

Effect of maternal position on fetal behavioural state and heart rate variability in healthy late gestation pregnancy

Peter R. Stone¹ , Wendy Burgess¹, Jordan P. R. McIntyre¹ , Alistair J. Gunn^{2,3} , Christopher A. Lear² , Laura Bennet² , Edwin A. Mitchell³, John M. D. Thompson^{1,3} and the Maternal Sleep In Pregnancy Research Group, The University of Auckland

¹Department of Obstetrics and Gynaecology, Faculty of Medical and Health Sciences, The University of Auckland, New Zealand

²Department of Physiology, Faculty of Medical and Health Sciences, The University of Auckland, New Zealand

³Department of Paediatrics: Child and Youth Health, Faculty of Medical and Health Sciences, The University of Auckland, New Zealand

Key points

- Fetal behavioural state in healthy late gestation pregnancy is affected by maternal position.
- Fetal state 1F is more likely to occur in maternal supine or right lateral positions.
- Fetal state 4F is less likely to occur when the woman lies supine or semi-recumbent.
- Fetal state change is more likely when the woman is supine or semi-recumbent.
- Fetal heart rate variability is affected by maternal position with variability reduced in supine and semi-recumbent positions.

Abstract Fetal behavioural states (FBS) are measures of fetal wellbeing. In acute hypoxaemia, the human fetus adapts to a lower oxygen consuming state with changes in the cardioclograph and reduced fetal activity. Recent studies of late gestation stillbirth described the importance of sleep position in the risk of intrauterine death. We designed this study to assess the effects of different maternal positions on FBS in healthy late gestation pregnancies under controlled conditions. Twenty-nine healthy women had continuous fetal ECG recordings under standardized conditions in four randomly allocated positions, left lateral, right lateral, supine and semi-recumbent. Two blinded observers, assigned fetal states in 5 min blocks. Measures of fetal heart rate variability were calculated from ECG beat to beat data. Compared to state 2F, state 4F was less likely to occur when women were semi-recumbent [odds ratio (OR) = 0.11, 95% confidence interval (95% CI) 0.02, 0.55], and supine (OR = 0.27, 95% CI 0.07, 1.10). State 1F was more likely on the right (OR = 2.36, 95% CI 1.11, 5.04) or supine (OR = 4.99, 95% CI 2.41, 10.43) compared to the left. State change was more likely when the mother was semi-recumbent (OR = 2.17, 95% CI 1.19, 3.95) or supine (OR = 2.67, 95% CI 1.46, 4.85). There was a significant association of maternal position to mean fetal heart rate. The measures of heart rate variability (SDNN and RMSSD) were reduced in both semi-recumbent and supine positions. In healthy late gestation pregnancy, maternal position affects FBS and heart rate variability. These effects are likely fetal adaptations to positions which may produce a mild hypoxic stress.

(Received 27 July 2016; accepted after revision 25 October 2016; first published online 21 November 2016)

Corresponding author P. Stone: Department of Obstetrics and Gynaecology, The University of Auckland, Private Bag 92019, Auckland 1142, New Zealand. Email: p.stone@auckland.ac.nz

Abbreviations CI, confidence interval; CTG, cardioclograph; FBS, fetal behavioural state; FHR, fetal heart rate; FHRV, fetal heart rate variability; OR, odds ratio; P_{aO_2} , arterial partial pressure of oxygen; RR interval, interval between successive R waves on the electrocardiograph; RMSSD, root mean square of successive differences (in the RR interval); SDNN, standard deviation of the RR interval.

Introduction

The presence of fetal behavioural states (FBS) has now been established for many years (Nijhuis *et al.* 1982; Arduini *et al.* 1986) and fetal heart rate (FHR) patterns have been used to deduce the fetal state (Timor-Tritsch *et al.* 1978; Pillai & James, 1990*a*), which is reliably determined by examination of the characteristics of the baseline FHR patterns alone (Pillai & James, 1990*b*). FBS and their transitions are measures of fetal wellbeing that reflect the neurological integrity of the fetus (Romanini & Rizzo, 1995) and the development of autonomic nervous control of heart rate (Brandle *et al.* 2015).

FBS may be defined as combinations of particular physiological variables which are stable over a period of time and recur (Martin, 2008). In the fetus at least three distinct behavioural or activity states have been identified and correspond to the early neonatal behavioural states 1 (quiet sleep – in the fetus termed 1F), 2 (active sleep – fetal 2F), 3 (quiet awake – in the fetus this is very infrequent or not seen) and 4 (active awake – in the fetus a period of considerable fetal activity with rapid heart rate and varying baseline FHR) (Nijhuis *et al.* 1982). During the third trimester of pregnancy, fetal activities are cycle- or state-dependent, so that prolonged and often repeated recording of behaviour is necessary before any adverse conclusions can be drawn about fetal wellbeing (Pillai & James, 1990*b*). The development and stability of FBS is disturbed in adverse situations such as maternal diabetes and in chronic fetal compromise such as growth restriction (van Vliet *et al.* 1985; Mulder *et al.* 1987). More acute compromise in a previously healthy fetus leads to suppression of fetal activity which may adapt over time in the absence of metabolic acidaemia (Martin, 2008). In acute hypoxaemia, the fetus makes adaptations to a lower oxygen consuming state, with effects on electrocortical activity shown in sheep (Boddy *et al.* 1974; Richardson *et al.* 1985; Bocking & Harding, 1986). The human fetus also makes adaptive changes to hypoxia (Martin, 2008) with changes in the cardiotocograph (CTG) and in reduced fetal activity (Bocking, 2003; Froen *et al.* 2008).

