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Influence of Physical Exercise on Baroreceptor Sensitivity during Pregnancy

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Abstract

Background: Baroreceptor sensitivity (BRS) refers to the magnitude of heart rate change in response to blood pressure change (e.g. upon standing). The impact of regular antenatal exercise on maternal BRS is unclear.

Aims: To determine whether supervised weekly exercise influences BRS, and to determine if posture and calculation method are important in antenatal BRS measurement.

Study design and subjects: Eighty-one healthy pregnant women were randomly assigned to an exercise or control group. The exercise group attended weekly classes from the 20th week of pregnancy onwards.

Outcome measures: Cardiovascular assessments (beat-to-beat blood pressure, heart rate) were performed at 12-16, 26-28, 34-36 weeks and 12 weeks following birth. BRS was calculated using two methods ('sequence' and 'beat-to-beat').

Results: Fifty-one women (63%) completed the study. Mean BRS reduced progressively in all women ($p < 0.025$) and was lowest in those who exercised ($0.046 < p < 0.002$). Postnatal increases in BRS were independent of posture. Training-induced BRS (beat-to-beat) reduction occurred earlier than BRS (sequence), and only BRS (sequence) was affected by posture. Heart rate variability reduced with advancing gestation ($p < 0.002$) and was more pronounced in the exercise group ($p < 0.029$).

Conclusions: Weekly exercise exaggerated the reductions in BRS and HRV during pregnancy and is likely linked to diminished parasympathetic activity.

1. Introduction

The term 'baroreceptor sensitivity' (BRS) refers to the change in cardiac interval that normally occurs in response to changes in blood pressure (as occur upon standing). Reduced BRS is associated with poor orthostatic tolerance [1]. Previous reports have conflicted regarding the influence of advancing gestation on maternal BRS: some have described a reduction of up to 50% by the end of pregnancy [2-4] whilst others have reported no change [5]. BRS can be enhanced by physical exercise in non-pregnant populations [6,7] but the influence of exercise conditioning on BRS in pregnancy is unclear. One previous study noted a decline in BRS during pregnancy in non-exercising women but no change in women who exercised, suggesting a possible 'maintenance' role of physical activity [8]. Blake et al. [2] found that posture influenced the trend in BRS: advancing gestation was associated with diminished BRS when supine but not when standing.

Two main confounders have likely hindered a consensus on the impact of antenatal exercise on BRS: previous studies have used neither standardised exercise programmes nor multiple postures during BRS assessment. We describe here an exercise training and assessment protocol that we believe is both explicit (and so is repeatable in other studies), rational (aligns with recommendations on antenatal exercise effort) and pragmatic (gives a realistic expectation of sustained engagement by women during pregnancy). The aim of this study was to determine the impact of our exercise programme on BRS during pregnancy, and in addition (1) to assess the influence of posture on repeated BRS measurement, and (2) to compare BRS calculated by both 'sequence' and 'beat-to-beat' methods.

2. Materials and Methods

2.1 Participants

Eligible participants were apparently healthy pregnant women aged 18 years or over, with no existing complications of pregnancy at their 12-week dating scan. Participants were recruited via the antenatal clinic (during the 12-week dating scan or by telephone) and via response to advertisements in local GP surgeries, sports centres and newspapers. Exclusion criteria were: a history of cardiovascular or chronic respiratory problems, sleep apnoea, or central/peripheral nervous system disorder. Potential participants were given details about

the study and were asked if they wished to take part one week later; those who did gave their written consent. Ethical approval was obtained from the local (South West Wales) Research Ethics Committee and all procedures were conducted in accordance with the Declaration of Helsinki. The trial was registered with ClinicalTrials.gov (registration number NCT02503995).

2.2 Study design

Participants were assigned to either an Exercise or Control group (no formal exercise programme). Ethical requirements meant that we could not randomly assign group membership before asking potential participants if they had a group preference – if they had no preference then random assignment occurred.

2.3 Exercise programmes

Participants assigned to the exercise group started an exercise programme at 20-weeks' gestation and attended weekly classes until full-term or until they felt they could no longer undertake physical activity. All exercise classes were led or supervised by a qualified midwife. Exercise classes comprised of eighteen minutes of recumbent cycling, ten minutes of stretching and toning exercises and fifteen minutes of pelvic floor exercises. The recumbent cycling exercise (V-Fit BST-RC Recumbent magnetic cycle, Beny Sports Co. UK Ltd., West Yorkshire, UK) consisted of a 3-minute warm-up (with no resistance on the bike) followed by 15-minutes of continuous cycling. Exercise workload was increased by one 'level' on the bike every two minutes, until the participant reached the heart rate target zones for aerobic exercise during pregnancy suggested by the Royal College of Obstetrics and Gynaecology [9].

