Development of fetal movement — fetal heart rate coupling from 20 weeks through term


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Abstract

This study documents the development of fetal heart rate (FHR) change in response to fetal movement (FM) in healthy fetuses from 20 weeks' gestational age through term. Thirty-one fetuses received 50 min of Doppler-based monitoring at 20, 24, 28, 32, 36 and 38–39 weeks. FHR and FM were continuously digitized. A coupling index was computed as the percentage of FMs associated with increases in FHR of 5 beats/min or more within -5 or +15 s of movement onset. The latency between FM onset and FHR change was also computed, as were the amplitude and duration of all movements. FM and FHR became more integrated with advancing gestation. Coupling increased and the latency between FM and FHR changes decreased. Maternal age, blood pressure and fetal sex did not affect FM-FHR coupling, but fetuses of women who reported greater stress in their daily lives and had faster heart rates displayed reduced coupling. These data suggest that the development of FM-FHR coupling reflects the development of the central nervous system during gestation, and that development may be affected by maternal factors.

Keywords: Fetal heart rate; Stress; Fetal movement; Neurologic development

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1. Introduction

The association between accelerations of fetal heart rate (FHR) and fetal movement (FM) has been documented since the 1930s [17]. In the third trimester, virtually all large fetal heart rate accelerations are associated with fetal activity, although a small percent are spontaneously generated [5,8,14,21]. The converse has also been reported to be true; most observable fetal movements are associated with an increase in FHR [18,19]. More vigorous and prolonged fetal movements are most likely to be associated with FHR accelerations. The degree of consistency with which FHR accelerations are coincident with fetal movement has been suggested as an index of fetal well-being [1,11], and as a potential substitute for the nonstress test [1].

It is unclear whether FHR accelerations are a consequence of fetal activity, or whether both are initiated simultaneously. Several investigators, including the earliest reporters of this association, have suggested that FHR changes do not merely reflect increased cardiac output as a result of increased motor activity. Instead, theories have focused on the role of sympathetic-parasympathetic balance in neural control of the heart [17] and synchronous central mediation of motoric and cardiac innervation [8,19].

A few provocative findings indicate that maternal factors can affect fetal autonomic function, although data on the topic are meager. Maternal emotional state, manipulated by observing a labor and delivery movie [20] or by listening to music [23] can influence fetal activity. Recently, a relation between exposure to repeated maternal stressors during pregnancy and reduced neuromotor behavior in squirrel monkey infants [15] has been documented, and it has been suggested that this effect is mediated by antenatal alterations in the adreno-pituitary axis [16].

The current study was designed to examine the development of the relation between FM and small changes in FHR in normal fetuses, and to determine the effect of maternal and fetal characteristics on this development. Specifically, we predict that maternal stress will hamper maturation of this integration, resulting in poorer linkage between FM and FHR, as this linkage is expressive of neural development. Previous studies on this subject have been limited by methods to ascertain fetal movement and calculation of FHR and FHR baseline through visual inspection of fetal monitor tracings. This research was conducted using a form of Doppler technology which recognizes and produces a continuous tracing of fetal movement data in addition to standard cardiotocographic methods for ascertaining FHR. This technology provides an opportunity to record FM data for long periods of time without the need for continuous ultrasound, which generally requires two transducers for adequate visualization of fetal extremities and trunk in the third trimester. All FHR and FM data were digitized on-line on a computer, affording precise quantification of FHR and FM variables.

