The Impact of Maternal Positive and Negative Affect on Fetal Physiology and Diurnal Patterns

Gillian E. Hanley, PhD, [2,4] Dan Rurak, PhD,[2,3] Ken Lim, MD, FRCSC,[2,3] Ursula Brain, BA,[1,2] and Tim F. Oberlander, MD, FRCPc[1,2]

[1] *Department of Pediatrics University of British Columbia, Vancouver BC, Canada*
[2] *Child & Family Research Institute, University of British Columbia, Vancouver BC, Canada*
[3] *Departments of Obstetrics & Gynecology, University of British Columbia, Vancouver BC, Canada*
[4] *School of Population and Public Health, University of British Columbia, Vancouver, BC, Canada*

ABSTRACT

Background: While research has shown that maternal mood (depression and/or anxiety) can have effects on the fetus, little is known about whether maternal positive and negative affect influences the fetus.

Method: We examined fetal vascular and heart rate changes at 36 weeks gestation in 53 euthymic mothers according to their Positive and Negative Affect Scale (PANAS) scores.

Results: Mothers who reported high levels of negative affect showed reduced uterine artery flow, decreased fetal heart rate (fHR) variability, an altered diurnal pattern, and decreased uterine artery cross-sectional area compared to mothers who reported low levels of negative affect. Mothers with low positive affect had a steeper diurnal pattern in fHR accelerations and decreased uterine artery mean velocity flow than mothers with high positive affect.

Limitations: Our observational study suffers from a small sample size.

Conclusion: Even in the absence of an Axis I Major Depressive Disorder (MDD), variations in maternal affect appear to be associated with variations in fetal and uterine physiology.

INTRODUCTION

The notion that a mother's mood during pregnancy shapes the developing fetal brain, which influences risks for mental and physical health across the life span has been a part of popular beliefs for millennia (1). Exposure to maternal mood disturbances during pregnancy is among the earliest of adverse experiences and has long-term effects on the offspring (2). While substantial evidence points to how early life adversity predisposes to poor mental health and stress adaptation across the life span (3) little is known about how such affect disorders, whether postive or negative, influence fetal development during a typical pregnancy.

An individual's affective state is now known to be correlated with their health status (4, 5), but why some are more prone than others to feel anxious, neurotic and threatened by life's stressors remains unclear. These tendencies, known as negative affect (NA), are generally maintained as relatively stable characteristics, with individuals expressing feelings like anger, contempt, shame, fear and depression (6). On the other hand, individuals with high positive affect (which reflects an individual's enthusiasm, activity, control and commitment) seem able to maintain a positive outlook over both time and in various situations (7).

Funding Source: G.E.H. is supported by the Canadian Institutes for Health Research, the Michael Smith Foundation for Health Research, Women's Health Research Institute and Neurodevnet. T.F.O. is the R. Howard Webster Professor in Early Child Development at the University of British Columbia and his work is supported by the Child and Family Research Institute and the Canadian Institutes for Health Research. This study was supported by the Child and Family Research Institute (UBC) and the Canadian Institutes of Health Research [MOP-57837].

Address for Correspondence: ✉ Tim F. Oberlander, MD, Child & Family Research Institute, F605 4480 Oak St., Vancouver, BC V6H 3V4, Canada
toberlander@cw.bc.ca

With respect to mother's mood, research examining maternal mood disturbances (depression and/or anxiety) during pregnancy has suggested that it is an independent risk factor for operative delivery (8), preterm birth (9) and low birth weight (9). Studies comparing the infants born to mothers with higher depression scores have noted that they are at increased risk for decreased motor tone, more abnormal reflexes, lower activity levels, less robustness and endurance, increased irritability, and inferior orientation compared to infants born to mothers with low depression scores (10, 11). Antenatal depressed mood during pregnancy has been associated with atypical frontal EEG patterns, reduced vagal tone, elevated cortisol and norepinephrine, and lower dopamine and serotonin levels in the offspring (12). Prenatal maternal anxiety predicts infant temperament and attention regulation during the first year of life (12, 13), even when accounting for postnatal maternal psychological state, consistent with a fetal progamming hypothesis.

Fetuses of mothers who are depressed display a higher baseline fetal heart rate (fHR), a slower fHR reaction to an external stimulus, and a longer period to return to fHR baseline levels after the stimulus compared with fetuses in a control group (14). Previous work examining how maternal psychological state affects the fetus has shown that fetuses of mothers who reported greater daily stress showed significantly lower fHR variability than the low stress group. Fetuses of depressed and/or anxious mothers also show significantly different reactivity to acute maternal stress and a significantly higher increase in fHR when the mother was introduced to a lab-induced stressor (15-17).

Thus, there is reason to believe that maternal affect may also influence fetal physiology and behavior; however, very little is known on the association between positive and negative maternal affect and human fetal physiologic functions during a typical pregnancy. Our aim was to investigate whether there is an association between maternal affect and fHR variability and Doppler blood flow velocity variables in the fetal middle cerebral artery (MCA), umbilical artery, and the uterine artery at 36 weeks gestation in euthymic mothers.

