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Fetal response to induced maternal stress

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Abstract

Background: Despite increased attention to the role of antenatal maternal psychological stress in postnatal development, remarkably little information is available on the nature of the intrauterine fetal response to maternal psychological state. *Aims*: To determine whether: (1) the fetus responds to maternal stress; (2) the fetal response changes over gestation; and (3) individual maternal and fetal response patterns are stable over time. *Study design*: Induced maternal stress at 24 and 36 weeks gestational age using the Stroop color–word task. *Subjects*: 137 low-risk pregnant women with normally developing fetuses. *Outcome measures*: Maternal (heart rate and skin conductance) and fetal (heart rate, heart rate variability, and motor activity) responses. *Results*: The manipulation evoked maternal sympathetic activation, which declined in magnitude from 24 to 36 weeks gestation. Fetuses responded to the manipulation with increased variability in heart rate ($F(2,256) = 7.80$, $p < 0.001$) and suppression of motor activity ($F(2,216) = 15.47$, $p < 0.001$). The magnitude of the fetal response increased over gestation. The degree of maternal reactivity to and recovery from the stressor were correlated over time (r's = 0.53 and 0.60 for heart rate; r's = 0.31 and 0.36 for skin conductance; p's < 0.001). There was moderate stability in the magnitude of the fetal motor response ($r = 0.25$, $p < 0.01$). *Conclusions*: Demonstration of fetal responses to maternal sympathetic activation evoked by a benign cognitive stressor suggests that fetal neurobehavioral regulation is routinely disrupted by maternal environmental intrusions. There is no evidence of a protective effect of diminished maternal sensitivity to stress on the fetus. Individual stability in the magnitude of the evoked maternal physiologic and psychological responses from 24 to 36 weeks and stability in the fetal motor response implies that characteristic response patterns emerge in utero. We propose that autonomic development is partially entrained through these processes.

Keywords: Fetal heart rate; Fetal movement; Stress; Pregnancy

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Persistent effects of maternal antenatal psychological stress on postnatal development have been demonstrated in animal models [1–3] and there is support for a similar association in humans [4–7]. Yet there is remarkably little understanding of the nature of the fetal response to maternal psychological state in situ, despite cultural and literary allusions to such a relationship from antiquity.

Provocative reports of linkage between maternal stress and fetal heart rate and behavior have appeared in the academic literature since the 1930s [8,9]. Interest was briefly rekindled some 40 years later by a series of studies in which presentation of relatively minor psychological stressors to pregnant monkeys generated a cascade of physiological fetal effects including changes in heart rate, blood pressure, and arterial oxygenation [10,11]. Somewhat earlier, fetal tachycardia was observed when stress was deliberately manipulated in pregnant women using a variety of conditions, including maternal startles elicited by loud noises and anxiety for fetal well-being after being led to believe that the fetus was inadequately oxygenated [12]. The use of a less threatening stimulus to induce maternal arousal, a tape recording of a crying infant, has been associated with a decelerative fetal heart rate response in anxious, but not in non-anxious or depressed women [13].

More recently, an increase in fetal heart rate to a common cognitive challenge (the Stroop Color–Word Test) has been observed in fetuses of women with high, but not low, trait anxiety [14]. Anecdotal evidence of the role of maternal psychological state also exists, including distress following a fall [15], an earthquake [16], and sounding of an air raid alarm during the Gulf War [17]. At least one study reported no effects of induced maternal anxiety on fetal heart rate or behavior [18], but it was based on a small sample ($n = 10$).

The current study examines the effect of induced maternal stress on fetal heart rate and motor activity at two gestational ages. Our primary goals are to determine whether there is a fetal response to induced maternal stress, and if so, whether the magnitude or nature of this response changes over gestation. Given the sparse literature, prediction of the direction of fetal effects is difficult. However, because the manipulation selected generates a well-documented sympathetic response, we expect that the fetal response will also reflect such activation, expressed as faster heart rate and greater motor activity. Moreover, we hypothesize that the magnitude of the response will increase as the patency of the fetal sympathetic response matures over gestation. Our secondary goal is to determine whether there is stability (i.e., preservation of relative ranking of individuals) [19] in maternal and fetal responses to stress over gestation, as a prelude to establishing whether individual variation in the intrauterine milieu may contribute to fetal ‘‘programming’’ of stress responsivity.