2.4 Physiological measurements

Physiological monitoring was carried out on four occasions: at 12-16, 24 -26 and 34-36 weeks gestational age, corresponding to end of the three trimesters (T1, T2, T3) and also at 12-weeks post-partum (PP). All participants were asked to perform a series of postural manoeuvres and various interventions designed to provoke changes in the cardiovascular and autonomic nervous systems. Participants were asked to refrain from drinking tea, coffee, alcohol or a heavy meal within 2 hours prior to assessment and to not exercise within 24 hours prior to assessment. Participants also completed a Pregnancy Physical

Activity Questionnaire (PPAQ) [10] during each of the three antenatal measurement sessions to monitor changes in physical fitness as pregnancy progressed.

2.4.1 Physiological variables quantified: As part of a larger protocol involving postural manoeuvres and exercise, participants were first asked to lie in a 45° reclined-supine position for six minutes, and then to stand for six minutes. Participants underwent continuous Holter ECG monitoring (Pathfinder/Lifecard Digital system; Spacelabs Medical Ltd., UK), providing ECG data with a 1024 Hz sampling frequency. The ECG recordings were assessed for quality by human observation using the Pathfinder system, primarily to verify the absence of excessive noise or artefact. Beat-to-beat cardiac interval (RR) was measured automatically by the Pathfinder system. HRV was quantified using RMSSD (square root of the mean squared differences in successive RR intervals) and HF_n (normalised high-frequency component), both of which are measures of parasympathetic activity. Beat-to-beat systolic blood pressure (SBP) was measured via vascular unloading photoplethysmography (Task Force Haemodynamic monitor, CNSystems Medizintechnik GMBH, Austria). RR and BP data were subsequently used to calculate BRS, whilst RMSSD and HF_n allowed us to explore possible co-variables of BRS (and thus potential mechanisms of antenatal BRS influence).

2.5 BRS calculations

We calculated BRS during the supine and standing states (to quantify the supine-to-standing response) using two methods:

1. The 'sequence method': sequences of three or more consecutive beats during which systolic BP and RR interval either both increased ('UP events') or both decreased ('DOWN events') were identified by the Task Force monitor and BRS values (BRS_{SEQUP} and $BRS_{SEQDOWN}$) were calculated from linear RR-BP regression models). Similarly, the mean BRS ($BRS_{SEQMEAN}$) was calculated using the combined set of UP/DOWN sequence events). Values were quantified separately for the six-minute Supine and Standing stages;
2. Beat-to-beat BRS: BRS was calculated as the ratio of beat-to-beat changes in RR interval and systolic blood pressure ($BRS = \Delta RR / \Delta SBP$). Using similar definitions as

discussed above, UP, DOWN and mean BRS were calculated for the supine and standing phases (and denoted as BRS_{BTBUP} , $BRS_{BTBDOWN}$, and $BRS_{BTBMEAN}$). The between-state change in BRS was also calculated by subtracting supine values from standing values. We defined our analysis data set as the array of twenty beat-to-beat data points on either side of the point of transition to the standing posture (20 points at the end of the Supine stage and the first 20 points at the start of the Standing stage). A threshold of $\pm 100 \text{ ms}\cdot\text{mmHg}^{-1}$ was applied to the data to remove values that were outside the physiologically accepted BRS range [11].

We quantified BRS using a BP-RR 'lag' of one cardiac cycle ('Lag 1', i.e. the RR value used in the calculation was delayed by one cardiac cycle relative to the BP value). Lag 1 was considered to be the most physiologically appropriate choice of lag as it corresponds most closely to the latency in the baroreflex response (in a steady-state, the baroreflex can elicit a reflex cardiac change 800ms following stimulation of the carotid baroreceptors [12,13]) .

2.6 Statistical analysis

Data from the water-based exercise class was excluded from the statistical analysis due to small numbers in this group. 'Exercise group' refers to participants who took part in the land exercise. Normality of the data was assessed using the Kolmogorov-Smirnof test. Repeated measures ANOVA with main factors 'Pregnancy Stage' (repeated measure) and 'Exercise Group' (between-group measure) was used to assess the influence of exercise and gestation on the measured physiological variables (separately for Supine, Standing and Supine-Standing values). Mauchly's test was consulted to assess the Sphericity of the data; if the assumption of Sphericity was violated then Wilks' Lambda multivariate tests were used. Post-hoc analysis was carried out with Bonferroni correction to identify the locations of significant difference effects as appropriate. Independent samples t-tests were used to assess between-group differences at each of the measurement points. Statistical significance was accepted as $p < 0.05$. Effect sizes were quantified as partial eta squared (η^2). All data are presented as Mean \pm SEM (standard error of the mean) and all error bars in the figures represent SEM.