METHOD

Participants were 53 healthy, pregnant women and their singleton fetuses. Mothers were recruited during their second trimester (at 26 weeks gestation) from community midwife clinics and family physician clinics in metropolitan Vancouver. Informed consent was obtained from all mothers and the study was approved by the University of British Columbia Research Ethics Board and the BC Women's Hospital Research Review Committee. Inclusion criteria for this study were singleton pregnancy, confirmed gestational age, ability to give informed consent, lack of substance abuse, and no known fetal anomalies. Exclusion criteria were bipolar disorder, use of psychotropic medications, and significant maternal medical, obstetrical, or fetal conditions.

MATERNAL AFFECT AND CHARACTERISTICS

We assessed maternal affect using the Positive and Negative Affect Scale (PANAS). We measured the study participants daily for 7 days at 36 weeks gestation. This was done to increase the reliability of the assessment, as it takes into account fluctuations in mood and provides more robust estimate of typical levels of positive and negative affect (18). The PANAS instrument estimates the degree of both negative and positive "affectiveness." We used the mean PA and NA scores for the 7-day period.

The PANAS instrument has been validated in many samples (7, 18-20) and it has been shown that positive and negative affect are not significantly correlated implying that there is divergent validity between the two measures. We also calculated the Pearson correlation coefficients between PA and NA scores in our sample and found that PA and NA were not strongly correlated ($\rho_{PA,NA} = -0.21$). Thus, each participant was categorized once according to their NA score and then again according to their PA score. Maternal characteristics and health history were obtained from a combination of maternal interviews and medical records. Mothers were also assessed for depression using the Edinburgh Postnatal Depression Scale (EPDS), a 10-item self-rated questionnaire intended to assess existence and severity of depression symptoms that was designed for use in pregnant women (21). The Hamilton Rating Scale for Depression (HAM-D) is a 21-item clinician rated scale that measures the severity of depression in adults with a range from 0-63. A trained research assistant administered the clinician rated HAM-D assessments (22).

EXPERIMENTAL PROTOCOL

The data collection for this protocol occurred between January 2007 and March 2010. Study recruits were healthy women, without any known significant medical conditions. The pregnancies were considered low risk at the time of the study. Study participants were asked to eat and drink normally before they arrived. Women were scanned as close to 36 weeks and 0 days as possible (sample mean was 36 weeks and 1 day) in an attempt to avoid risk of delivery in healthy women. They were placed in a semi-recumbant,

left lateral decubitus position throughout the ultrasound and the fHR monitoring. The study protocol involved two 2-hour monitoring sessions, a morning session (starting at approximately 8:15 am) and an afternoon session (starting at approximately 1:00 pm) on the same day. Fetal and placental positions were documented by ultrasound. Amniotic fluid assessment was done to rule out oligohydramnios and polyhydramnios prior to the start of the study period. The Doppler ultrasound vascular studies were performed with an Aloka ProSound 5500 with a curvilinear 4-7 MHz probe using B mode, color flow and pulse wave Doppler. All scans were performed by a single Obstetrician/Gynecologist (KL) who was blinded to the mothers' PANAS results. In the first monitoring session, high resolution B mode and pulse wave Doppler ultrasound was used to measure blood flow velocity variables (diameter, pulsatility index, peak velocity, blood flow) in three arterial vessels: umbilical, uterine and fetal middle cerebral arteries (23). Each variable was measured five times with the mean being used for analysis. Following the ultrasound portion of the session, the fHR characteristics were recorded using computerized cardiotocography (Oxford Sonicaid 8002; Oxford Instruments, U.K.). The Sonicaid system was used for 50 minutes to collect data on baseline fHR, accelerations, decelerations, short- and long-term variation, minutes of high episode, as well as maternally perceived fetal movements. These fHR variables are commonly used in fetal monitoring procedures to identify fetuses at risk of metabolic compromise (24, 25). This protocol was repeated in the afternoon sessions. Between the two sessions, participants were provided a standard lunch and mothers were encouraged to get up and move around during the break.

DATA ANALYSIS

We separated mothers into low and high negative and positive affect groups using a median split for each dimension. We then used repeated measures analysis of variance (ANOVA) to examine time (morning versus afternoon) by group (low or high negative or positive affect) differences in physiological parameters. Univariate analysis of variance was used to determine differences in maternal group characteristics. A p-value of <0.05 was considered significant. All statistical analyses were carried out using Stata version 12.0 (StataCorp, College Station, Texas).

RESULTS

This study sample is drawn from a cohort that included women who were depressed and/or exposed to selective serotonin reuptake inhibitor (SSRI) antidepressants; 156 women were contacted and 92 of those women met study inclusion criteria and were enrolled - 39 of these women were experiencing depression or were using SSRI antidepressants and were thus excluded from this study. Our final study sample included 53 healthy, pregnant women and their singleton fetuses.

MATERNAL AND FETAL/NEONATAL CHARACTERISTICS

Table 1 illustrates maternal and fetal characteristics according to positive and negative affect. There were no differences in maternal age at birth across any affect groups. Mothers with high negative affect were more likely to be nulliparous than mothers with low negative affect (68.0% versus 55.6%); however, differences were not statistically significant. The same was true of mothers with high positive affect (65.4% versus 57.7%). Education levels also differed slightly according to affect with mothers reporting high negative affect indicating they had some postsecondary or less, more often than mothers reporting low negative affect (30.7% versus 18.5%). The opposite was true for mothers reporting high positive affect - 19.3% of those mothers reported having some postsecondary education or less compared to 29.6% of mothers reporting low positive affect. However, there were no statistically significant differences in education level across affect groups and all mothers were highly educated relative to the general population.