Behavioural state transitions have also been found to be different in length of time and characteristics in the growth-restricted compared with the normally grown fetus (Arduini *et al.* 1989). Measures of fetal habituation and behavioural state transitions have been proposed as methods of assessing fetal wellbeing and predicting neonatal outcome (Krasnegor *et al.* 1998).

Recent developments in transabdominal fetal ECG have permitted ambulatory recording of the beat to beat FHR (Narayan *et al.* 2015). A conventional CTG may be derived from this and fetal behavioural state determined.

Fetal heart rate variability (FHRV) calculated from beat to beat heart rate intervals is an established marker of fetal

wellbeing as it reflects the development and function of the fetal autonomic nervous system in both health and in stress such as hypoxia (Dawes *et al.* 1994; Schneider *et al.* 2008). Reduction in FHRV is known to precede fetal distress and alterations in the inter-beat interval may occur before any noticeable change in the heart rate itself is detected (Dalton *et al.* 1983). The changes in fetal behavioural state may be associated with changes in FHRV (Romanini & Rizzo, 1995).

A recent study of factors associated with late (third trimester) stillbirth described the importance of maternal sleep position where non-left-sided sleeping, particularly supine, was found to be associated with an increased risk of stillbirth (Stacey *et al.* 2011). Two further studies have confirmed adverse effects of supine sleeping (Owusu *et al.* 2013; Gordon *et al.* 2015). The mechanisms by which a normally formed fetus in a healthy pregnancy should be at risk of stillbirth remain unclear as does the reason why maternal position should be of importance. However, a triple risk model has been proposed as a method of understanding the pathogenesis of late stillbirth involving the interplay of maternal factors, a vulnerable fetus and the imposition of a stressor (such as maternal supine position) which then produces a lethal combination (Warland & Mitchell, 2014). An aim of our studies was to investigate the effects of maternal position in healthy late gestation prior to examining vulnerable pregnancies such as those in obese woman or with fetal growth restriction. Vulnerable groups at increased risk of late stillbirth have been identified as a priority area for research in high-income countries (Flenady *et al.* 2011).

Therefore, as part of ongoing studies of stillbirth, we designed this study to assess the effects of different maternal positions in healthy late gestation pregnancies under controlled conditions on FBS as a marker of fetal wellbeing. We hypothesised that FBS would be affected by maternal position.

Methods

Ethical approval

This study was approved by the Northern Regional Human Ethics Committee (NTX/11/09/084). All subjects gave written informed consent. All studies approved by the Northern Regional Human Ethics Committee conform to the *Declaration of Helsinki*.

Subjects

Twenty-nine healthy women aged ≥ 18 years with a normal singleton pregnancy, late in the third trimester (35–38 weeks of gestation), were recruited from low risk midwifery care at National Women's Hospital, Auckland, New Zealand.

Maternal exclusion criteria included: current smoking or alcohol use, early pregnancy body mass index > 30, any medical or obstetric complications (e.g. pre-eclampsia, any known cardiovascular disorder including hypertension or use of antihypertensive treatments, respiratory or renal disorders, all forms of diabetes), not regularly attending scheduled obstetric appointments, any orthopaedic or musculoskeletal conditions which would make adopting different maternal positions difficult and inadequate English speaking to give consent. Fetal exclusion criteria included: abnormal biometry for the gestation, reduced amniotic fluid volume, abnormal umbilical arterial Doppler measurements and multiple pregnancy.

A maternal echocardiogram and ECG were performed immediately prior to the study to ensure normal maternal cardiac anatomy and function.

Fetal biometry using customized centile charts (McCowan *et al.* 2004) and fetal Doppler measures of the umbilical and middle cerebral arteries were also recorded using standard methodologies. Fetal biometry < 10th centile was considered abnormal and was an exclusion factor. Pulsatility indices in the umbilical artery < 95th centile, and in the middle cerebral artery > 5th centile and a cerebroplacental pulsatility index ratio > 5th centile on reference charts (Ebbing *et al.* 2007) were considered normal and were required for inclusion in the study. In addition, a measurement of the single deepest pool of amniotic fluid was performed, all assessments being performed to confirm normal fetal wellbeing. Birth outcome data were collected to confirm the health status of the mother and neonate.

Procedures

Participants were told to abstain from alcohol, caffeine, chocolate and strenuous exercise on the day of the assessment, and not eat within 2 h of the assessment. All assessments were performed in the afternoon between 14.00 and 15.00 h.

