	14724.351	13.580	1084.280	1.715	.053
Error(time)	240403.140	380.236	632.248		

Between-Subjects

Source	Type III Sum of Squares	df	Mean Square	F	Sig.
Intercept	461.943	1	461.943	.184	.670
GAtesteddays	4152.136	1	4152.136	1.651	.204
mumbaseFHR	198022.927	1	198022.927	78.718	.000
Group	10644.883	2	5322.441	2.116	.130
Error	140873.754	56	2515.603		

90 s Surrounding Offset of the Mother's Voice Forward

Within-Subjects

Source	Type III Sum of Squares	df	Mean Square	F	Sig.
condition	16.027	1.000	16.027	.019	.890
condition * GAtesteddays	16.545	1.000	16.545	.020	.888
condition * Group	2897.924	2.000	1448.962	1.745	.184
Error(condition)	46495.926	56.000	830.284		
time	4369.250	6.413	681.333	1.042	.399
time * GAtesteddays	4297.725	6.413	670.179	1.025	.410
time * Group	13762.525	12.826	1073.051	1.642	.073
Error(time)	234719.646	359.117	653.603		
condition * time	8274.501	4.675	1770.020	1.825	.113
condition * time * GAtesteddays	8026.383	4.675	1716.944	1.770	.124
condition * time * Group	12137.345	9.350	1298.165	1.338	.215
Error(condition*time)	253939.612	261.789	970.016		

Between-Subjects

Source	Type III Sum of Squares	df	Mean Square	F	Sig.
Intercept	75612.402	1	75612.402	6.304	.015
GAtesteddays	19883.895	1	19883.895	1.658	.203
Group	83236.753	2	41618.376	3.470	.038
Error	671661.519	56	11993.956		

90 s Prior to Offset of the Mother's Voice Forward

Within-Subjects

Source	Type III Sum of Squares	df	Mean Square	F	Sig.
Time	15246.128	5.937	2567.957	3.455	.003
Time * meanmumFHR	27104.075	5.937	4565.231	6.143	.000
Time * GAtesteddays	7537.615	5.937	1269.586	1.708	.119
Time * Group	13573.102	11.874	1143.082	1.538	.110
Error(Time)	225037.718	302.790	743.213		

Between-Subjects

Source	Type III Sum of Squares	df	Mean Square	F	Sig.
Intercept	1376.851	1	1376.851	.386	.537
meanmumFHR	117634.832	1	117634.832	32.963	.000
GAtesteddays	8156.340	1	8156.340	2.286	.137
Group	9157.102	2	4578.551	1.283	.286
Error	182004.190	51	3568.710		

90 s immediately Following Offset of the Mother's Voice Played Forward

Within-Subjects

Source	Type III Sum of Squares	df	Mean Square	F	Sig.
time	3172.547	6.594	481.095	.752	.620
time * GAtesteddays	3165.166	6.594	479.976	.751	.621
time * Group	14098.825	13.189	1068.995	1.672	.064
Error(time)	236133.444	369.288	639.429		

Between-Subjects

Source	Type III Sum of Squares	df	Mean Square	F	Sig.
Intercept	38915.034	1	38915.034	5.441	.023
GAtesteddays	9376.651	1	9376.651	1.311	.257
Group	56939.829	2	28469.915	3.981	.024
Error	400514.562	56	7152.046		

Mother's Voice Backward – 30 s

30 s Surrounding Onset of the Mother's Voice Backward

Within-Subjects

Source	Type III Sum of Squares	df	Mean Square	F	Sig.
condition	247.118	1.000	247.118	.343	.561
condition * GAtesteddays	241.968	1.000	241.968	.335	.565
condition * Group	2038.955	2.000	1019.478	1.413	.252
Error(condition)	38227.546	53.000	721.274		
time	355.057	3.702	95.909	.390	.801
time * GAtesteddays	331.091	3.702	89.435	.364	.820
time * Group	1669.858	7.404	225.533	.918	.498
Error(time)	48214.178	196.207	245.731		
condition * time	804.125	4.104	195.928	.893	.471
condition * time * GAtesteddays	906.826	4.104	220.951	1.007	.406
condition * time * Group	3540.251	8.208	431.297	1.966	.050
Error(condition*time)	47709.659	217.522	219.332		