Not surprisingly, there were significant differences across affect groups in mean Edinburgh Postnatal Depression Scale (EPDS) scores and Hamilton Depression Scale (HAM-D); however, mean scores were significantly below the cut-off values for a positive screen for depressive symptomatology in all groups (relevant cutoff values are 13 or more for the EPDS and 18 or more for the HAM-D) (26, 27). There were no significant differences in neonatal outcomes across the groups.

FETAL MOVEMENTS, HEART RATE AND HEART RATE VARIABILITY

Figure 1 illustrates fetal movements, heart rate and heart rate variability across low and high negative affect groups. Fetal movement counts (as perceived by the mother) did not differ between low and high negative affect groups ($F=0.21$, $P=0.65$), nor did they differ across the day ($F=0.00$, $P=0.95$) (Fig. 1F).

Basal heart rate at the onset of each study session was also not significantly different between high and low negative affect groups ($F=0.57$, $P=0.45$), and again there were

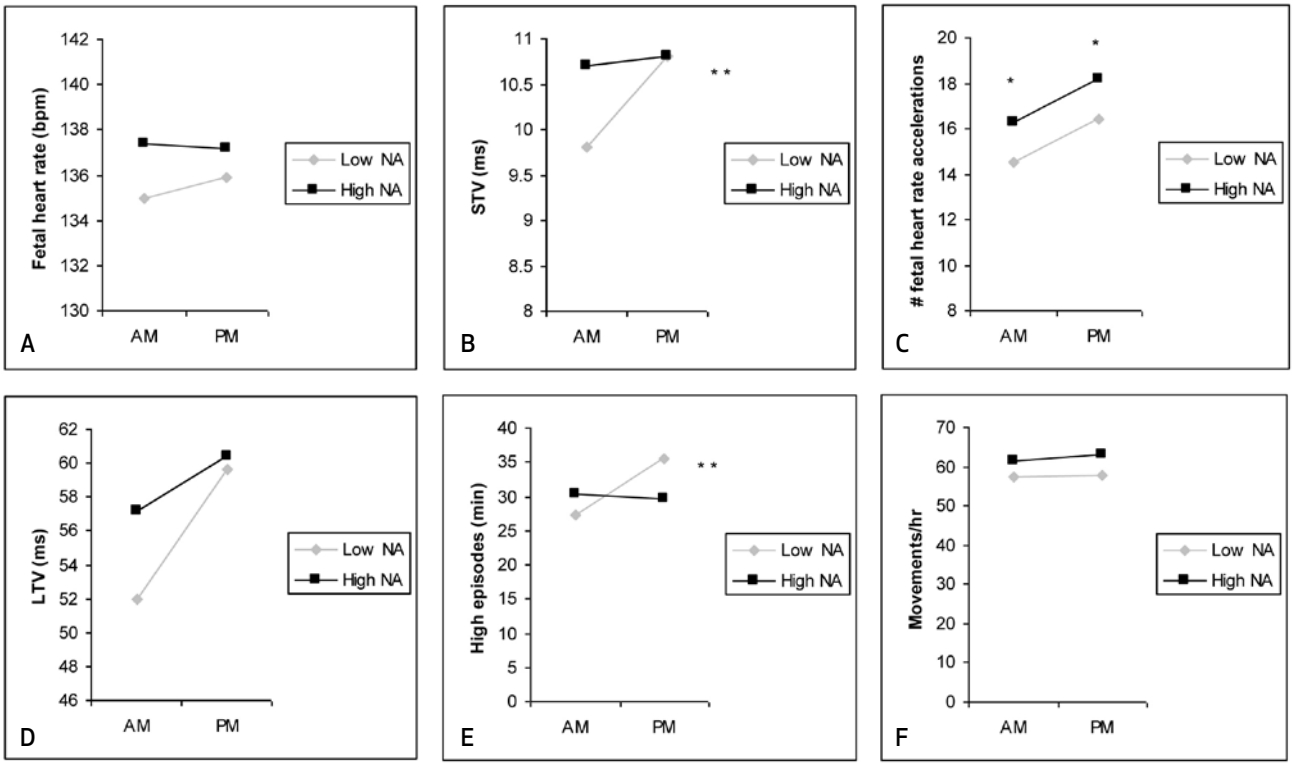
Table 1. *Maternal and neonatal characteristics according to positive and negative affect*