1. Methods

1.1. Participants

Participants were 137 women with uncomplicated pregnancies and their singleton fetuses. Eligibility was restricted to nonsmoking women at least 20 years old with consistent pregnancy dating validated by early first trimester pregnancy testing, examination, and/or ultrasound. Efforts were made during recruitment to yield comparable

representation in terms of parity (nulliparous vs. multiparous) and fetal sex, determined through ultrasound and confirmed at birth. Participant and offspring characteristics are presented in Table 1. The sample represents a fairly mature, well-educated group of low-risk pregnant women. The study was approved by the Institutional Review Board at Johns Hopkins University and women provided written informed consent.

1.2. Design

This protocol was part of a larger study of fetal neurobehavioral development in which baseline recordings were collected monthly beginning at 20 weeks gestation. Visits were scheduled at either 1 or 3 pm, consistent for each participant. Women were asked to refrain from eating 1 1/2 h prior to their visit. Following a brief ultrasound examination to determine fetal position for monitoring, 50 min of baseline fetal and maternal recording ensued for the parent study. The experimental manipulation was provided at 24 and 36 weeks gestation immediately following this undisturbed period. The manipulation was the Stroop Color–Word Test, a procedure that has been extensively used to invoke a sympathetic, autonomic response since its origination 60 years ago [20]. The task requires disassociating word meaning from printed word color, performed under time pressure. Participants viewed the stimuli on a projector and provided responses orally.

Data streaming was begun anew for the Stroop procedure at the conclusion of the 50 min period. A Stroop baseline period corresponded to settling the projector into place on an over-bed table and providing instructions. An event marker was then used to signal the onset of the first Stroop stimulus in the computer file. A series of slides were used that included both traditional color–word combinations as well as pregnancy-based emotionally evocative words. Women were asked to respond as quickly and accurately as possible; slides were advanced at a predetermined interval to increase urgency. Termination of the procedure, the duration of which was dependent on the amount of time it took each participant to complete all the stimuli, was signaled with the event marker. Maternal–fetal monitoring continued for the period of time during which the equipment was dismantled and concluding information was provided. Immediately following administration, women reported the degree to which they experienced the Stroop as stressful and difficult on 5-point scales ranging from low (1) to high (5). Women's overt responses indicative of stress were also rated on a similar 5-point scale by an observer.

Table 1
Maternal and infant characteristics ($n = 137$)

Maternal demographic characteristics	
Age (S.D.)	31.3 (4.1)
Education in years (S.D.)	16.7 (2.1)
Married	94%
Nulliparous	55%
Infant characteristics	
Birth weight (g) (S.D.)	3520 (440)
Gestational age (weeks) at delivery (S.D.)	39.4 (1.2)
Male	50%

Given time constraints, fetal state was not standardized at Stroop administration. However, fetal state during the last 3 min of the 50-min recording was used as a control measure. This was limited to 36-week analyses because states are not sufficiently developed prior to this gestational age. State attribution was based on standard methods of categorizing fetal heart rate and motor activity patterns [21]. Eye movement data, which require continuous ultrasound visualization, were not available but the correspondence between fetal heart rate and movement patterns near term is high [22]. Scoring was based on consensus by two coders who had achieved reliability during a training period.

1.2.1. Maternal–fetal monitoring

Maternal and fetal data were collected simultaneously on a personal computer. Data were sampled at 1000 Hz using an internal A/D board and digitized via streaming software. Maternal data collection used a multichannel, electrically isolated, bioamplifier (James Long, Caroga Lake, NY) that amplified the physiological signals. Electrocardiogram (ECG) was recorded from three carbon fiber disposable electrodes in triangulated placement (right mid sub-clavicle, left mid axillary thorax, and upper left thigh for ground lead). Electrodermal activity (skin conductance) was monitored from two Ag/AgCl electrodes with a gelled skin contact area placed on the distal phalanxes of the first and index fingers of the nondominant hand affixed with adhesive collars to limit gel contact to a 1-cm-diameter circle, and velcro. Maternal variables were computed off-line using software developed in our laboratory (GESTATE; James Long). Maternal ECG data underwent R-wave detection, manual editing for artifact, and interbeat interval (IBI) computation. To maintain consistency with fetal measures, IBI values were prorated to second by second heart rate in beats per minute (bpm). Skin conductance was measured by administering a constant 0.5-V root-mean-square 30-Hz AC excitation signal and detecting the current flow. Skin conductance level (SCL) was quantified and scaled from 0 to 25 μS. This measure reflects changes in conductivity of the skin as modulated by eccrine glands that are sympathetically activated [23].