2. Materials and methods

Thirty-one women with unremarkable pregnancy histories, who were high school graduates, at least 20 years old, and who did not smoke were recruited for this longi-
tudinal study. Given the gestational age-based nature of the study, accurate ascertained gestational age was also a criterion for inclusion. Age determination criteria included the following: pregnancy test within 2 weeks of missed period and/or first trimester obstetric or sonographic examination. Actual dating criteria were more stringent than required by the protocol: the mean gestational age at pregnancy confirmation was 5.4 weeks. Volunteers were predominantly well-educated, employed women (mean maternal age = 28.5 years, range = 22–36; mean years of education completed = 16.5, range = 13–20). Six women were African-American, the remainder were white. Most (20) were primiparous, 10 had one other child, the remainder had two. There were a range of minor risk factors present in the sample (e.g. mild pre-eclampsia or oligohydramnios at 38 weeks), but all neonates were considered healthy at delivery and discharged on normal nursery schedules (mean birthweight = 3349 g, range 2720–4160 g; mean 5-min Apgar = 8.9, range = 8–10). Seventeen (55%) were girls.

Subjects were tested at each of the following gestational ages: 20, 24, 28, 32, 36 and 38–39 weeks. To control for potential diurnal and prandial effects, subjects were tested at the same time each visit, either at 13:00 or 15:00 h, and were instructed to eat lunch 1.5 h prior to testing. The research protocol was approved by the institution’s Joint Committee on Clinical Investigation.

Maternal pregnancy history and demographic data were collected upon enrolment. At each visit, women completed the Hassles and Uplifts Scale [6]. This scale includes 53 items which are rated on a 4-point scale in terms of the degree to which they were hassling and/or uplifting in the past 24 h. For example, ‘Your spouse’ may be appraised as both an uplift, a hassle, or both, and the intensity of the appraisal may vary from mildly to highly stressful for each. Reliability and validity for this, and other similar scales, have been established [6,9]. Because positive and negative stressors typically have similar physiologic effects, a combined Hassles and Uplifts score (Hassles intensity + Uplifts intensity + frequency of each) was computed.

Maternal pulse rate and blood pressure were measured at the beginning of each fetal recording. Blood pressure data were quantified as mean arterial pressure \((MAP = \frac{2 \times \text{diastolic value} + \text{systolic value}}{3})\). Women were then monitored in the left lateral recumbent position for a period of 50 min using a Toitu MT320 Fetal Actocardiograph. This monitor simultaneously records fetal movement and fetal heart rate through the use of a single wide array transabdominal Doppler transducer. FHR is ascertained using autocorrelation techniques based on sampling the Doppler generated waveform every 1.5 ms. The innovation in this and other similar monitors is Doppler-based fetal movement detection. Higher frequency Doppler signals (150–220 Hz) are generated by motion of the fetal heart. Thus, standard FHR monitoring requires a Doppler signal sensitive enough to detect movement changes that are as small as 1–2 mm. Lower frequency signals, which would be produced by maternal and fetal body activity, are typically filtered out as noise and discarded. Instead of discarding these signals, the actograph bandpasses both the highest frequency (i.e. FHR) and the lowest frequency signals (i.e. maternal movement and respiration). Actograph signals are generated by a change in the returned Doppler waveform; if there is no movement, the returned signal will retain
the same frequency as the emitted signal. If the fetus is moving, the echo will be returned at a different frequency which is proportional to the velocity with which the fetal body part moves towards or away from the transducer. The resultant signal is output in the form of spikes on a polygraphic tracing in arbitrary voltage units, and corresponds almost exclusively to limb and body movement of the fetus [12].

The actocardiograph detects 95.9% of all movements observed on ultrasound, including 100% of all large, complex movements [3]. Similar validity in movement detection has been reported for other Doppler-based fetal movement monitors [13]. Both reports indicated that fetal actographs are somewhat better at detecting larger and longer movements than they are at smaller, more discrete movements. Note, however, that estimates of both false positive and negative rates are limited by the lack of a true 'gold standard' in ascertainment of fetal movement; ultrasound transducers can visualize only portions of the fetal body and may miss localized movements which are produced by limbs beyond this field and which do not affect the rest of the body.

Fetal heart rate and movement output from this monitor were sampled at 5 Hz and digitized on-line on a microcomputer (Macintosh IIci, Apple, Inc.) using an A-D converter board (Labview NB, National Instruments). Data collection and analysis software applications were developed for this and related projects. Quantification of all FM, FHR, and coupling measures reported here was accomplished through these customized programs.