	N=53					
	Negative affect			Positive affect		
Variables	Low (n=27)	High (n=26)	P-value	Low (n=27)	High (n=26)	P-value
Maternal characteristics, mean (sd) or count (%)						
Gestational age on fetal study day, weeks	36.2 (0.15)	36.0 (0.10)	0.16	36.1 (0.14)	36.1 (0.12)	0.76
Age, yrs	34.2 (4.5)	33.9 (5.2)	0.80	34.6 (5.1)	33.5 (4.6)	0.41
Number of previous live births						
0	15 (55.6)	17 (68.0)		15 (57.7)	17 (65.4)	
1	10 (37.0)	8 (32.0)		10 (38.5)	8 (30.8)	
2	2 (7.4)	0 (0.0)	0.21	1 (3.9)	1 (3.9)	0.63
Number of pregnancies						
1	8 (29.6)	10 (40.0)		8 (30.8)	10 (38.5)	
2	11 (40.7)	10 (40.0		11 (42.3)	10 (38.5)	
3	3 (11.1)	4 (16.0)		4 (15.4)	3 (11.5)	
4	5 (18.5)	1 (4.0)	0.21	3 (11.5)	3 (11.5)	0.68
Maternal education						
High school or less	1 (3.7)	3 (11.5)		3 (11.1)	1 (3.9)	
Some postsec	4 (14.8)	5 (19.2)		5 (18.5)	4 (15.4)	
Postsec completed	10 (37.0)	12 (46.1)		11 (44.0)	10 (38.5)	
Post-graduate	11 (40.7)	6 (23.1)	0.54	7 (28.0)	10 (38.5)	0.72
EPDS score	2.7 (3.2)	6.8 (4.7)	<0.01	6.3 (5.1)	3.0 (2.9)	0.01
HAM-D score	5.0 (4.7)	9.8 (5.9)	<0.01	9.6 (3.4)	5.0 (4.1)	<0.01
Neonatal characteristics						
Birth weight (grams)	3450.96 (432.3)	3621.4 (643.0)	0.16	3556.7 (426.4)	3509.2 (442.0)	0.69
Birth length (cm)	51.9 (2.6)	51.9 (2.4)	0.99	52.2 (2.7)	51.6 (2.2)	0.38
Head circ, (cm)	35.0 (1.3)	35.4 (1.3)	0.25	35.3 (1.3)	35.2 (1.4)	0.77
Gestational age at birth, (weeks)	39.9 (1.2)	40.2 (1.1)	0.38	40.2 (1.1)	39.9 (1.2)	0.39
1 min Apgar	8.6 (0.8)	8.5 (1.2)	0.80	8.5 (1.2)	8.6 (0.8)	0.89
5 min Apgar	9.0 (0.4)	9.0 (0.3)	0.95	9.0 (0.4)	8.9 (0.3)	0.42

no significant differences between morning and afternoon (F=0.59, P=0.44) (Fig. 1A). However, differences in fHR variability indices emerged between groups and across the day. There was a significant time-by-group interaction regarding short-term variations across the day (F=3.89, P=0.05) (Fig. 1B). There was little or no change across the day among the high NA group whereas among the low NA group, short-term variations increased significantly from morning to afternoon. The number of fHR accelerations in the high NA group was significantly higher than in the low NA group (F=6.40, P=0.01) (Fig. 1C). Similar to short-term variations, durations of high-HR variability episodes remained unchanged in the high NA group, while it increased significantly in the low NA group between the morning and afternoon sessions (F=7.36, P=0.009) (Fig. 1E). Long-term variations did not differ between NA groups (F=0.54, P=0.46) (Fig. 1D).

Figure 2 illustrates fetal movements, heart rate and heart rate variability across low and high positive affect groups. Once again there were no statistically significant differences in fetal movements or basal heart rate between groups (Fig. 2A and 2F). There were also no statistically significant differences in short-term variability, long-term variation, and duration of high variability (Fig. 2B, 2D, 2E). However, there were significant time-group interactions in fHR accelerations (F=10.5, P=0.002). The high PA group showed very little change between morning and afternoon sessions, while the low PA group showed a statistically significant increase in fHR accelerations between the morning and afternoon session (Fig. 2C).

Figure 1. *Means of: basal fetal heart rate (A); short-term variability (B); fetal heart rate accelerations (C); long-term variation (D); duration of high variability (E); and fetal movements/h (F) in the low and high NA group*



*p<0.05; **Group-time interaction significantly different from corresponding AM value

Table 2. *Mean and standard deviations for: umbilical artery pulsatility index (PI); mean uterine artery (UtA) PI; Middle Cerebral Artery (MCA) PI; MCA mean flow velocity (MVC); MCA vessel cross-sectional area; and MCA artery blood flow, in the low and high negative and positive affect groups.*