Fetal data were collected from the output port of a Toitu (MT320) fetal actocardiograph. This monitor detects fetal heart rate and movement through a single wide array transabdominal Doppler transducer and processes this signal using a series of filtering techniques. Digitized heart rate data underwent error rejection procedures based on moving averages of acceptable values as necessary. The fetal cardiac response was quantified in two variables: (1) mean rate and (2) variability, defined as the standard deviation of rate during each period. The actograph feature of the monitor detects fetal movements by preserving the remaining signal after band passing frequency components of the Doppler signal that are associated with fetal heart rate and maternal somatic activity. Reliability studies comparing actograph based vs. ultrasound visualized fetal movements have found the performance of the Toitu monitor to be accurate in detecting both fetal motor activity and quiescence [24–26]. The Toitu generates calibrated values in arbitrary units (a.u.s) ranging from 0 to 100, represented as a series of spikes corresponding to individual movements. Fetal motor activity was quantified as the mean of all actograph values exceeding a threshold of 5 a.u.s, established to eliminate background noise and motion of the fetal diaphragm.

1.3. Data analyses

Technical problems compromised availability or quality of complete data for some cases; analyses are based on 135 and 128 subjects at 24 and 36 weeks, respectively. Maternal and fetal responses to the manipulation were analyzed using 2×3 repeated measures analysis of variance of mean values by gestational age (24 and 36) for the following segments: pre-Stroop (average duration = 2.3 min), Stroop (3.8 min), and post-Stroop (1.2 min). Interaction terms for response by gestational age were included. When significant interactions were detected, post hoc analyses were conducted for 24- and 36-week results separately. Evaluation of maternal and fetal stability in individual responsiveness from 24 to 36 weeks gestation was conducted using Pearson correlations of change scores from pre-stimulus to stimulus periods (reactivity) and stimulus to post-stimulus periods (recovery). Analysis of the association between maternal and fetal physiological responsiveness was also based on correlations of change scores, controlling for the value of the fetal measure in the initial interval.

2. Results

2.1. Response to manipulation

Maternal heart rate and skin conductance responses to the manipulation are presented in Figs. 1 and 2. In general, women reacted to the manipulation with increased heart rate

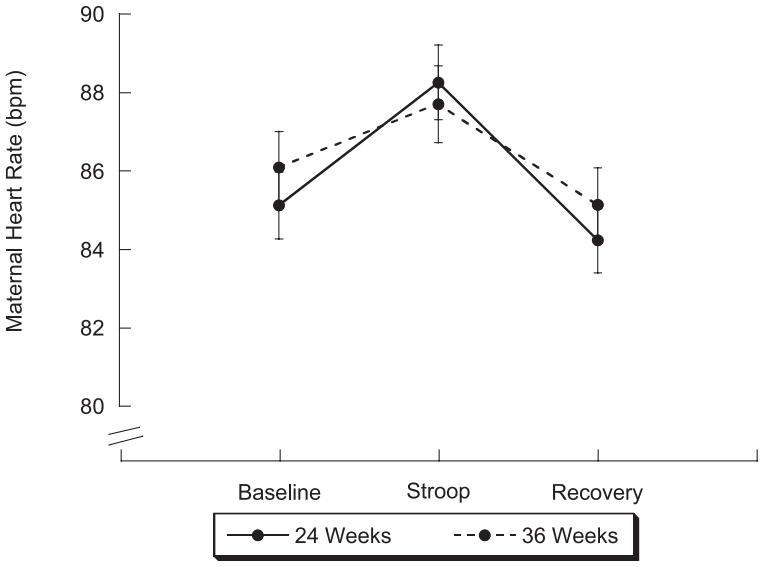

Fig. 1. Maternal heart rate (bpm) immediately before, during, and following exposure to stressor at 24 and 36 weeks gestation.