3. Results

3.1 Participant Characteristics

Eighty-one pregnant women were recruited into the study and allocated to Control or Exercise groups. Sixteen out of thirty-three women (49%) in the Exercise group completed the study (attended the complete exercise programme and all four assessments), whilst thirty-five women in the Control group (61%) completed the study. These fifty-one participants attended the clinic for physiological assessment at mean gestational ages of 15.1 ± 1.9 weeks, 25.5 ± 1.2 , 34.6 ± 1.4 weeks and post-natally at 13.4 ± 1.7 weeks. Participants were physically active but were not athletes and had not engaged in any substantive pre-pregnancy exercise training. Participant characteristics and pregnancy outcomes are shown in Table 1.

Table 1. Participant characteristics and pregnancy outcomes

| | Control (n=35) | | Exercise (n=16) | |
|---------------------------------------------------------------------|----------------|-------------|-----------------|-------------|
| | n | % | n | % |
| Maternal Age at Initial Measurement (Years) | | | | |
| 19-24 | 2 | 5.7 | 3 | 18.8 |
| 25-29 | 12 | 34.3 | 4 | 25.0 |
| 30-34 | 16 | 45.7 | 6 | 37.5 |
| 35-39 | 5 | 14.3 | 2 | 12.5 |
| 40+ | 0 | 0 | 1 | 6.3 |
| BMI at Initial Measurement (kg·m⁻²) | | | | |
| 18.5-24.9 | 23 | 65.7 | 8 | 50 |
| 25.0-29.9 | 6 | 17.1 | 2 | 12.5 |
| >30 | 6 | 17.1 | 6 | 37.5 |
| BMI at 34 weeks (kg·m⁻²) | | | | |
| 18.5-24.9 | 9 | 25.7 | 3 | 18.8 |
| 25.0-29.9 | 14 | 40.0 | 6 | 37.5 |
| >30 | 12 | 34.3 | 7 | 43.8 |
| Parity | | | | |
| Nulliparous | 19 | 54.3 | 10 | 62.5 |
| Primi/Multiparous | 16 | 45.7 | 6 | 37.5 |
| Smoking Status | | | | |
| Previous (Prior to pregnancy) | 8 | 22.9 | 8 | 50.0 |
| Current | 3 | 8.6 | 1 | 6.3 |
| Method of Delivery | | | | |
| Vaginal | 28 | 80 | 11 | 68.8 |
| Caesarean Section | 7 | 20 | 5 | 31.2 |
| Delivery Time (hours:min)¹ | | | | |
| | 4:42 | 0:27-21:15 | 4:27 | 1:05-15:48 |
| Birth Weight (g) | | | | |
| | 3500 | 2620-4820 | 3470 | 2780-4340 |
| Initial Fitness Status² (MET·h·week⁻¹) | | | | |
| Total Activity | 313.2 | 284.3-449.0 | 177.0 | 113.9-590.9 |

¹ Vaginal delivery group only

² Questionnaire completed by a subset of participants (Control, n=5; Exercise, n=14)

3.2 Cardiovascular profiles

Table 2 shows the values for each of the cardiovascular variables during the supine and standing postures, as well as the corresponding standing-supine change (Δ) values.

Table 2. Heart rate variability and haemodynamic variables (Mean \pm SEM) for control and exercise groups.

(* Significantly different from control values at the same time point)