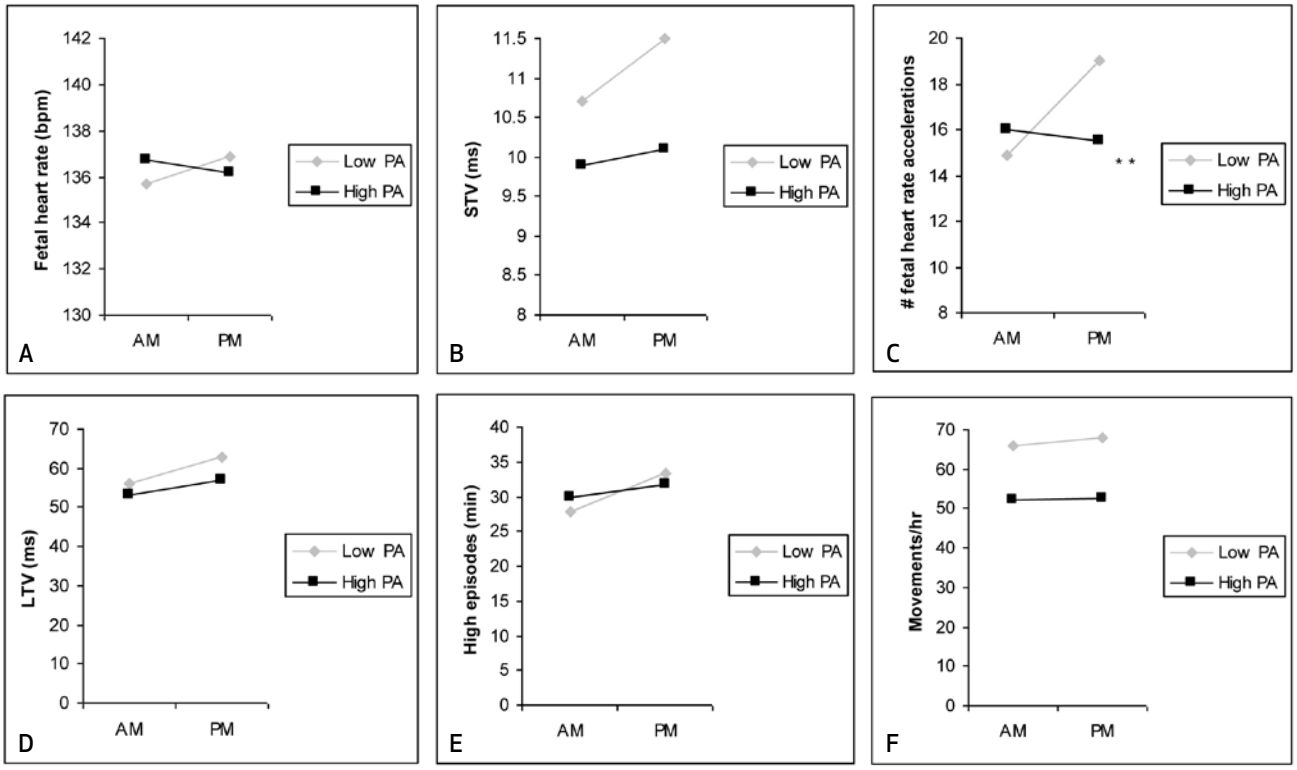
	Negative affect			Positive affect		
Variable	Low	High	P-value	Low	High	P-value
Umbilical artery PI	0.93 (0.13)	0.90 (0.17)	0.40	0.93 (0.13)	0.90 (0.17)	0.54
MCA PI	1.73 (0.35)	1.74 (0.30)	0.97	1.73(0.35)	1.74 (0.30)	0.63
MCA MVC (cm/s)	27.9 (.6)	26.4 (5.8)	0.28	27.9 (6.6)	26.4 (5.8)	0.67
MCA area (cm^2)	0.10 (0.05)	0.10 (0.03)	0.93	0.10 (0.05)	0.10 (0.03)	0.36
MCA flow	167.6 (114.4)	158.9 (78.9)	0.60	167.6 (114.4)	158.9 (78.9)	0.66

MIDDLE CEREBRAL, UMBILICAL AND UTERINE ARTERY FLOW CHARACTERISTICS

Table 2 presents mean middle cerebral artery (MCA) pulsatility index, MCA flow velocity, MCA vessel cross-sectional area, and MCA total artery blood flow. There were no significant differences in any of these measures across groups, nor were there any significant time-group interactions. Table 2 also illustrates the umbilical artery pulsatility index. There were no significant differences in any of these measures across groups, nor were there any significant time-group interactions (P>0.05).

Figure 3 illustrates uterine artery mean blood flow velocity, volume flow, pulsatility index and vessel cross-sectional area. In fetuses of mothers with high PA mean uterine artery blood flow velocity was significantly higher than in fetuses of mothers with low PA (F=6.03, P=0.02), and the decrease in UtA mean velocity flow between morning and afternoon was significantly different in

Figure 2. *Means of: basal fetal heart rate (A); short-term variability (B); fetal heart rate accelerations (C); long-term variation (D); duration of high variability (E); and fetal movements/h (F) in the low and high PA group*



Note: * p<0.05; ** Group-time interaction significantly different from corresponding AM value