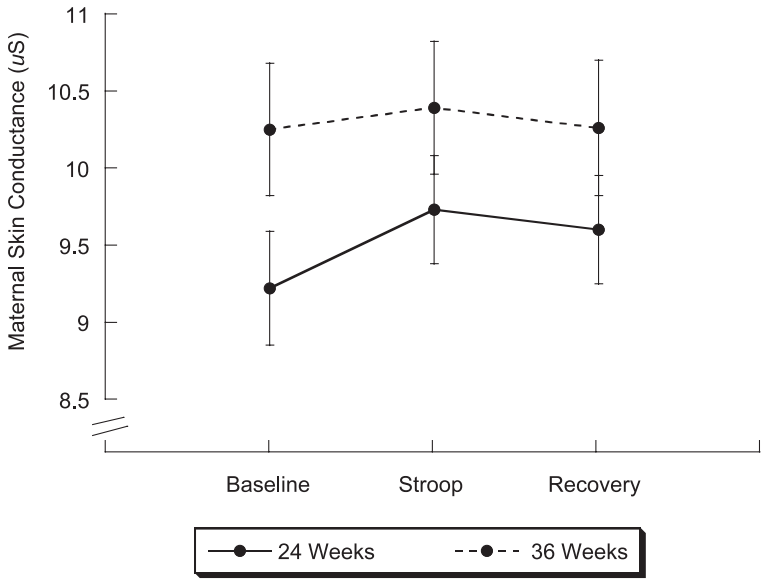

Fig. 2. Maternal skin conductance (μS) immediately before, during, and following exposure to stressor at 24 and 36 weeks gestation.

followed by return to pre-baseline levels during the recovery periods. However, there was a significant interaction with gestational age ($F(2,250)=7.62$, $p<0.001$). Post hoc analyses indicate greater maternal responsiveness at 24 weeks ($F(2,268)=44.97$, $p<0.0001$) than at 36 weeks ($F(2,254)=19.85$, $p<0.0001$). Skin conductance also increased and then decreased in response to the Stroop ($F(2,252)=21.03$, $p<0.0001$) although overall skin conductance was higher at 36 weeks than at 24 weeks ($F(1,126)=6.25$, $p<0.01$). A significant interaction with gestational age was also apparent ($F(2,252)=12.31$, $p<0.0001$). The skin conductance response was significant at 24 weeks ($F(2,268)=29.45$, $p<0.001$) but blunted at 36 weeks ($F(2,256)=2.79$, $p=0.06$). Based on 5-point scales, women reported that the Stroop manipulation was moderately difficult and stressful (median = 3 at each gestational age), corresponding to the observer's ratings (median = 3). Self-reported or observer-rated stress to the Stroop did not change significantly from 24 to 36 weeks. However, women tended to regard the Stroop as more difficult at 36 weeks ($F(1,134)=3.73$, $p=0.056$).

Fetal heart rate and variability results are presented in Figs. 3 and 4. Mean fetal heart rate was unaffected by the manipulation ($F(2,252)=0.20$). Fetal heart rate variability changed significantly ($F(2,252)=9.23$, $p<0.0001$) but there was a significant main effect for gestational age at test ($F(1,126)=22.33$, $p<0.001$); post hoc analyses revealed a greater increase in variability at 36 weeks ($F(2,256)=7.80$; $p<0.001$) than at 24 weeks ($F(2,268)=2.72$, $p=0.07$). In contrast, fetal motor activity (Fig. 5) was suppressed in response to the Stroop ($F(2,216)=15.47$, $p<0.001$). There was also a significant interaction with gestational age ($F(2,216)=4.42$, $p<0.01$) such that the suppressive effect