Between-Subjects

Source	Type III Sum of Squares	df	Mean Square	F	Sig.
Intercept	128175.942	1	128175.942	23.090	.000
GAtesteddays	12579.066	1	12579.066	2.266	.138
Group	3460.506	2	1730.253	.312	.734
Error	294216.400	53	5551.253		

30 s Immediately Prior to Onset of the Mother's Voice Played Backward

Within-Subjects

Source	Type III Sum of Squares	df	Mean Square	F	Sig.
time	440.364	3.996	110.190	.445	.776
time * GAtesteddays	464.969	3.996	116.347	.470	.757
time * Group	3226.929	7.993	403.728	1.632	.117
Error(time)	53389.710	215.806	247.397		

Between-Subjects

Source	Type III Sum of Squares	df	Mean Square	F	Sig.
Intercept	70231.145	1	70231.145	21.029	.000
GAtesteddays	8321.030	1	8321.030	2.492	.120
Group	3859.391	2	1929.696	.578	.565
Error	180347.254	54	3339.764		

30 s Immediately Following Onset of the Mother's Voice Played Forward

Within-Subjects

Source	Type III Sum of Squares	df	Mean Square	F	Sig.
time	1030.544	4.060	253.799	1.159	.330
time * GAtesteddays	1088.657	4.060	268.111	1.224	.301
time * Group	2444.239	8.121	300.980	1.374	.208
Error(time)	48903.768	223.326	218.979		

Between-Subjects

Source	Type III Sum of Squares	df	Mean Square	F	Sig.
Intercept	53695.350	1	53695.350	17.401	.000
GAtesteddays	3311.836	1	3311.836	1.073	.305
Group	1694.892	2	847.446	.275	.761
Error	169719.171	55	3085.803		

30 s Immediately Surrounding Onset of the Mother's Voice Backward

Within Subjects

Source	Type III Sum of Squares	df	Mean Square	F	Sig.
BeforeAfter	1751.316	1.000	1751.316	1.555	.218
BeforeAfter * GAtesteddays	1678.639	1.000	1678.639	1.490	.227
BeforeAfter * Group	2812.580	2.000	1406.290	1.248	.295
Error(BeforeAfter)	61953.978	55.000	1126.436		
Time	1107.002	3.805	290.912	1.384	.242
Time * GAtesteddays	1093.140	3.805	287.269	1.367	.248
Time * Group	2492.551	7.611	327.512	1.558	.143
Error(Time)	43992.805	209.291	210.200		
BeforeAfter * Time	1159.274	3.243	357.481	1.402	.242
BeforeAfter * Time * GAtesteddays	1176.447	3.243	362.776	1.423	.235
BeforeAfter * Time * Group	1265.227	6.486	195.077	.765	.608
Error(BeforeAfter*Time)	45465.483	178.359	254.909		

Between Subjects

Source	Type III Sum of Squares	df	Mean Square	F	Sig.
Intercept	111268.692	1	111268.692	13.684	.001
GAtesteddays	7084.067	1	7084.067	.871	.355
Group	12704.433	2	6352.217	.781	.463
Error	447235.581	55	8131.556		

Last 30 s Prior to Offset of the Mother's Voice Backward

Within-Subjects

Source	Type III Sum of Squares	df	Mean Square	F	Sig.
Time	347.897	3.949	88.103	.391	.812
Time * GAtesteddays	338.488	3.949	85.720	.381	.820
Time * Group	1078.432	7.897	136.554	.606	.770
Error(Time)	48915.260	217.181	225.228		

Between-Subjects

Source	Type III Sum of Squares	df	Mean Square	F	Sig.
Intercept	70469.468	1	70469.468	14.137	.000
GAtesteddays	7829.772	1	7829.772	1.571	.215
Group	11178.137	2	5589.068	1.121	.333
Error	274168.738	55	4984.886		

30 s Immediately following Offset of the Mother's Voice Backward

Within-Subjects

Source	Type III Sum of Squares	df	Mean Square	F	Sig.
time	1900.007	3.077	617.507	2.559	.055
time * GAtesteddays	1920.445	3.077	624.149	2.587	.053
time * Group	2895.010	6.154	470.442	1.950	.074
Error(time)	41573.018	172.306	241.274		