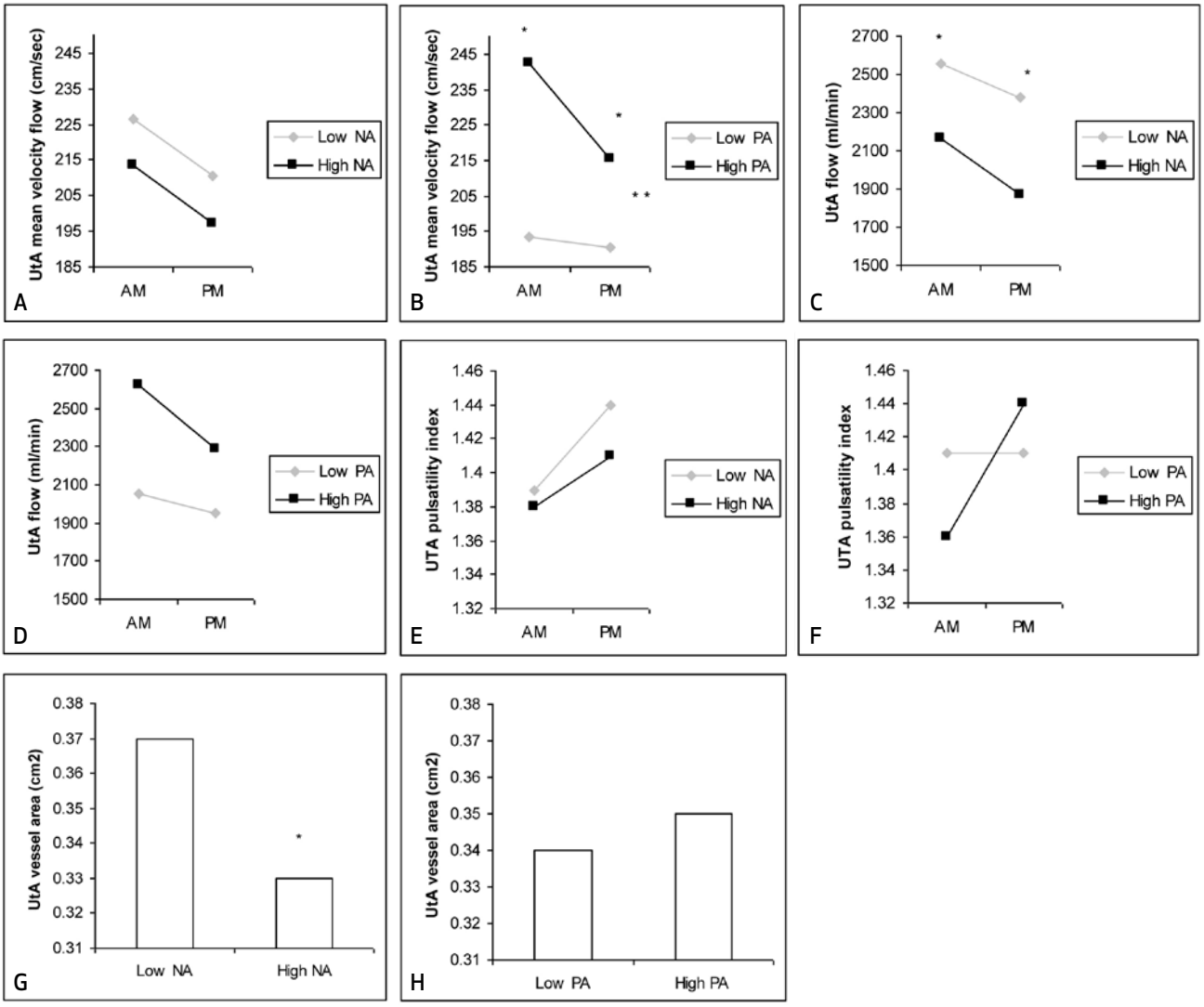
mothers with high PA (F=6.03, P=0.04) (Fig. 3B). Fetuses of mothers with low NA had significantly higher UtA volume flow than mothers with high NA (F=3.83, P=0.05), and in both groups this appeared to decrease slightly between morning and afternoon (Fig. 3C). Overall uterine blood flow in the low and high NA groups when normalized to birth weight averaged 691.1±59.1 ml/kg and 345.5±27.0 ml/kg, respectively and were significantly different (p<0.01). There was no difference in the uterine artery pulsatility index by negative or positive affect (Fig. 3E, 3F). UtA vessel cross-sectional area (calculated from the vessel diameter) was significantly lower in the high NA group compared with the low NA group (P=0.04) (Fig. 3G). There was no significant difference in UtA vessel cross-sectional area between PA groups (P=0.70).

DISCUSSION

We report that in a non-clinical cohort (i.e., non-psychiatric setting) a mother's affect, measured using the Positive and Negative Affect Scale (PANAS), was associated with differences in fHR characteristics and uterine flow measures at 36 weeks gestation. Among fetuses of mothers reporting high levels of negative affect, there were higher rates of accelerations compared with fetuses of mothers who reported low NA. Although the higher rates of accelerations were not associated with an increase in fetal movements as perceived by the mother, this measure may underestimate fetal movements (28). Among fetuses of high NA mothers, there were no increases in fHR variability from morning to afternoon that had occurred in the low NA groups. This included measures of short-term variability and the duration of high variability episodes. Among fetuses of mothers reporting high levels of positive affect, there was also less variability between morning and afternoon for fHR accelerations, than among fetuses whose mother reported low positive affect.

Among mothers reporting high NA, uterine artery mean volume flow was lower and stayed lower across the day. Mothers with high PA had higher UtA mean velocity flow across the day and showed a larger change from morning to afternoon session than mothers with low PA.

Figure 3. *Uterine artery mean blood flow velocity according to NA (A) and PA (B), mean volume flow according to NA (C) and PA (D), uterine pulsatility index according to NA (E) and PA (F), and mean vessel cross-sectional area presented as a mean according to NA (G) and PA (H)*



*p<0.05; **Group-time interaction significantly different from corresponding AM value

Uterine artery cross-sectional area was also significantly lower in mothers with high NA compared to mothers reporting low NA.

Our finding of increased fHR variability across the study day in the fetuses whose mothers reported low NA is consistent with the typical diurnal variation in fHR that has been previously reported in the near-term human fetus (23, 29). While an exact mechanism involved in humans is not evident, in pregnant sheep the maternal melatonin rhythm influences fetal rhythms in activity, behavior and cardiovascular function via placental transfer (30, 31). It is unclear why the fHR variables in the high NA group did not show the same morning to afternoon pattern; however, we have long known that there is a link between mood disorders that present with high levels of negative emotions and circadian rhythm disturbances (32, 33).