Four maternal positions, supine, semi-recumbent, left lateral and right lateral, were studied. In supine the woman lay on her back with one pillow. The semi-recumbent position was defined as having the woman supine with the cephalad end of the examination couch raised to a measured 30 deg from the horizontal and one pillow was provided. The lateral positions involved the women being placed lying on their side and at least 30 deg from supine, with the head of the couch flat and one or two pillows provided.

On arrival in the laboratory, the participants were randomised to the order of maternal positions from a computer-generated list created in MS Excel. Each woman was monitored for 30 min in each position. The participant would move directly from one position to the

next unless she needed to use the bathroom. Assessments were all performed in the same room, by the same investigators (PS, JM).

A continuous fetal ECG, electrohysterogram and maternal heart rate were recorded using the Monica AN24 ambulatory transabdominal fetal ECG device (Monica Healthcare, Nottingham, UK). Skin preparation, electrode placement and impedance testing were performed as per the manufacturer's instructions. This device enabled monitoring of the fetus without need to reposition bulky transducers when the mothers moved between each position. In addition, in contrast to conventional CTG, the device recorded a fetal ECG with true beat to beat intervals in 1 min epochs without autocorrelation as used in commercial CTG machines.

Data processing

The data from the Monica device were uploaded to a PC computer with the Monica (VS) analysis software. The Monica VS software uses beat to beat data to construct a fetal cardiograph, which when combined with the hysteroogram produced a printout analogous to a standard CTG suitable for interpreting FBS.

The Monica device has a built in proprietary algorithm to deal with signal loss (any epoch with > 30 s signal loss in the 1 min epochs used for the analysis of the raw ECG signal is disregarded and no result is given for that epoch). The manufacturer's analysis program (Monica DK v1.9) was used to calculate FHRV. Mean FHR was assessed for each minute analysed, giving up to 30 samples (30 1 min epochs) per position in each subject. Each epoch was quantified by the mean FHR, the standard deviation of RR intervals (SDNN) and the root mean square of successive RR intervals (RMSSD). The left lateral position was used as the referent from which the other positions were compared. For analysis of the relationship of these variables in relation to fetal state, the observations over each block of time were averaged to correspond with the block of time in which the fetal state had been determined.

Fetal state was based on the classic features of the CTG as described by Pillai & James (1990a). The CTGs were scored independently by two obstetricians (PS, WB), blinded to maternal position. Each block was scored for fetal state as either 1F, 2F, 4F, transition or indeterminate using the methods of Pillai & James (1990a). Consistent heart rate patterns were defined as a state when the duration was at least 3 min. Comparison of the scoring found a kappa of 0.68, which is considered substantial, with complete agreement in 82% of observations. When the agreement analysis was limited to observations where a fetal state had been defined by both scorers kappa was 0.86 (considered almost perfect) and there was complete agreement for 95% of observations. For observations where there was disagreement, the scorers reviewed the

Table 1. Number (%) of blocks of time in relation to maternal position and fetal state

Maternal position	State 1F	State 2F	State 4F
Left	13 (11.3)	91 (79.1)	11 (9.6)
Right	28 (22.0)	91 (71.7)	8 (6.3)
Semi-recumbent	23 (16.3)	113 (81.9)	2 (1.4)
Supine	45 (34.4)	83 (63.3)	3 (2.3)

observations together, blinded to the original scoring and reached a consensus view. These observations are those used in the analysis.

Statistical analyses

Odds ratios (ORs) were determined to estimate the risk of the fetus being in state 1F or state 4F compared to the predominant state 2F by maternal position. This was carried out using repeated measures analyses (i.e. the repeated measures over the 30 min in each position of fetal state) in the GLIMMIX procedure in SAS. The models used a binary outcome with a logit link and a random intercept term.

Differences in FHR and FHRV were assessed using the GLIMMIX procedure to compare differences in these measures when the fetus was in 1F or 4F compared to the referent 2F group. The analyses to compare FHR and FHRV by maternal position (with referent left position) for state 1F and 2F were carried out in the same manner. The sample size did not allow for this analysis to be carried out for data where the fetus was in state 4F ($n = 24$).

All analyses were carried out in SAS for Windows v9.3 (SAS Institute, Cary, NC, USA).

Results

There were analysable data for 511 (88.1%) of the observations (blocks of time); data loss was due to loss of signal (8.3%), fetus in transition (1.7%) or indeterminable state (1.9%). Visual analysis of the FHR data showed that there were no decelerations at times of state change, nor periods of fetal bradycardia.

Distribution of fetal state

The distribution of FBS by maternal position is shown in Table 1. As would be expected, the primary FBS was 2F (74.0% of the time) followed by 1F (21.3%) and 4F (4.7%).

Effect of maternal position on fetal state

In Table 2, the likelihood of being in a state other than 2F related to maternal position is shown. In comparing state 2F to 1F, those on the right [OR = 2.36, 95% confidence

interval (CI) 1.11, 5.04] or supine (OR = 4.99, 95% CI 2.41, 10.43) were significantly more likely to be in 1F compared to those on the left. Compared to state 2F, state 4F was less likely to occur when the women were in the semi-recumbent position (OR = 0.11, 95% CI 0.02, 0.55). In the supine position, the likelihood of being in 4F was also reduced but did not reach statistical significance (OR = 0.27, 95% CI 0.07, 1.10).