Between-Subjects

Source	Type III Sum of Squares	df	Mean Square	F	Sig.
Intercept	42432.705	1	42432.705	10.066	.002
GAtesteddays	922.659	1	922.659	.219	.642
Group	3960.471	2	1980.235	.470	.628
Error	236053.452	56	4215.240		

90 s Surrounding Onset of the Mother's Voice Backward

Within-Subjects

Source	Type III Sum of Squares	df	Mean Square	F	Sig.
condition	129.861	1.000	129.861	.077	.783
condition * GAtesteddays	113.238	1.000	113.238	.067	.797
condition * Group	1158.465	2.000	579.233	.343	.711
Error(condition)	84400.164	50.000	1688.003		
time	2873.808	7.897	363.896	.761	.636
time * GAtesteddays	2894.570	7.897	366.525	.766	.631
time * Group	7118.884	15.795	450.714	.942	.520
Error(time)	188908.107	394.867	478.410		
condition * time	5926.342	6.556	903.897	1.356	.227
condition * time * GAtesteddays	5720.265	6.556	872.466	1.309	.248
condition * time * Group	23293.794	13.113	1776.407	2.665	.001
Error(condition*time)	218531.271	327.822	666.616		

Between-Subjects

Source	Type III Sum of Squares	df	Mean Square	F	Sig.
Intercept	485623.164	1	485623.164	24.542	.000
GAtesteddays	76347.810	1	76347.810	3.858	.055
Group	61990.704	2	30995.352	1.566	.219
Error	989351.888	50	19787.038		

90 s Immediately Prior to Onset of the Mother's Voice Backward

Within-Subjects

Source	Type III Sum of Squares	df	Mean Square	F	Sig.
time	2431.381	6.499	374.089	.538	.793
time * GAtesteddays	2369.978	6.499	364.642	.525	.803
time * Group	10887.698	12.999	837.584	1.206	.273
Error(time)	230304.596	331.473	694.792		

Between-Subjects

Source	Type III Sum of Squares	df	Mean Square	F	Sig.
Intercept	253401.594	1	253401.594	19.833	.000
GAtesteddays	41926.296	1	41926.296	3.282	.076
Group	32054.108	2	16027.054	1.254	.294
Error	651602.473	51	12776.519		

First 90 s of Mother's Voice Backward

Within-Subjects

Source	Type III Sum of Squares	df	Mean Square	F	Sig.
time	4848.946	6.463	750.261	1.215	.296
time * GAtesteddays	4791.859	6.463	741.428	1.201	.304
time * Group	19246.526	12.926	1488.975	2.411	.004
Error(time)	215498.923	349.003	617.471		

Between-Subjects

Source	Type III Sum of Squares	df	Mean Square	F	Sig.
Intercept	208780.336	1	208780.336	19.904	.000
GAtesteddays	23539.131	1	23539.131	2.244	.140
Group	22090.520	2	11045.260	1.053	.356
Error	566418.214	54	10489.226		

90 s Surrounding Offset of the Mother's Voice Backward

Within Subjects

Source	Type III Sum of Squares	df	Mean Square	F	Sig.
BeforeAfter	23732.893	1.000	23732.893	10.425	.002
BeforeAfter * GAtesteddays	23794.681	1.000	23794.681	10.452	.002
BeforeAfter * Group	22916.484	2.000	11458.242	5.033	.010
Error(BeforeAfter)	122928.777	54.000	2276.459		
Time	5720.916	6.021	950.202	1.257	.277
Time * GAtesteddays	5951.702	6.021	988.534	1.307	.253
Time * Group	4601.976	12.041	382.177	.505	.911
Error(Time)	245811.369	325.120	756.064		
BeforeAfter * Time	8817.671	6.445	1368.124	2.135	.044
BeforeAfter * Time * GAtesteddays	8773.064	6.445	1361.203	2.124	.046
BeforeAfter * Time * Group	17593.936	12.890	1364.912	2.130	.012
Error(BeforeAfter*Time)	223000.020	348.034	640.741		

Between Subjects

Source	Type III Sum of Squares	df	Mean Square	F	Sig.
Intercept	269685.058	1	269685.058	13.201	.001
GAtesteddays	7664.059	1	7664.059	.375	.543
Group	21694.318	2	10847.159	.531	.591
Error	1103214.966	54	20429.907		