2.1. Fetal data collection and quantification

2.1.1. Fetal heart rate. Raw fetal heart rate data sampled every 200 ms from the continuous, autocorrelated output of the monitor underwent processing for artifact and baseline computation in the following manner:

(1) Artifact rejection. The digital data underwent a series of error rejection procedures. A data point was rejected if its value was beyond a predefined range and/or was not within a predefined factor range of previously acceptable data points. Following this, the median for each sequential second (i.e. five data points) was computed, and compared to previous medians. Again, the median was rejected if it was not within an acceptable range of previous medians. For each second that was rejected, the range of acceptability increased incrementally to a maximum range. This range decreased to initial values as soon as an acceptable median was detected. Rejected data points were interpolated to preserve temporal integrity. However, interpolated values were not used in quantification of FHR measures. Our final algorithm was developed after comparing the polygraphic output of the monitor to the computerized output of several hundred records and ultimately validated against visual inspection of 7500 min of collected polygraphic data.

(2) Baseline computation. A moving baseline was fit to these data based on computation of the FHR power spectrum. The modal FHR was subtracted from each point and the resulting data were then filtered in a backward and forward series to reduce phase shift, removing all but the lowest frequency variations (0.0017 Hz low pass). The modal value was then re-added to each resultant data point. Thus, the baseline reflects a lower frequency version of the original data series centered at
its modal value. This baseline was superimposed against the raw data and used to detect excursions in heart rate.

2.1.2. Fetal movement. The actographic signal output is calibrated in arbitrary units (a.u.s.) which range from 0 to 100. Signals of less than 25 a.u.s. can be produced by fetal breathing or hiccups, which generate incidental fetal movement but are not considered motor activity. Fetal movement detection was thus based on a 25 a.u.s. threshold. A discrete movement was defined as commencing each time the actograph signal attained or exceeded 25 a.u.s. and terminating when the signal fell below 25 a.u.s. for at least 10 consecutive seconds. The duration and amplitude of each movement were calculated.

2.1.3. FHR-FM coupling. Coupling was defined as occurring each time a fetal movement was accompanied by an excursion in FHR ≥ 5 beats/min for ≥5 s above the FHR baseline within 5 s before the FM or 15 s following the movement. Because the baseline is a smoothed version of the actual data, fetuses with high levels of background FHR variability must exceed their baseline rate to meet these criteria. Previous research has determined that using the 5 beats/min criteria in measurement of coupling has good sensitivity and specificity in predicting nonstress test results [1].

If coupling was detected, the latency between the onset of the FHR change relative to the onset of the FM was calculated. Negative latency values were transformed into absolute values, thus latencies may range from 5 to 15 s. If a movement occurred during an already coupled acceleration, that movement was also included as coupled. The coupling index was computed as: (total coupled FM ÷ all FM) × 100.

Because fetal activity is a primary cause of poor FHR signal quality, FMs were excluded from the coupling index if 50% or more of the 20-s window surrounding the movement was rejected as artifactual.

2.1.4. Data analysis. Weighted least squares analysis was used to model the developmental trends of the two coupling measures over time. This method estimates and corrects for the non-independence of longitudinally collected variables and weights observations based on estimated correlational structures. Robustness of these estimated correlational structures was tested using Generalized Estimating Equations method [22]. Lowess, a non-parametric smoothing technique [4], was used for each measure to determine the shape of the developmental trend over time. If the trend appeared non-linear, a knotted spline was included in the model. This procedure permits detection of one or more changes in the rate of development during the observation period by allowing the slope of the regression line to change. The following covariates were included in the model for both coupling and latency: gestational age (GA), fetal sex, maternal age, maternal mean arterial blood pressure (MAP), maternal heart rate, and Hassles/Uplifts (perceived stress). The terms for maternal blood pressure, heart rate and perceived stress were specific to each gestational age point. Thus, each fetal measure was modelled as follows:

$$\beta_0 \text{ (intercept)} + (\beta_1 \times \text{GA}) + (\beta_2 \times \text{fetal sex}) + (\beta_3 \times \text{maternal age}) + (\beta_4 \times \text{daily maternal heart rate}) + (\beta_5 \times \text{daily maternal MAP}) + (\beta_6 \times \text{hassles/uplifts})$$

An additional term for the spline function at the gestational age at which the model appeared to change slope was included if indicated.