In comparison with the left lateral position, when mothers were placed semi-recumbent or supine, the fetus was significantly more likely to change behavioural state (OR = 2.17, 95% CI 1.19, 3.95 and OR = 2.67, 95% CI 1.46, 4.85, respectively). There was no pattern as to what state change took place.

Effect of fetal state on measures of FHRV

In Table 3 the effect of fetal state on FHR and FHRV is shown. Compared with state 2F, in state 1F there was a significant reduction in FHR, SDNN and RMSSD. In state 4F the mean FHR was higher with significant reduction in RMSSD.

Association of maternal position with heart rate variability

Maternal position was significantly associated with mean FHR and variability. During state 1F, FHR was higher when the mother was supine or semi-recumbent compared to the left lateral position (Table 4). The measures of variability (SDNN and RMSSD) were reduced in both the semi-recumbent and the supine positions compared to the left (Table 4). There was no difference in the measures of variability between left and right during state 1F, as shown in Table 4. In state 2F, the effects were not as notable, with a decrease in FHR in the right compared to left, and a decrease in SDNN when semi-recumbent compared to left.

Discussion

This study has shown that in healthy late gestation pregnancy, maternal position has a significant relationship with both fetal behavioural state as determined by features of FHR and its variability. Both the time the fetus spent in the particular state and the likelihood that a change of state would occur were significantly related to maternal position. In the supine and semi-recumbent positions, the fetus was more likely to be in state 1F and also more likely to change state.

State 1F is a condition of fetal quiescence. In the presence of a stressor such as reduced uteroplacental perfusion or hypoxia, a move to a low oxygen consuming state would be a protective reaction to an adverse stimulus. Doppler ultrasound studies in the human fetus late in the

Table 2. Univariable odds ratios (95% CI) associated with being in fetal state 1F and 4F compared to state 2F according to maternal position (left lateral position referent)

Position	Fetal state 1 vs. 2	Fetal state 4 vs. 2	State change
	$P = 0.0001$	$P = 0.033$	$P = 0.0005$
Left	ref	ref	ref
Right	2.36 (1.11, 5.04)	0.57 (0.19, 1.71)	0.96 (0.49, 1.85)
Semi-recumbent	1.60 (0.74, 3.46)	0.11 (0.02, 0.55)	2.17 (1.19, 3.95)
Supine	4.99 (2.41, 10.43)	0.27 (0.07, 1.10)	2.67 (1.46, 4.85)

Figures in bold show significant differences from referent position.

Table 3. Differences in measures of FHR according to fetal state

Fetal state	FHR	SDNN	RMSSD
	$P < 0.0001$	$P < 0.0001$	$P < 0.0001$
1F (OR, 95% CI)	-6 (-4, -7)	-8.1 (-9.7, -6.4)	-1.8 (-1.2, -2.3)
2F	Mean = 139 (SEM = 0.35)	Mean = 23.0 (SEM = 0.40)	Mean = 9.9 (SEM = 0.14)
4F (OR, 95% CI)	13 (10, 16)	-2.9 (-5.1, 1.2)	-2.8 (-1.7, -3.9)

Figures in bold show significant differences from referent position.

Table 4. Differences in measures of HRV by position for states 1F and 2F

	FHR	SDNN	RMSSD
State 1F ($n = 109$)	$P = 0.013$	$P = 0.0005$	$P = 0.14$
Left	Mean = 128.2 (SEM = 2.0)	Mean = 19.9 (SEM = 2.0)	Mean = 9.5 (SEM = 0.6)
Right (OR, 95% CI)	2.8 (-2.0, 7.6)	-1.8 (-6.6, 3.1)	-1.3 (-2.9, 0.2)
Semi-recumbent (OR, 95% CI)	7.4 (2.4, 12.4)	-5.7 (-10.8, -0.7)	-1.7 (-3.3, -0.1)
Supine (OR, 95% CI)	5.6 (1.1, 10.1)	-7.9 (-12.5, -3.4)	-1.6 (-3.1, -0.2)
State 2F ($n = 375$)	$P = 0.014$	$P = 0.07$	$P = 0.25$
Left	Mean = 139 (SEM = 0.67)	mean = 24.3 (SEM = 0.78)	mean = 9.62 (SEM = 0.3)
Right (OR, 95% CI)	-2.3 (-4.2, -0.5)	-0.3 (-2.5, 1.9)	0.7 (-0.1, 1.5)
Semi-recumbent (OR, 95% CI)	0.0 (-1.7, 1.8)	-2.3 (-4.4, -0.3)	-0.0 (-0.8, 0.8)
Supine (OR, 95% CI)	0.5 (-1.4, 2.4)	-2.0 (-4.2, 0.2)	0.3 (-0.5, 1.2)

Figures in bold show significant differences from referent position.

third trimester show significantly lower resistive indices in the internal carotid artery (decreased cerebral vascular resistance) when the fetus is in state 2F as compared to 1F, suggesting increased cerebral blood flow in 2F (van Eyck *et al.* 1987; Connors *et al.* 1991). Non-reactive non-stress testing or prolonged periods in 1F are fetal responses to hypoxia. In the normal mature fetus, state 1F has a reported mean duration of 20 min with a range up to 38 min (Pillai & James, 1990a). The frequency of the state changes seen in this study appear to exceed that found in observational studies where the mother maintained a constant semi-recumbent position (Pillai & James, 1990a), further suggesting that maternal position and the position change had an effect on FBS and was a stressor.