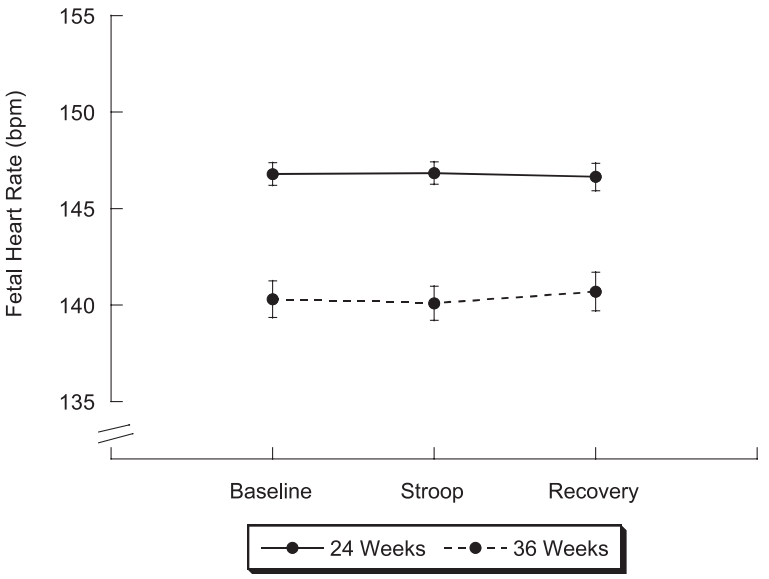

Fig. 3. Fetal heart rate (bpm) immediately before, during, and following maternal exposure to stressor at 24 and 36 weeks gestation.

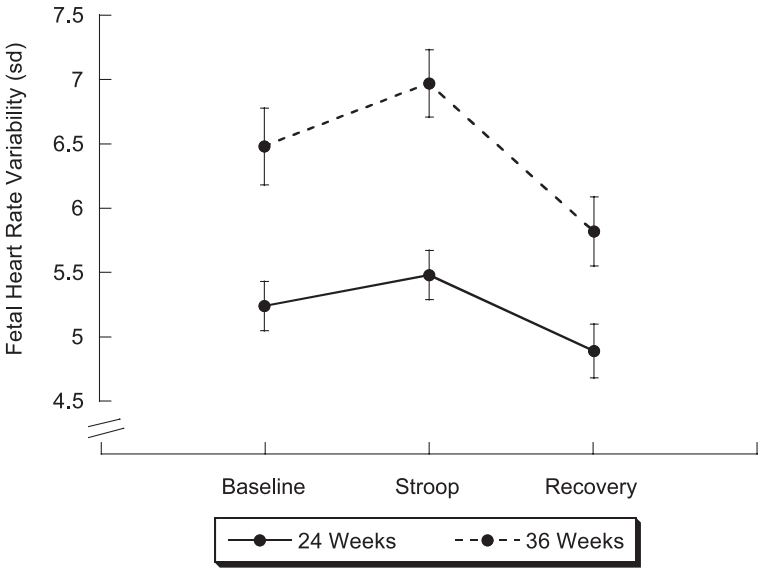

Fig. 4. Fetal heart rate variability (S.D.) immediately before, during, and following maternal exposure to stressor at 24 and 36 weeks gestation.

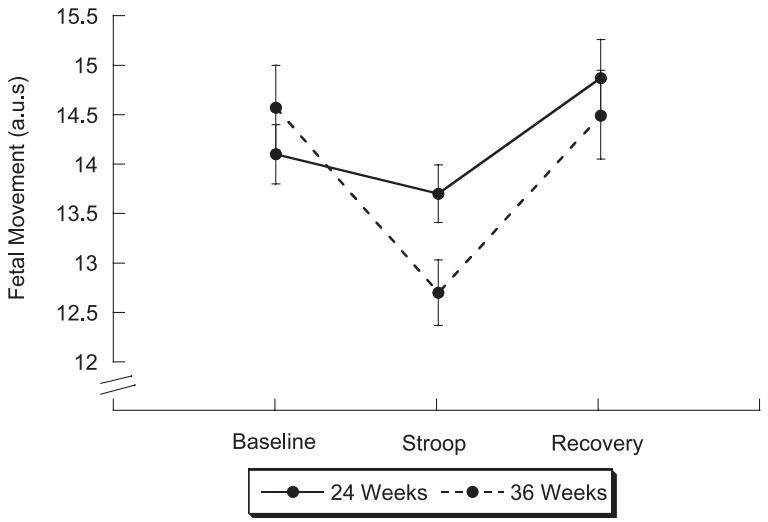

Fig. 5. Fetal motor activity (a.u.s.) immediately before, during, and following maternal exposure to stressor at 24 and 36 weeks gestation.

on fetal motor activity was heightened at 36 weeks ($F(2,232) = 13.64$, $p < 0.0001$) compared to 24 weeks ($F(2,252) = 7.47$, $p < 0.001$).