Fourteen of the 31 subjects delivered prior to their term appointment (i.e. prior
to 38/39 weeks), so data at term are based on the remaining 17 subjects only. Pearson product-moment correlations were computed to investigate the relations between the two coupling measures and *-tests were used to compare the characteristics of coupled and uncoupled movements.

3. Results

Coupling of FHR and FM increased with advancing gestation. The percentage of FM onsets associated with increases in FHR increased from 21 to 57% between 20 weeks and term, while the latency or lag time between FM onset and FHR change decreased from 5.0 to 2.7 s (Fig. 1). Results of the least squares regression are presented in Table 1, and the highly significant Z-scores indicate that both of these values change significantly over gestation. Maturation of the coupling index occurred most rapidly between 20 and 32 weeks (i.e. the spline term, which detects a change in slope, is significant at 32 weeks), while after this time the rate of change slows. Fig. 2 presents examples of actocardiograph tracings from the same fetus at
Table 1
Results of weighted least squares analysis: developmental trends during gestation

<table>
<thead>
<tr>
<th>Gestation</th>
<th>Spline</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>GA</td>
</tr>
<tr>
<td>Est.</td>
<td>S.E.</td>
</tr>
<tr>
<td>Coupling index</td>
<td>2.51</td>
</tr>
<tr>
<td>Coupling latency</td>
<td>-0.14</td>
</tr>
</tbody>
</table>

Total model df = 164. The table columns are defined as follows: the estimated parameter (Est.), the estimated standard error of the parameter estimate (S.E.), the ratio of the estimate to its standard error (Z-value), and the P-value corresponding to the Z-statistic. These statistics are computed separately for the general trend over gestation as well as the tested spline term. In the case of coupling index, 32 weeks is the gestational age at which the regression line undergoes a significant change in slope.

20 weeks and at term to illustrate the developmental nature of the relation between FM and FHR.

In most cases, onset of FM preceded FHR change, but for one or two fetuses at each gestational age latencies were negative, indicating that FHR changes often preceded FM in these subjects. By the last two recordings, the two measures of coupling were negatively related ($r = -0.31$ at 36 weeks and $r = -0.65$ at term); fetuses that displayed a higher rate of coupling also had a closer temporal association between the movement onset and FHR change.

Table 2 presents additional data on the characteristics of FM that were associated with FHR increase at each age tested through a series of paired t-tests between coupled and uncoupled movements for each movement characteristic. Beginning at 20 weeks, coupled movements were significantly longer in duration than were uncoupled ones, and this relation was independent of movement amplitude until 32 weeks. From this time until term, coupled movements were both longer and more vigorous. Significantly more movements were uncoupled than coupled through 28 weeks.

Table 3 presents the effects of covariates. Maternal perceived stress was significantly associated with the degree of coupling; higher reported stress was associated with less FM-FHR coupling. In addition, faster maternal heart rate was negatively associated with coupling latency. Fetuses of women with faster heart rates had longer latencies for the movements which were coupled. Maternal age, blood pressure, and fetal sex were not significantly associated with either measure.