Heart rate variability is a measure of cardiac autonomic control and in the fetus it is made up of sympathetic

and parasympathetic nervous system activity as well as intrinsic pacemaker rhythms of the sino-atrial node (Jensen *et al.* 2009; Papaioannou *et al.* 2013; Koome *et al.* 2014). In addition, there is some evidence that there are also non-neural influences such as fetal body and breathing movements (Visser *et al.* 1982; Dalton *et al.* 1983). Sympathetic activity is important in the maintenance of fetal blood pressure, for example during repeated asphyxia (Galinsky *et al.* 2014; Lear *et al.* 2016). In this study both RMSSD and SDNN were decreased in the supine and semi-recumbent positions. This is highly likely to reflect the concomitant changes in FBS with the increased risk of being in state 1F. State 1F is associated with reduced fetal body movements, a key contributor to FHRV, while preclinical evidence strongly supports that changes in FBS are also associated with marked changes

in autonomic activity (Schneider *et al.* 2008; Gustafson *et al.* 2012). Although decreased FHRV is accepted to predict fetal distress, decreased FHRV in the present study is unlikely to reflect the direct effect of the stressors associated with maternal supine and semi-recumbent position. Acute hypoxia, in contrast, is associated with an increase in FHRV in both fetal sheep (Parer, 1980) and humans (Thaler *et al.* 1985) while more severe asphyxia is also associated with an initial increase in FHRV in fetal sheep (Westgate *et al.* 1999). Reduced uterine blood flow after fluoxetine infusion in an ovine model was found to cause transient, mild fetal hypoxaemia and acidosis for 12 h, which were associated with a small increase in FHR (Morrison *et al.* 2002) although measures of HRV were not reported. The findings were consistent with the sustained adaptation to longer periods of mild to moderate hypoxia. In our study, we did not observe FHR decelerations, suggesting that the observed changes in FBS and FHRV were not due to acute moderate to severe hypoxia but rather a much milder change in fetal oxygen tension, sufficient to trigger a change in fetal sleep state to a lower oxygen consuming state, but not the autonomic adaptive responses. In a study of women with pre-eclampsia, markedly reduced fetal movements were associated with episodes of haemoglobin desaturation in sleep. Treatment with overnight continuous positive airways pressure improved fetal movements (Blyton *et al.* 2013), which lends support to the concept that the fetus adapts to hypoxia by switching to a low oxygen consumption state.

The explanations for our findings are speculative. No women in the study reported symptoms suggestive of supine hypotension while they were supine or semi-recumbent. Continuous maternal brachial arterial blood pressure recording was undertaken and no hypotensive episodes were detected. In addition, there were no clinically nor statistically significant differences in maternal pulse rate between the four positions (data not shown). Notwithstanding that, there is evidence that the supine position can alter uterine blood flow in the third trimester of pregnancy (Jeffreys *et al.* 2006), although in that study fetal responses were not recorded. Studies of the effects of tilt positions in late pregnancy have shown reductions in leg blood flow on changing from the left lateral to supine positions, but without effects on Doppler measures of uterine arterial resistance or changes in fetal Doppler or heart rate (Kinsella *et al.* 1990). A recent study of ten singleton pregnant women using magnetic resonance imaging to investigate aortocaval compression did not confirm aortic but only caval compression, which was relieved by 30 deg but not 15 deg tilt (Higuchi *et al.* 2015), suggesting that arterial blood flow may not be reduced by the supine position, at least in healthy non-obese subjects. However, in a smaller study than ours, it has been suggested that the supine position in late

pregnancy was associated with changes to the fetal middle cerebral arterial and umbilical arterial Doppler pulsatility indices, suggesting a fetal response to the physiological stress of position change (Khatib *et al.* 2014). There do not appear to have been studies demonstrating changes in FBS with maternal position.

In addition to the consideration of blood flow changes with maternal position, body position may affect oxygenation. Changes in maternal P_{aO_2} have been found when a subject in late pregnancy is changed from a supine to a sitting position (Spiropoulos *et al.* 2004), although fetal parameters were not assessed in that study.

The strengths of our study include the standardisation of experimental conditions within a realistic clinical environment and the blinding of the data and analysis. Outcome data on all women (not shown) confirmed that all pregnancies were delivered at term without maternal or fetal complications and all neonates were normal. The benefit of using a crossover method meant each mother and fetus acted as its own control, increasing the power of the study. We controlled for external factors known to affect FBS such as gestation, time of day, exercise, caffeine intake and time from last meal. Other strengths of this study were the small amount of data loss and that the same investigators performed the studies on every woman.