In the 3 min prior to onset of the 36-week Stroop data collection, the majority of fetuses displayed fetal heart rate and motor parameters consistent with state 2F (active sleep) ($n = 95$; 69%). The remainder displayed quiet sleep (1F; 11%), active waking (4F; 5%) or indeterminate (14%) states. Repeated measures analyses were conducted excluding fetuses not displaying active sleep; effects on fetal heart rate and movement were unchanged.

There were no sex differences in fetal responsiveness to the maternal manipulation at 24 weeks. At 36 weeks, there was a significant time by sex interaction for fetal movement ($F(2,230) = 4.35$, $p < 0.01$). Although the values for the baseline ($M = 14.5$ vs. 14.4 for males and females, respectively) and Stroop periods ($M = 13.00$ vs. 12.50) did not differ, male fetuses responded to termination of the Stroop with greater motor activity ($M = 15.6$ vs. 13.3).

Correlations among fetal heart rate, variability, and motor activity change scores to the Stroop are presented in Table 2. Coordination of the degree of cardiac and motor responsiveness among the fetal measures increased over gestation for both reactivity and recovery responses.

2.2. Individual stability in responsiveness during gestation

The degree of maternal heart rate ($r = 0.53$, $p < 0.001$) and skin conductance ($r = 0.31$, $p < 0.001$) reactivity to the manipulation were significantly correlated from 24 to 36 weeks gestation. There was also stability in the degree to which women experienced the manipulation as stressful based on self ($r = 0.49$, $p < 0.001$) and observer ($r = 0.46$, $p < 0.001$) reports. Maternal recovery of physiological activity following the Stroop was

Table 2
Associations between fetal heart rate and movement responses

	24 weeks		36 weeks	
	Reactivity	Recovery	Reactivity	Recovery
FHR–FHRV	0.07	−0.24*	0.16	0.31**
FHR–FM	0.17	0.10	0.31**	0.20*
FHRV–FM	0.15	0.04	0.34**	0.37**

FHR, fetal heart rate; FHRV, fetal heart rate variability; FM, fetal movement.
* $p < 0.01$.
** $p < 0.001$.

also stable over time ($r = 0.60$, $p < 0.001$ for heart rate and $r = 0.36$, $p < 0.001$ for skin conductance). No fetal consistency in responsiveness over gestation was detected for fetal heart rate or variability. However, the degree to which individual fetuses responded with changes in motor activity exhibited moderate stability from 24 to 36 weeks ($r = 0.25$, $p < 0.01$). Recovery change scores for fetal measures were not related at 24 and 36 weeks.

2.3. Maternal physiological and psychosocial associations with fetal responsiveness

The degree of change in maternal heart rate and skin conductance in response to onset (reactivity) or offset (recovery) of the Stroop did not correspond to changes in fetal heart rate, variability, or motor activity at either gestational age with one exception: modest but significant correspondence between the degree of reactivity in skin conductance and fetal movement ($r = 0.21$, $p < 0.05$) at 36 weeks. Because the maternal measures used in this study do not represent an exhaustive ascertainment of the stress response, analyses based on women's perception of the stressfulness of the procedure were also conducted. Perceived stress was unrelated to reactivity magnitude at either gestation, but recovery magnitudes were significantly related for fetal heart rate ($r = -0.28$, $p < 0.01$), fetal heart rate variability ($r = -0.21$, $p < 0.05$), and fetal movement ($r = -0.18$, $p < 0.05$). Fetuses of women who perceived the Stroop as more stressful showed less decline in these measures following Stroop offset.