The lower value of uterine blood flow in the high NA group compared to the low NA group was due to reduced values of both mean uterine artery blood flow velocity and uterine artery cross-sectional area, the two determinants of volume flow. These differences may be related to the changes in uterine blood flow during pregnancy. Although

total uterine blood flow increases progressively during gestation, uterine blood flow normalized to fetal weight decreases progressively from at least 20 weeks gestation (34). This decline in relative blood flow is associated with progressive decreases in pro-angiogenic (placental growth factor) and increases in anti-angiogenic (soluble endoglin and soluble VEGF receptor-1) factors in maternal blood with advancing gestation (35), suggesting a decrease in placental angiogenesis. Fowles et al. (36) have reported that maternal serum levels of VEGF (another pro-angiogenic factor) had a negative relationship with Center for Epidemiologic Studies – Depression scale in low income women. Furthermore, Helbig et al. (37) found a reduction in fetal weight normalized umbilical venous volume flow with no change in umbilical arterial pulsatility index in relation to increasing maternal psychological distress. They also found no changes in uterine artery pulsatility index, suggesting the volume flow rather than vascular resistance indices is a more important variable to measure in such studies. In the current study the lower value of uterine blood flow in the high NA group was not associated with a lower birth weight. However, birth weight is a poor indicator of fetal growth; rather it is the extent to which individual fetuses meet their growth potential that is more important (38).

A number of key limitations need mentioning. First, we assumed the mood differences were the main independent variables, and randomization between the groups was not possible. As a result, not accounting for unmeasured maternal illness characteristics may have contributed to an ascertainment bias. Second, our sample size was small and there were frequently differences between the groups that did not reach statistical significance. Further research should examine the effect of maternal affect on fetal vascular and fHR in a larger sample. Finally, we did have two mothers who delivered before 37 weeks, but their blood flow measures were not significantly different from the mothers who delivered after 37 weeks, making it unlikely that we observed early signs of preterm labor. It is possible that the PANAS measurements may suffer from some social desirability bias; however, as there is considerable variation in scores, and many mothers who reported high negative affect and low positive affect, we consider the possibility of social desirability bias unlikely. While we excluded mothers who suffered from significant maternal, obstetrical and fetal conditions, it is possible that there were differences in maternal health status across the affect groups. Finally, we were also unable to examine neonatal short- and long-term outcomes in this study.

In summary, even in euthymic mothers, those who report high levels of negative affect showed reduced uterine artery flow, decreased fHR variability, an altered diurnal pattern, and decreased uterine artery cross-sectional area. These findings suggest that even in the absence of an Axis I MDD, maternal affect may impact on fetal and uterine physiology. Further studies are needed to examine the mechanisms that link maternal affect and fetal cardiovascular function, as well as to investigate all of the potentially relevant and interacting physiologic variables. While we report no difference in birth weight, birth length, head circumference, gestational age, and 1- and 5-minute Apgar scores of infants according to maternal affect groups (Table 1), further research should examine alternative neonatal outcomes. Implications for maternal care during gestation remain to be determined.

References

1. Murphy PA. Origins: How the nine months before birth shape the rest of our lives. New York: Free Press, 2010.
2. Vesga-Lopez O, Blanco C, Keyes K, Olfson M, Grant BF, Hasin DS. Psychiatric disorders in pregnant and postpartum women in the United States. Arch Gen Psychiatry 2008;65:805-815.
3. Charney DS. Psychobiological mechanisms of resilience and vulnerability: Implications for successful adaptation to extreme stress. Am J Psychiatry 2004;161:195-216.
4. Pressman SD, Cohen S. Does positive affect influence health? Psychol Bull 2005;131:925.
5. Veenhoven R. Healthy happiness: Effects of happiness on physical health and the consequences for preventive health care. J Happiness Stud 2008;9:449-469.
6. Watson D, Pennebaker JW. Health complaints, stress, and distress: Exploring the central role of negative affectivity. Psychol Rev 1989;96:234.
7. Bood SÅ, Archer T, Norlander T. Affective personality in relation to general personality, self-reported stress, coping, and optimism. Indiv Diff Res 2004;2:26-37.
8. Chung TKH, Lau TK, Yip ASK, Chiu HFK, Lee DTS. Antepartum depressive symptomatology is associated with adverse obstetric and neonatal outcomes. Psychosom Med 2001;63:830-834.
9. Grote NK, Bridge JA, Gavin AR, Melville JL, Iyengar S, Katon WJ. A meta-analysis of depression during pregnancy and the risk of preterm birth, low birth weight, and intrauterine growth restriction. Arch Gen Psychiatry 2010;67:1012-1024.
10. Field T, Diego M, Hernandez-Reif M. Prenatal depression effects and interventions: A review. Infant Behav Dev 2010;33:409-418.
11. Misri S, Oberlander TF, Fairbrother N, Carter D, Ryan D, Kuan AJ, et al. Relation between prenatal maternal mood and anxiety and neonatal health. Can J Psychiatry 2004;49:684-689.
12. Talge NM, Neal C, Glover V. Antenatal maternal stress and long-term effects on child neurodevelopment: How and why? J Child Psychol Psychiatry 2007;48:245-261.
13. Austin MP, Hadzi-Pavlovic D, Leader L, Saint K, Parker G. Maternal trait anxiety, depression and life event stress in pregnancy: Relationships with infant temperament. Early Hum Dev 2005;81:183-190.
14. Allister L, Lester BM, Carr S, Liu J. The effects of maternal depression on fetal heart rate response to vibroacoustic stimulation. Dev Neuropsychol 2001;20:639-651.
15. Monk C, Fifer WP, Myers MM, Sloan RP, Trien L, Hurtado A. Maternal

stress responses and anxiety during pregnancy: Effects on fetal heart rate. Dev Psychobiol 2000;36:67-77.