Limitations included the difficulties in studying maternal haemodynamic parameters non-invasively, and some signal loss from the Monica AN24 device. However, we and others have found long-term recordings generally are feasible with good quality signals (Graatsma *et al.* 2009), including in the obese subject (Cohen & Hayes-Gill, 2014). The definition of fetal sleep states in the study was based on analysis of FHR patterns. Whilst such an approach enabled us to distinguish clearly the heart rate patterns attributed to states 1F, 2F and 4F, short periods of indeterminate patterns were not included in the analysis.

We could also not control for maternal discomfort or need for bathroom breaks. If a woman requested, she was allowed to stop between (but not during) positions and get up before returning and carrying on with the next position. It was not possible to estimate the effect that this might have on the experimental paradigm and FBS.

This study demonstrates that maternal position affects the state in which the fetus is in and that FBS changes occur with maternal position change. During this study where the women were awake, the fetus was most active when the woman lay on the left side. State 4F occurred infrequently when the woman was supine or semi-recumbent. State 1F – fetal quiescence – was more commonly seen in the supine position. Changes in FHRV were also seen that were consistent with the changes in FBS. Should the supine position indeed be a physiological stressor, these findings strongly suggest that healthy fetuses make adaptive responses into states which use less oxygen.

Conclusions

In this controlled experiment in normal healthy late third trimester pregnancy, maternal position was significantly associated with FBS and FHRV. Maternal supine position reduced the time the fetus spent in active 4F with a switch to quiet sleep state (1F). These findings are consistent with the concept that state changes occur as an adaptive response and shift the fetus to a lower oxygen consuming state. The supine position may be disadvantageous for fetal wellbeing and in compromised pregnancies may be a sufficient stressor to contribute to fetal demise.

References

- Arduini D, Rizzo G, Giorlandino C, Valensise H, Dell'Acqua S & Romani C (1986). The development of fetal behavioural states: a longitudinal study. *Prenat Diagn* **6**, 117–124.
- Arduini D, Rizzo G, Caforio L, Boccolini MR, Romanini C & Mancuso S (1989). Behavioural state transitions in healthy and growth retarded fetuses. *Early Hum Dev* **19**, 155–165.
- Blyton DM, Skilton MR, Edwards N, Hennessy A, Celermajer DS & Sullivan CE (2013). Treatment of sleep disordered breathing reverses low fetal activity levels in preeclampsia. *Sleep* **36**, 15–21.
- Bocking AD & Harding R (1986). Effects of reduced uterine blood flow on electrocortical activity, breathing and skeletal muscle activity in fetal sheep. *Am J Obstet Gynecol* **154**, 655–662.
- Bocking A (2003). Assessment of fetal heart rate and fetal movements in detecting oxygen deprivation in-utero. *Eur J Obstet Gynecol Reprod Biol* **110**, S108–S112.
- Boddy K, Dawes GS, Fisher R, *et al.* (1974). Foetal respiratory movements, electrocortical activity and cardiovascular responses to hypoxaemia and hypercapnia in sheep. *J Physiol* **243**, 599–618.
- Brändle J, Preissl H, Draganova R, Ortiz E, Kagan KO, Abele H, Brucker SY & Kiefer-Schmidt I (2015). Heart rate variability parameters and fetal movement complement fetal behavioural states detection via magnetography to monitor Neurovegetative development. *Front Hum Neurosci* **9**, 147.
- Cohen WR & Hayes-Gill B (2014). Influence of maternal body mass index on accuracy and reliability of external fetal monitoring techniques. *Acta Obstet Gynecol Scand* **93**, 590–595.
- Connors G, Gillis S, Hunse C, Gagnon R & Richardson B (1991). The interaction of behavioural state, heart rate and resistance index in the human fetus. *J Dev Physiol* **15**, 331–336.
- Dalton KJ, Dawes GS & Patrick JE (1983). The autonomic nervous system and fetal heart rate variability. *Am J Obstet Gynecol* **146**, 456–462.
- Dawes G, Meir YJ & Mandruzzato GP (1994). Computerized evaluation of fetal heart-rate patterns. *J Perinat Med* **22**, 491–499.
- Ebbing C, Rasmussen S & Kiserud T (2007). Middle cerebral artery blood flow velocities and pulsatility index and the cerebroplacental pulsatility ratio: longitudinal reference ranges and terms for serial measurements. *Ultrasound Obstet Gynecol* **30**, 287–296.
- Flenady V, Middleton P, Smith GC, Duke W, Erwich JJ, Khong TY, Neilson J, Ezzati M, Koopmans L, Ellwood D, Fretts R, Froen JF & for The Lancet's Stillbirth Series steering committee (2011). Stillbirths: the way forward in high-income countries. *Lancet* **377**, 1703–1717.
- Froen FF, Heazell AEP, Tviet JVH, Saastad E, Fretts RC & Flenady V (2008). Fetal movement assessment. *Semin Perinatol* **32**, 243–246.
- Galinsky R, Jensen EC, Bennet L, Mitchell CJ, Gunn ER, Wassink G, Fraser M, Westgate JA & Gunn AJ (2014). Sustained sympathetic nervous system support of arterial blood pressure during repeated brief umbilical cord occlusions in near-term fetal sheep. *Am J Physiol Regul Integr Comp Physiol* **306**, R787–R795.
- Gordon A, Raynes-Greenow C, Bond D, Morris J, Rawlinson W & Jeffery H (2015). Sleep position, fetal growth restriction, and late-pregnancy stillbirth: the Sydney stillbirth study. *Obstet Gynecol* **125**, 347–355.
- Graatsma E, Jacod B, van Egmond L, Mulder E & Visser G (2009). Fetal electrocardiography: feasibility of long-term fetal heart rate recordings. *BJOG* **116**, 334–338.
- Gustafson KM, May LE, Yeh HW, Million SK & Allen JJ (2012). Fetal cardiac autonomic control during breathing and non-breathing epochs: the effect of maternal exercise. *Early Hum Dev* **88**, 539–546.
- Higuchi H, Takagi S, Zhang K, Furui I & Ozaki M (2015). Effect of lateral tilt angle on the volume of the abdominal aorta and inferior vena cava in pregnant and nonpregnant women determined by magnetic resonance imaging. *Anaesthesiology* **122**, 286–293.
- Jeffreys R, Stepanchak W, Lopez B, Hardis J & Clapp III J (2006). Uterine blood flow during rest and exercise after 28 weeks of gestation. *BJOG* **113**, 1239–1247.
- Jensen EC, Bennet L, Guild SJ, Booth LC, Stewart J & Gunn AJ (2009). The role of the neural sympathetic and parasympathetic systems in diurnal and sleep state related cardiovascular rhythms in the late gestation ovine fetus. *Am J Physiol Regul Integr Comp Physiol* **297**, R998–R1008.
- Khatib N, Weiner Z, Beloosesky R, Vitner D & Thaler I (2014). The effect of maternal supine position on umbilical and cerebral blood flow indices. *Eur J Obstet Gynecol Reprod Biol* **175**, 112–114.
- Kinsella SM, Lee A & Spencer JA (1990). Maternal and fetal effects of the supine and pelvic tilt positions in late pregnancy. *Eur J Obstet Gynecol Reprod Biol* **36**, 11–17.
- Koome ME, Bennet L, Booth LC, Davidson JO, Wassink G & Gunn AJ (2014). Ontogeny and control of the heart rate power spectrum in the last third of gestation in fetal sheep. *Exp Physiol* **99**, 80–88.
- Krasnegor NA, Fifer W, Maulik D, McNellis D, Romero R & Smotherman W (1998). Fetal behavioural development: measurement of habituation, state transitions, and movement to assess fetal well being and to predict outcome. *J Matern Fetal Investig* **8**, 51–57.