Last 90 s Prior to Offset of the Mother's Voice Backward

Within-Subjects

Source	Type III Sum of Squares	df	Mean Square	F	Sig.
Time	2841.477	6.213	457.374	.692	.661
Time * GAtesteddays	2831.924	6.213	455.836	.690	.663
Time * Group	8342.184	12.425	671.394	1.016	.434
Error(Time)	221699.209	335.480	660.842		

Between-Subjects

Source	Type III Sum of Squares	df	Mean Square	F	Sig.
Intercept	226711.518	1	226711.518	18.397	.000
GAtesteddays	29233.585	1	29233.585	2.372	.129
Group	42058.496	2	21029.248	1.706	.191
Error	665462.159	54	12323.373		

90 s Immediately Following Offset of the Mother's Voice Backward

Within Subjects

Source	Type III Sum of Squares	df	Mean Square	F	Sig.
time	11567.611	6.315	1831.877	2.523	.019
time * GAtesteddays	11793.277	6.315	1867.614	2.573	.017
time * Group	14683.577	12.629	1162.665	1.602	.085
Error(time)	256713.404	353.619	725.961		

Between-Subjects

Source	Type III Sum of Squares	df	Mean Square	F	Sig.
Intercept	67440.293	1	67440.293	6.659	.013
GAtesteddays	2091.431	1	2091.431	.207	.651
Group	3874.818	2	1937.409	.191	.826
Error	567165.779	56	10127.960		

Auditory-Elicited Body Movements

Mother's Voice Forward

Number of Movements in the 2 min Prior to Mother's Voice Forward

Within Subjects

Source	Type III Sum of Squares	df	Mean Square	F	Sig.
time	1.035	2.336	.443	1.098	.343
time * GAtesteddays	1.009	2.336	.432	1.071	.354
time * Group	1.830	4.671	.392	.971	.434
Error(time)	50.872	126.125	.403		

Between Subjects

Source	Type III Sum of Squares	df	Mean Square	F	Sig.
Intercept	.718	1	.718	1.182	.282
GAtesteddays	.440	1	.440	.725	.398
Group	2.899	2	1.450	2.386	.102
Error	32.803	54	.607		

Number of Movements in the 2 min Mother's Voice Forward Period

Within Subjects

Source	Type III Sum of Squares	df	Mean Square	F	Sig.
time	.870	2.800	.311	.919	.428
time * GAtesteddays	.857	2.800	.306	.904	.435
time * Group	1.589	5.600	.284	.838	.535
Error(time)	53.056	156.789	.338		

Between Subjects

Source	Type III Sum of Squares	df	Mean Square	F	Sig.
Intercept	.137	1	.137	.160	.691
GAtesteddays	.014	1	.014	.016	.898
Group	.322	2	.161	.188	.829
Error	47.923	56	.856		

Number of Movements in the 2 min Following Mother's Voice Forward Offset

Within Subjects

Source	Type III Sum of Squares	df	Mean Square	F	Sig.
time	.400	2.719	.147	.408	.728
time * GAtesteddays	.378	2.719	.139	.386	.744
time * Group	1.051	5.437	.193	.537	.763
Error(time)	53.835	149.522	.360		

Between Subjects

Source	Type III Sum of Squares	df	Mean Square	F	Sig.
Intercept	.008	1	.008	.010	.920
GAtesteddays	.093	1	.093	.117	.733
Group	.827	2	.413	.521	.597
Error	43.604	55	.793		

Number of Movements in the 2 min Prior to Mother's Voice Backward

Within Subjects

Source	Type III Sum of Squares	df	Mean Square	F	Sig.
time	1.411	1.864	.757	.584	.548
time * GAtesteddays	1.313	1.864	.705	.544	.570
time * Group	2.160	3.728	.579	.447	.761
Error(time)	120.777	93.204	1.296		

Between Subjects

Source	Type III Sum of Squares	df	Mean Square	F	Sig.
Intercept	1.932	1	1.932	2.107	.153
GAtesteddays	1.303	1	1.303	1.421	.239
Group	1.591	2	.796	.868	.426
Error	45.847	50	.917		