16. Monk C, Myers MM, Sloan RP, Ellman LM, Fifer WP. Effects of women's stress-elicited physiological activity and chronic anxiety on fetal heart rate. J Dev Behav Pediatr 2003;24:32.
17. Monk C, Sloan RP, Myers MM, Ellman L, Werner E, Jeon J, et al. Fetal heart rate reactivity differs by women's psychiatric status: An early marker for developmental risk? J Am Acad Child Adolesc Psychiatry 2004;43:283-290.
18. Steptoe A, Wardle J. Positive affect and biological function in everyday life. Neurobiol Aging 2005;26:108-112.
19. Archer T, Adolfsson B, Karlsson E. Affective personality as cognitive-emotional presymptom profiles regulatory for self-reported health predispositions. Neurotox Res 2008;14:21-44.
20. Norlander T, Bood SAK, Archer T. Performance during stress: Affective personality, age, and regularity of physical exercise. Soc Behav Pers 2002;30:495-508.
21. Cox J, Holden J, Sagovsky R. Detection of postnatal depression. Development of the 10-item Edinburgh Postnatal Depression Scale. Br J Psychiatry 1987;150:782-786.
22. Hamilton M. A rating scale for depression. J Neurol Neurosurg Psychiatry 1960;23:56-62.
23. Rurak D, Lim K, Sanders A, Brain U, Riggs W, Oberlander TF. Third trimester fetal heart rate and Doppler middle cerebral artery blood flow velocity characteristics during prenatal selective serotonin reuptake inhibitor exposure. Pediatr Res 2011;70:96.
24. Dawes GS, Moulden M, Redman CW. Improvements in computerized fetal heart rate analysis antepartum. J Perinat Med 1996;24:25-36.
25. Hamilton EF, Warrick PA. New perspectives in electronic fetal surveillance. J Perinat Med 2013;41:83-92.
26. Matthey S, Henshaw C, Elliott S, Barnett B. Variability in use of cut-off scores and formats on the Edinburgh Postnatal Depression Scale - implications for clinical and research practice. Arch Womens Ment Health 2006;9:309-315.
27. Cusin C, Yan H, Yeung A, Fava M. Rating scales for depression. In: Bair L, Blais MA, editors. Handbook of clinical rating scales and assessment in psychiatry and mental health. New York: Humana, 2010: pp. 7-35.
28. Hijazi ZR, East CE. Factors affecting maternal perception of fetal movement. Obstet Gynecol Surv 2009 quiz 499; 64:489-497.
29. Visser G, Goodman J, Levine D, Dawes G. Diurnal and other cyclic variations in human fetal heart rate near term. Am J Obstet Gynecol 1982;142:535.
30. Houghton D, Walker DW, Young IR, McMillen IC. Melatonin and the light-dark cycle separately influence daily behavioral and hormonal rhythms in the pregnant ewe and sheep fetus. Endocrinology 1993;133:90-98.
31. Zemdegs I, McMillen IC, Walker W, Thorburn G, Nowak R. Diurnal rhythms in plasma melatonin concentrations in the fetal sheep and pregnant ewe during late gestation. Endocrinology 1988;123:284-289.
32. Wirz-Justice A. Chronobiology and mood disorders. Dialogues Clin Neurosci 2003;5:315.
33. Wirz-Justice A. Biological rhythm disturbances in mood disorders. Int Clin Psychopharmacol 2006;21:S11.
34. Konje JC, Kaufmann P, Bell SC, Taylor DJ. A longitudinal study of quantitative uterine blood flow with the use of color power angiography in appropriate for gestational age pregnancies. Am J Obstet Gynecol 2001;185:608-613.
35. Romero R, Nien JK, Espinoza J, Todem D, Fu W, Chung H, et al. A longitudinal study of angiogenic (placental growth factor) and anti-angiogenic (soluble endoglin and soluble vascular endothelial growth factor receptor-1) factors in normal pregnancy and patients destined to develop preeclampsia and deliver a small for gestational age neonate. J Matern Fetal Neonatal Med 2008;21:9-23.
36. Fowles ER, Murphey C, Ruiz RJ. Exploring relationships among psychosocial status, dietary quality, and measures of placental development during the first trimester in low-income women. Biol Res Nurs 2011;13:70-79.
37. Helbig A, Kaasen A, Malt UF, Haugen G. Does antenatal maternal psychological distress affect placental circulation in the third trimester? PLoS ONE 2013;8:e57071.
38. Bukowski R. Fetal growth potential and pregnancy outcome. Semin Perinatol 2004;28:51-58.