- Lear CA, Galinsky R, Wassink G, Mitchell CJ, Davidson JO, Westgate JA, Bennet L & Gunn AJ (2016). Sympathetic neural activation does not mediate heart rate variability during repeated brief umbilical cord occlusions in near-term fetal sheep. *J Physiol* **594**, 1265–1277.
- Martin CB (2008). Normal fetal physiology and behaviour, and adaptive responses with hypoxemia. *Semin Perinatol* **32**, 239–242.
- McCowan L, Stewart AW, Francis A & Gardosi J (2004). A customised birthweight centile calculator developed for a New Zealand population. *Aust N Z J Obstet Gynaecol* **44**, 428–431.
- Morrison JL, Chien C, Riggs KW, Gruber N & Rurak D (2002). Effect of maternal fluoxetine administration on uterine blood flow, fetal blood gas status, and growth. *Pediatr Res* **51**, 433–442.
- Mulder EHJ, Visser GHA, Bekedam DJ & Prechtl HF (1987). Emergence of behavioural states in the fetuses of type-1 diabetic women. *Early Hum Dev* **15**, 231–252.
- Narayan HK, Vignola EF, Fifer WP & Williams IA (2015). Assessment of cardiac rate and rhythm in fetuses with arrhythmia via maternal abdominal fetal electrocardiography. *Am J Perinatol Rep* **5**, e176–e182.
- Nijhuis JG, Prechtl HFR, Martin CB Jr & Bots RSGM (1982). Are there behavioural states in the human fetus? *Early Hum Dev* **6**, 177–195.
- Owusu JT, Anderson FJ, Coleman J, Oppong S, Seffah JD, Aikins A & O'Brien LM (2013). Association of maternal sleep practices with pre-eclampsia, low birth weight, and stillbirth among Ghanaian women. *Int J Gynaecol Obstet* **121**, 261–265.
- Papaioannou VE, Verkerk AO, Amin AS & de Bakker JM (2013). Intracardiac origin of heart rate variability, pacemaker funny current and their possible association with critical illness. *Curr Cardiol Rev* **9**, 82–96.
- Parer JT, Dijkstra HR, Vredereg PP, Harris JL, Krueger TR & Reuss ML (1980). Increased fetal heart rate variability with acute hypoxia in chronically instrumented sheep. *Eur J Obstet Gynecol Reprod* **10**, 393–399.
- Pillai M & James D (1990a). Behavioural states in normal mature human fetuses. *Arch Dis Child* **65**, 39–43.
- Pillai M & James D (1990b). The development of fetal heart rate patterns during normal pregnancy. *Obstet Gynecol* **76**, 812–816.
- Richardson BS, Patrick JE & Abduljabbar H (1985). Cerebral oxidative metabolism in fetal sheep: relationship to electrocortical activity state. *Am J Obstet Gynecol* **153**, 426–431.
- Romanini C & Rizzo G (1995). Fetal behaviour in normal and compromised fetuses. An overview. *Early Hum Dev* **43**, 117–131.
- Schneider U, Frank B, Fiedler A, Kaehler C, Hoyer D, Liehr M, Hauelsen J & Schleussner E (2008). Human fetal heart rate variability—characteristics of autonomic regulation in the third trimester of gestation. *J. Perinat Med* **36**, 433–441.
- Spiropoulos K, Prodromaki E & Tsapanos V (2004). Effect of body position on PaO₂ and PaCO₂ during pregnancy. *Gynecol Obstet Invest* **58**, 22–25.
- Stacey T, Thompson J, Mitchell EA, Ekeroma AJ, Zuccollo JM & McCowan LME (2011). Association between maternal sleep position and risk of late stillbirth: a case control study. *BMJ* **342**, d3403.
- Thaler I, Timor-Tritsch IE & Blumenfeld Z (1985). Effect of acute hypoxia on human fetal heart rate. The significance of increased heart rate variability. *Acta Obstet Gynecol Scand* **64**, 47–50.
- Timor-Tritsch IE, Dierker LJ, Hertz RH, Deagan C & Rosen MG (1978). Studies of antepartum behavioural states in the human fetus at term. *Am J Obstet Gynecol* **132**, 524–528.
- Van Eyck J, Wladimiroff JW, van den Wijngaard JA, Noordam MJ & Prechtl HF (1987). The blood flow velocity waveform in the internal carotid and umbilical artery; its relation to fetal behavioural states in normal pregnancy at 37–38 weeks. *Br J Obstet Gynaecol* **94**, 736–741.
- van Vliet MAT, Martin CB Jr, Nijhuis JG & Prechtl HF (1985). Behavioural states in growth-retarded human fetuses. *Early Hum Dev* **12**, 183–197.
- Visser GH, Goodman JD, Levine DH & Dawes GS (1982). Diurnal and other cyclic variations in human fetal heart rate near term. *Am J Obstet Gynecol* **142**, 535–544.
- Warland J & Mitchell EA (2014). A triple risk model for unexplained late stillbirth. *BMC Pregnancy Childbirth* **14**, 142.
- Westgate JA, Bennet L & Gunn AJ (1999). Fetal heart rate variability changes during brief repeated umbilical cord occlusion in near term fetal sheep. *Br J Obstet Gynaecol* **106**, 664–667.