2 min Mother's Voice Backward Period

Within Subjects

Source	Type III Sum of Squares	df	Mean Square	F	Sig.
time	.915	2.734	.335	.762	.506
time * GAtesteddays	.865	2.734	.316	.720	.529
time * Group	.834	5.468	.153	.347	.897
Error(time)	61.247	139.442	.439		

Between Subjects

Source	Type III Sum of Squares	df	Mean Square	F	Sig.
Intercept	2.910	1	2.910	3.183	.080
GAtesteddays	2.109	1	2.109	2.307	.135
Group	3.492	2	1.746	1.910	.159
Error	46.629	51	.914		

2 min Following Offset of Mother's Voice Backward

Within Subjects

Source	Type III Sum of Squares	df	Mean Square	F	Sig.
time	1.852	2.698	.687	1.572	.203
time * GAtesteddays	1.812	2.698	.672	1.538	.211
time * Group	1.430	5.395	.265	.607	.707
Error(time)	61.263	140.275	.437		

Between Subjects

Source	Type III Sum of Squares	df	Mean Square	F	Sig.
Intercept	3.777	1	3.777	4.586	.037
GAtesteddays	4.827	1	4.827	5.861	.019
Group	.030	2	.015	.018	.982
Error	42.830	52	.824		

Duration of Movements in the 2 min Prior to Mother's Voice Forward

Within Subjects

Source	Type III Sum of Squares	df	Mean Square	F	Sig.
time	43.628	2.754	15.842	.484	.678
time * GAtesteddays	41.196	2.754	14.959	.457	.696
time * Group	279.001	5.508	50.654	1.548	.172
Error(time)	4867.732	148.716	32.732		

Between Subjects

Source	Type III Sum of Squares	df	Mean Square	F	Sig.
Intercept	8.177	1	8.177	.150	.700
GAtesteddays	1.873	1	1.873	.034	.854
Group	216.312	2	108.156	1.987	.147
Error	2939.106	54	54.428		

Duration of Movements in the 2 min Mother's Voice Forward Period

Within Subjects

Source	Type III Sum of Squares	df	Mean Square	F	Sig.
time	47.191	2.760	17.099	.461	.694
time * GAtesteddays	49.057	2.760	17.775	.479	.681
time * Group	47.426	5.520	8.592	.232	.958
Error(time)	5733.668	154.557	37.097		

Between Subjects

Source	Type III Sum of Squares	df	Mean Square	F	Sig.
Intercept	85.708	1	85.708	1.254	.267
GAtesteddays	53.563	1	53.563	.784	.380
Group	65.977	2	32.988	.483	.620
Error	3826.212	56	68.325		

Duration of Movements in the 2 min Following Offset of Mother's Voice Forward

Within Subjects

Source	Type III Sum of Squares	df	Mean Square	F	Sig.
time	84.064	2.858	29.408	.805	.487
time * GAtesteddays	83.809	2.858	29.319	.803	.489
time * Group	103.864	5.717	18.168	.498	.801
Error(time)	5740.122	157.217	36.511		

Between Subjects

Source	Type III Sum of Squares	df	Mean Square	F	Sig.
Intercept	1.228	1	1.228	.015	.902
GAtesteddays	8.941	1	8.941	.112	.740
Group	56.863	2	28.431	.355	.703
Error	4403.983	55	80.072		

Duration of Movements in the 2 min Prior to Mother's Voice Backward

Within Subjects

Source	Type III Sum of Squares	df	Mean Square	F	Sig.
time	113.621	2.754	41.258	1.071	.360
time * GAtesteddays	110.485	2.754	40.119	1.042	.372
time * Group	244.072	5.508	44.313	1.151	.337
Error(time)	5302.625	137.697	38.509		

Between Subjects

Source	Type III Sum of Squares	df	Mean Square	F	Sig.
Intercept	227.805	1	227.805	2.096	.154
GAtesteddays	168.173	1	168.173	1.547	.219
Group	116.367	2	58.183	.535	.589
Error	5433.763	50	108.675		

Duration of Movements in the 2 min Mother's Voice Backward Period

Within Subjects

Source	Type III Sum of Squares	df	Mean Square	F	Sig.
time	230.623	2.483	92.869	2.186	.105
time * GAtesteddays	224.959	2.483	90.588	2.132	.111
time * Group	375.801	4.967	75.665	1.781	.122
Error(time)	5381.287	126.650	42.490		