4. Comment

With maturation, the relation between FM and FHR becomes more synchronized and temporally associated in healthy fetuses. This relation is evident as early as 20
Fig. 2. Output from Toitu Actocardiograph Monitor. Upper line of each strip is FHR, lower line represents fetal movement output of actograph. Each dark vertical line is 1 min. Top tracing shows little coupling in a 20-week fetus; lower tracing demonstrates good coupling in the same fetus at 39 weeks.
Table 2

Characteristics of coupled and uncoupled movements at six gestational ages

<table>
<thead>
<tr>
<th>GA</th>
<th>Coupled movements</th>
<th></th>
<th>Uncoupled movements</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Mean duration (s)</td>
<td>Mean amplitude (a.u.s.)</td>
<td>N</td>
<td>Mean duration (s)</td>
</tr>
<tr>
<td>-----</td>
<td>------------------</td>
<td>-------------------------</td>
<td>-----</td>
<td>------------------</td>
</tr>
<tr>
<td>20</td>
<td>22.2* (19.2)</td>
<td>36.3 (3.7)</td>
<td>11*** (5)</td>
<td>14.4 (6.6)</td>
</tr>
<tr>
<td>24</td>
<td>15.6* (12.6)</td>
<td>38.0 (4.9)</td>
<td>17*** (6)</td>
<td>10.8 (6.6)</td>
</tr>
<tr>
<td>28</td>
<td>14.4** (7.2)</td>
<td>38.4 (4.2)</td>
<td>24*** (8)</td>
<td>8.4 (7.2)</td>
</tr>
<tr>
<td>32</td>
<td>14.4*** (11.4)</td>
<td>38.7** (4.1)</td>
<td>27 (10)</td>
<td>8.4 (7.2)</td>
</tr>
<tr>
<td>36</td>
<td>13.8*** (11.4)</td>
<td>41.0*** (4.1)</td>
<td>26 (8)</td>
<td>7.8 (7.2)</td>
</tr>
<tr>
<td>38–39</td>
<td>12.6* (14.7)</td>
<td>40.8* (5.0)</td>
<td>28 (11)</td>
<td>7.8 (7.8)</td>
</tr>
</tbody>
</table>

Values in parentheses are standard deviations.

*P < 0.05; **P < 0.01; ***P < 0.001. Indicates significant difference with uncoupled movements.

weeks, when 21% of all movement onsets are associated with small increments in FHR. Between 20 weeks and term, the time lag between the onset of movement and FHR change diminishes from approximately 5 to 2.5 s, and the percentage of coupled movements triples. A transition in the rate of development occurred at 32 weeks, after which time the rate of coupling began to level off. We have noted similar developmental transitions in other aspects of fetal functioning, including FHR variability, activity level, state concordance, and responsivity to vibroacoustic stimulation at about the same gestational age [7] and have proposed that this reflects a critical period for neural integration. However, the coexistence of similar patterns of development for other neuroregulatory processes in the fetus reveals that the rise in coupling does not exist in isolation, and the role of potential mediators of the relation between fetal movement and heart rate, such as behavioral state, are not well-known at present.

A prevailing view in the literature has been that FM does not cause FHR accelerations by increasing demands on the heart, but rather that both cardiac and somatic systems are activated simultaneously. For example, Timor-Tritsch et al. [19] speculated that the nearly synchronous onset of FHR accelerations with movement indicates centrally coordinated control of both functions, and implicated diffusion of neural signal between loci of motor and cardiovascular function in the cortex. We agree with this position and suggest that FM-FHR coupling reflects coactivation of the parasympathetic and sympathetic components of the autonomic nervous system of both motor and cardiac function. The branches of the autonomic nervous system can act both reciprocally and in union; simultaneous vagal withdrawal and sympathetic activation produces a phasic response in target organs with minimal impact on tonic, baseline control [2]. In addition, stimulation of single central nervous system (i.e. hypothalamic) sites has been demonstrated to rapidly increase both heart rate and blood flow to muscles in animal preparations [10]. Based on this
### Table 3
Results of weighted least squares analysis: maternal and fetal covariates