3. Discussion

Central to consideration of the influence of antenatal maternal stress on the postnatal development of offspring are putative effects of episodes of stress on the fetus. Results from this study establish that the fetus can indeed respond to manipulated maternal psychological state. As expected, the Stroop elicited significant maternal sympathetic activation, as indicated by transient elevations in heart rate and skin conductance. In contrast to expectations, fetuses responded to maternal stress with increased variability in heart rate and reduced fetal movement which reverted to original levels following offset of the stressor. The Stroop did not elicit a change in fetal heart rate, a finding consistent with a recent report on a smaller number of third trimester subjects [27]. The same pattern of fetal responsiveness for both heart rate variability and motor activity was demonstrated at

both gestational ages studied, although the fetal response was more robust at 36 weeks than at 24 weeks. The fetal response was also better integrated in terms of correspondence between cardiac and motor parameters at the later age. Taken together, these findings confirm our expectations that fetal responsivity to maternal stress reflects the maturity of the developing autonomic nervous system.

In most respects, male and female fetuses responded to the manipulation similarly, although male fetuses showed enhanced recovery in fetal motor activity following offset of the stressor at 36 weeks. If male fetuses consistently respond to maternal stressors with rebound in motor activity, this may contribute to the persistent clinical and public perception that male fetuses are more active despite lack of empirical documentation of a sex difference in samples of adequate size [28,29]. The current results suggest further investigation into the possibility that there is a differential response in motor activity under challenge conditions.

In contrast to the potentiation of the fetal response from 24 to 36 weeks, the maternal physiological response became more blunted, although neither women nor the observer reported diminution in psychological or behavioral indicators of stress. The reduction in maternal physiological responsivity may simply reflect increased familiarity with the procedure, although women tended to perceive the Stroop as *more* difficult the second time. Pregnancy is associated with hyporesponsiveness to physiological challenges [30,31]. One of the few other investigations to examine changes in maternal physiologic responsiveness over the course of pregnancy reports a reduction in blood pressure responsiveness to cognitive and physical challenges over the same 3-month period of gestation [32]. Thus, while we are not able to discount the role of familiarity, the current results are consistent with the prevailing expectations concerning diminished physiological responsiveness to stress with advancing gestation. This phenomenon is widely regarded as a protective mechanism for the fetus; however, our observations of increased fetal effects at 36 weeks do not provide support for this position.

We are unaware of any other report of the significant increase in basal maternal skin conductance as term approached that was observed here. Unlike heart rate, skin conductance is innervated by only the sympathetic branch of the autonomic nervous system [23]. The rise in skin conductance is consistent with parallel changes in other stress-related domains, including glucocorticoids [33,34], and suggests further support that diminution of physiologic responsiveness over gestation is generated by alterations to autonomic regulation during pregnancy [30,32,35].

Although we were able to show that the manipulation evoked a maternal physiological response, we were unable to link the magnitude of individual maternal responses on these parameters to individual fetal responsivity. The only significant association, found between the degree of change in maternal skin conductance response and fetal movement suppression at 36 weeks, was modest. However, maternal skin conductance and fetal movement emerge as the two most temporally linked features of maternal–fetal functioning when time series analyses are applied to undisturbed baseline conditions [36]. Nonetheless, although maternal heart rate and skin conductance changes provide confirmation of maternal sympathetic activation, they do not appear to represent the mechanisms through which the fetal response was effected. Independence between maternal (i.e., blood pressure and heart rate) and fetal (i.e. heart rate) reactivity has also

been reported in two other investigations using the Stroop during pregnancy [14,27]. However, the latter reported significant correlations between the degree of maternal sympathetic deactivation and fetal heart rate changes only following termination of the stressor during a 5-min recovery period. In the current study, the most consistent relations between fetal and maternal responses were detected between the degree to which women experienced the Stroop as stressful and fetal functioning during the recovery period. Both sets of findings confirm the notion that the immediate post-stressor period provides a unique source of information regarding maternal stress effects on the fetus [37].

The duration of the three time periods of data collection in this study is brief. On one hand, this can be regarded a limitation of the study design that may have introduced an unidentified quantitative bias and compromised interpretation of the data. On the other, detection of changes in both maternal and fetal measures across the windows of study suggests a relatively fast fetal response to both onset and offset of maternal stimulation. The relatively high correlations for the magnitude of the maternal reaction to and recovery from the stressor for heart rate (i.e., r's = 0.53 and 0.60) and the lesser but consistent stability in skin conductance (i.e., r's = 0.31 and 0.36) suggests that these periods were long enough to capture individual differences in maternal physiological patterns, and that at least one element of the stress response may be characterized in terms of relatively brief phasic activity.