Additional information

Competing interests

The authors declare no competing financial interests.

Author contributions

Fetal Behavioural State scoring was performed by PS and WB. Position sensing, initial analysis of FHR variability and conversion of FHR data to conventional CTG was carried out by JM. JT performed all the statistical analyses. AG, LB and CL contributed to analytical design. PS, JT and EM wrote the manuscript with input from all authors. All authors have approved the final version of the manuscript. All persons listed as authors qualify for authorship, and all those who qualify for authorship are listed. The Maternal Sleep in Pregnancy Research Group also includes: A.W. Stewart, A. Veale, S. Jones, K. Ellyett, L. McCowan, R. Cronin and S. Woodall.

Funding

This work was funded in part by Cure Kids and The University of Auckland. CL was supported by the Auckland Medical Research Foundation. AG and LB were supported by the Health Research Council of NZ. The New Zealand Respiratory and Sleep Institute and the Wilson Sweet Paediatric Fellowship supported J.M.

Translational perspective

Late stillbirth is independently related to the position women adopt during sleep. We hypothesised that fetal behavioural state as an indicator of fetal welfare would be affected by maternal position. We studied 29 healthy normal singleton pregnancies between 35 and 38 weeks of gestation and examined the effects of four maternal positions of fetal behavioural state, which was determined by blinded assessment of FHR patterns and ultrasound assessment of fetal activity. The results show that in normal healthy third trimester pregnancy, maternal position influences the behavioural state of the fetus. Changes were also seen in measures of FHRV, a marker of autonomic responsiveness. Compared with the left lateral position, there was almost a 5-fold risk of the fetus being in 1F when the mother was supine. It was also more than twice as likely that the fetus would change state (towards 1F) when the mother was supine. A switch to state 1F or fetal quiescence when the mother is supine suggests the fetus is adopting a low oxygen consuming state. The results offer insights into physiological mechanisms that the fetus may utilise to adapt to the effects of maternal position. We speculate that the findings may be due to reduced uterine perfusion and that vulnerable fetuses, which may already be hypoxic, are unable to adapt to the stressor of maternal supine position. Further research into the effects of maternal position overnight and in vulnerable fetuses is indicated.