<table>
<thead>
<tr>
<th>Maternal stress</th>
<th>Maternal pulse</th>
<th>Maternal blood pressure</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Est.</td>
<td>S.E.</td>
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<td>Coupling index</td>
<td>-8.56</td>
<td>3.39</td>
</tr>
<tr>
<td>Coupling latency</td>
<td>0.29</td>
<td>0.35</td>
</tr>
<tr>
<td>Maternal age</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Est.</td>
<td>S.E.</td>
</tr>
<tr>
<td>Coupling index</td>
<td>-0.52</td>
<td>0.37</td>
</tr>
<tr>
<td>Coupling latency</td>
<td>0.01</td>
<td>0.03</td>
</tr>
</tbody>
</table>
physiologic model, the increase in coupling observed during gestation reflects development of components of the nervous system. Several of our empirical findings lend support to this speculation. These include the close temporal relation between the two events, the initiation of FHR acceleration prior to FM in some instances (although this is not the typical relation), and the association between coupling and movement duration. Longer movements were more likely to be coupled. Because the mean duration of coupled movements was 22 s at 20 weeks, and the mean latency between FM onset and FHR acceleration above 5 beats/min was only 5 s, coupling occurred early in the movement; thus the FHR change occurred at the beginning, not at the end of the movement. This suggests that FHR accelerations and FM may both be initiated and maintained by the intensity of the neural innervation.

Anecdotal support for the position is provided by an example from a subject presented in Fig. 3. This 38-week fetus, which developed oligohydramnios several days prior to recording, moved less frequently and vigorously (13 movements per 50-min recording) than any other fetus, probably as a result of positioning and uterine constraint. However, large accelerations are evident in the figure, almost all of which are coincident with very small, brief, movements. The coupling index for this fetus was 77%. The movements do not appear to be large enough to require compensatory cardiac output and argue for the role of synchronous mediation.

The percentage of FM associated with FHR changes is lower than has been reported by other investigators. At term, only 57% of FM onset was coupled in this study compared to reports of over 90% by other investigators [19]. This discrepancy

Fig. 3. Actocardiograph tracing from a 38-week, breech fetus with oligohydramnios. Note large accelerations associated with small, brief, movements.
is probably due to criterial differences in defining FHR changes and FM. Computerized quantification of FM and small increments in FHR (i.e. 5 beats/min above baseline) permitted us to quantify fetal functioning in more precise ways than are available by visual inspection of polygraphic tracings or in those studies in which FM is detected by maternal perception. Others have found that both the size of the FHR change used as criteria and the type of movement data used affects coupling rates [14]. Our coupling index was based on Doppler-based data which include all FMs, including isolated limb excursions. However, our data indicate that movement duration is the most consistent determinant of FHR acceleration, which confirms observations of other investigators using different methods [19]. If we had limited our FM data to prolonged movements only, the percentage of movements associated with FHR changes would have been greater and more in accord with other reports. Also, it is important to understand the nature of the associations reported in the literature; many investigations study the degree to which FHR changes are associated with movements. Because our goal was to investigate the role of movement in instigating FHR changes, our denominator was fetal movements, not FHR accelerations. It seems likely that while most accelerations are associated with some form of fetal movement [8,21] the reverse would be less common. Decisions on how coupling was calculated in this study were made to provide the most sensitive description of the developmental relation between the onset of a movement and resulting change in FHR while keeping arbitrary or clinical judgments based on acceleratory or movement size to a minimum.

There was a wide range of coupling within this group of healthy fetuses. At term the coupling index ranged from 31 to 81%. The data indicate that at least part of this variability is a function of maternal perceptions of daily stress. Fetuses of women who reported higher levels of current stress displayed less FM-FHR coupling. This finding was supported by a relation between maternal pulse rate and coupling latency. Decoupling may be a fetal response to the neuroendocrine milieu produced by sympathetic maternal arousal and/or a reduction in parasympathetic tone. These results suggest that maternal psychologic stress may impede neurologic maturation of the fetus and illustrates the potentially complex interaction between maternal emotions and fetal functioning.

Acknowledgements

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References