Between Subjects

Source	Type III Sum of Squares	df	Mean Square	F	Sig.
Intercept	215.298	1	215.298	3.251	.077
GAtesteddays	163.424	1	163.424	2.468	.122
Group	316.090	2	158.045	2.386	.102
Error	3377.688	51	66.229		

Duration of Movements in the 2 min Following Offset of Mother's Voice Backward

Within Subjects

Source	Type III Sum of Squares	df	Mean Square	F	Sig.
time	351.966	2.511	140.151	2.988	.042
time * GAtesteddays	351.247	2.511	139.865	2.982	.042
time * Group	290.374	5.023	57.813	1.232	.297
Error(time)	6125.777	130.589	46.909		

Between Subjects

Source	Type III Sum of Squares	df	Mean Square	F	Sig.
Intercept	247.662	1	247.662	3.201	.079
GAtesteddays	315.570	1	315.570	4.078	.049
Group	77.777	2	38.888	.503	.608
Error	4023.839	52	77.382		

APPENDIX G

Correlation Tables

Results of Pearson Product-moment correlation, maternal cardiac autonomic measures and spontaneous fetal behaviour while the mother was in the supine position for the overweight group.

	LF power (n=14)	HF power (n=14)	Total power (n=14)	PNS indicator (n=14)	SNS indicator (n=14)	Slope (n=12)	Systolic arterial BP (n=12)	RR interval (n=12)
Supine FHR accel ≥ 10								
Supine FHR accel ≥ 15								
Supine FHR decel ≥ 10								
Supine FHR decel ≥ 15								
Body movements								
Breathing movements		0.611*		0.695*	0.625*			

* $p < 0.05$

Results of Pearson Product-moment correlation, maternal cardiac autonomic measures and spontaneous fetal behaviour while the mother was in the supine position for the normal weight comparison group.

	LF power (n=19)	HF power (n=19)	Total power (n=19)	PNS indicator (n=19)	SNS indicator (n=19)	Slope (n=18)	Systolic arterial BP (n=18)	RR interval (n=18)
Supine FHR accel ≥ 10								
Supine FHR accel ≥ 15								
Supine FHR decel ≥ 10								
Supine FHR decel ≥ 15							0.621*	
Body movements	0.564*							
Breathing movements								

$p < 0.05$

Results of Pearson Product-moment correlation, maternal cardiac autonomic measures and spontaneous fetal behaviour while the mother was in the standing position for the hypertensive group.

	LF power (n=13)	HF power (n=13)	Total power (n=13)	PNS indicator (n=13)	SNS indicator (n=13)	Slope (n=11)	Systolic arterial BP (n=11)	RR interval (n=11)
Standing FHR accel ≥ 10								
Standing FHR accel ≥ 15								
Standing FHR decel ≥ 10							0.702*	
Standing FHR decel ≥ 15								
Body movements								
Breathing movements								

$p < 0.05$

Results of Pearson Product-moment correlation, maternal cardiac autonomic measures and spontaneous fetal behaviour while the mother was in the standing position for the overweight group.

	LF power (n=15)	HF power (n=15)	Total power (n=15)	PNS indicator (n=15)	SNS indicator (n=15)	Slope (n=12)	Systolic arterial BP (n=12)	RR interval (n=12)
Standing FHR accel ≥ 10								
Standing FHR accel ≥ 15								
Standing FHR decel ≥ 10								
Standing FHR decel ≥ 15								
Body movements								
Breathing movements					0.629*			

* $p < 0.05$

Results of Pearson Product-moment correlation, maternal cardiac autonomic measures and spontaneous fetal behaviour while the mother was in the standing position for the normal weight comparison group.

	LF power (n=16)	HF power (n=16)	Total power (n=16)	PNS indicator (n=16)	SNS indicator (n=16)	Slope (n=14)	Systolic arterial BP (n=14)	RR interval (n=14)
Standing FHR accel ≥ 10								
Standing FHR accel ≥ 15							0.693*	
Standing FHR decel ≥ 10								
Standing FHR decel ≥ 15								
Body movements	0.585*							
Breathing movements								

* $p < 0.05$