Consideration of potential mechanisms that mediate the observed fetal responses must be based on the temporal features of the study period. Maternal sympathetic activation can generate a cascade of metabolic and neurohormonal effects, including glucocorticoid responses, but these are likely to be too slow to account for the observed effects. In contrast, vasomotor indicators such as maternal diastolic blood pressure have been shown to recover within the first 2 min following Stroop offset [14]. This raises the possibility that the Stroop generates transient maternal vasoconstriction with reductions in uterine perfusion. Acutely induced mild fetal hypoxemia in ovine [38] and nonhuman primate [39] studies generates a similar increase in heart rate variability, although this effect was not found during induced hypo-oxygenation in women at term [40]. However, increased variability in heart rate is a consequence of the physiologic stress associated with labor [41,42]. The other fetal response observed in the present study was reduced motor activity; decreases in motor tone and activity are commonly observed consequences of decreased oxygen availability [43].

Fetal heart rate responses have been observed within seconds of disruptions of the maternal environment in investigations of sensory capacities, including maternal postural changes [44] and auditory stimuli [45]. Recently, a similarly rapid onset of a fetal response to induced maternal psychological stress, including increased fetal heart rate variability, has been reported in catheterized macaques leading the authors to suggest that fetal response represents detection of alterations to the intrauterine sensory environment [46]. Maternal vasculature sounds are prominent in the uterine auditory environment [47], and it is possible that sudden accelerations in maternal heart rate and accompanying blood pressure changes may provide the fetus with signals generated by maternal sympathetic activation. Thus the predominant mechanism would entail a sensory response and not direct physiological mediation. An additional potential stimulus, maternal speech, is an

inadvertent component of the current study design. Maternal speech sounds are both detected and discriminated by the fetus [48]. The nature of the maternal speech generated by the present study differs from normal, fluent speech and may present a novel stimulus, particularly to the near-term fetus. Inhibition of motor activity is a core component of an orienting or attentional response, which is consistent with the fetal motor quieting observed here. However, in contrast to the observed increase in heart rate variability, attentional responses generally evoke transient suppression of vagal tone, apparent as early as the second postnatal month [19]. However, existing studies of fetal responses to stimuli have not traditionally examined effects on heart rate variability, so it is premature to consider this incompatible with an attentional response to changes in the intrauterine milieu. Moreover, induced maternal stress may generate a complex response that includes a rapid sensory-mediated component as well as a secondary response mediated by adrenergic or vasoconstrictive processes.

The current study is one of the few to document the nature of the fetal response during induced maternal psychological stress. Given the relatively benign nature of the maternal manipulation, results suggest that the fetus is periodically exposed to threats to homeostasis promulgated by maternal emotional arousal. With respect to individual maternal–fetal pairs, there is stability in both maternal physiological and psychological response to the stressor over time and a lesser, but significant, consistency in the fetal motor response to maternal stress. The frequency of such events between individuals is likely to vary, in part, with the degree to which women's lives are stressful and also with more characteristic response tendencies inherent in personality traits, such as anxiety. We previously reported that fetal motor activity is elevated in women who display persistent emotional arousal during pregnancy [49], suggesting that arousal may exert both phasic and tonic influences. Anecdotal observations also support a biphasic motor response [16].

The contribution of nongenetic, constitutional influences of the maternal "womb environment" on postnatal develop is gradually being recognized [50]. The documentation of fetal responses to maternal arousal evoked by a benign stressor that is consistent with naturally occurring events in the lives of pregnant women suggests that fetal neurobehavioral regulation is routinely disrupted by environmental intrusions. The consistency in the degree of evoked maternal physiologic responsiveness over time suggests that there is systematic variability in the manner in which the uterine environment provides a stimulus to individual fetuses. We propose that patterns in the maternal–fetal dyad may serve to entrain autonomic development in the fetus and that characteristic response patterns begin in utero. These findings may serve to inform about the processes through which the intrauterine environment acts to set the stage for later life.

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