| Variable | Control | | | | Exercise | | | |
|----------------------------------------------|------------------|------------------|------------------|------------------|------------------|------------------|------------------|------------------|
| | T1 | T2 | T3 | PP | T1 | T2 | T3 | PP |
| Supine | | | | | | | | |
| RMSSD (ms) | 31.5 \pm 2.7 | 21.7 \pm 1.8 | 22.8 \pm 2.7 | 45.3 \pm 5.4 | 26.3 \pm 2.9 | 21.9 \pm 2.9 | 14.4 \pm 1.8* | 42.8 \pm 2.8 |
| HF _n | 0.39 \pm 0.01 | 0.34 \pm 0.01 | 0.35 \pm 0.01 | 0.36 \pm 0.01 | 0.35 \pm 0.01 | 0.34 \pm 0.02 | 0.29 \pm 0.01* | 0.36 \pm 0.01 |
| HR (bpm) | 80.9 \pm 1.5 | 87.3 \pm 1.8 | 89.1 \pm 1.7 | 74.7 \pm 1.7 | 83.0 \pm 3.1 | 86.6 \pm 2.4 | 94.6 \pm 2.5 | 71.2 \pm 2.3 |
| SBP (mmHg) | 109.0 \pm 1.7 | 108.1 \pm 1.6 | 109.6 \pm 1.2 | 108.5 \pm 1.6 | 105.8 \pm 1.9 | 105.1 \pm 1.9 | 111.0 \pm 2.4 | 105.4 \pm 2.8 |
| Standing | | | | | | | | |
| RMSSD (ms) | 24.0 \pm 2.3 | 20.1 \pm 1.5 | 20.6 \pm 2.0 | 28.3 \pm 2.3 | 21.6 \pm 1.9 | 19.5 \pm 2.2 | 15.7 \pm 1.5 | 31.5 \pm 3.6 |
| HF _n | 0.33 \pm 0.01 | 0.33 \pm 0.01 | 0.32 \pm 0.01 | 0.30 \pm 0.01 | 0.31 \pm 0.01 | 0.29 \pm 0.01* | 0.29 \pm 0.04* | 0.31 \pm 0.01 |
| HR (bpm) | 92.9 \pm 1.7 | 97.0 \pm 2.0 | 98.4 \pm 1.6 | 87.4 \pm 1.8 | 93.0 \pm 3.5 | 94.8 \pm 2.9 | 100.9 \pm 2.6 | 82.9 \pm 2.5 |
| SBP (mmHg) | 114.1 \pm 2.9 | 114.8 \pm 3.0 | 115.0 \pm 1.9 | 112.9 \pm 1.9 | 111.0 \pm 2.3 | 109.3 \pm 2.6 | 118.3 \pm 2.9 | 109.4 \pm 3.0 |
| Supine-Standing (Δ) | | | | | | | | |
| RMSSD (ms) | -7.5 \pm 1.8 | -1.6 \pm 1.0 | -2.2 \pm 1.7 | -17.1 \pm 3.9 | -4.6 \pm 1.9 | -2.3 \pm 1.4 | 1.2 \pm 1.5 | -11.4 \pm 2.7 |
| HF _n | -0.06 \pm 0.01 | -0.02 \pm 0.01 | -0.03 \pm 0.01 | -0.06 \pm 0.01 | -0.04 \pm 0.02 | -0.05 \pm 0.02 | 0.00 \pm 0.01 | -0.05 \pm 0.02 |
| HR (bpm) | 12.1 \pm 1.0 | 9.7 \pm 1.1 | 9.3 \pm 1.0 | 12.7 \pm 1.0 | 10.0 \pm 1.3 | 8.2 \pm 1.1 | 6.3 \pm 1.5 | 11.7 \pm 1.0 |
| SBP (mmHg) | 5.1 \pm 1.8 | 6.7 \pm 1.9 | 5.4 \pm 1.4 | 4.4 \pm 1.5 | 5.2 \pm 1.2 | 4.2 \pm 2.3 | 7.3 \pm 1.9 | 4.0 \pm 3.1 |

Repeated measures ANOVA indicated a significant interaction effect between main factors Pregnancy Stage and Exercise Group for HR ($p < 0.01$), RMSSD ($p < 0.04$) and HF_n ($p < 0.01$) in the supine state only (i.e. the trend in these variables with advancing gestation was group-dependent). Exercise Group did not influence any of the measured variables, whilst each of the measured variables (except BP) was dependent on Pregnancy Stage (all $p < 0.0005$). Significant pairwise (between-stage) and Group differences are noted in Table 3.

Table 3. Influence of gestation and exercise on HRV and BP

| Variable | Change with advancing gestation? | Antenatal/Postpartum change? | Exercise influence? |
|----------|----------------------------------------------|-------------------------------------------|---------------------|
| HR | \uparrow $p < 0.002$ (Supine and Standing) | \downarrow $p < 0.0005$ (Standing only) | No |

| | | | |
|--------------|--------------------------------------------------|---------------------------------------------------|-------------------------------------------------------|
| | ↓ p<0.032 (Δ) | ↑ p<0.003 (Δ) | |
| RMSSD | ↓ p<0.002 (Supine and Standing) ↓ p=0.004 (Δ) | ↑ p<0.0005 (Supine and Standing) ↑ p<0.048 (Δ) | ↓ p=0.029 (SUP, T3) |
| HFn | ↓ p<0.0005 (Supine only) | ↑ p<0.006 (Supine only) | ↓ p=0.002 (Supine, T3) ↓ p<0.032 (Standing, T2,T3) |
| BP | No | No | No |

3.3 Baroreceptor Sensitivity

Table 4 shows the values for each of the BRS variables during the supine and standing postures as well as the standing-supine change (Δ) values.

Table 4. Baroreceptor Sensitivity for each gestational stage, using the Sequence Method and the Beat-to-Beat Method of analysis. Data are presented as Mean ± SEM. (* Significant difference between control and exercise groups, p<0.05)

| BRS_{SEQ} (ms·mmHg ⁻¹) | Supine | | | Standing | | | Δ Supine - Standing | | |
|------------------------------------------------------|---------------|------------|-------------|-----------------|------------|-------------|----------------------------|------------|-------------|
| | Mean | Up | Down | Mean | Up | Down | Mean | Up | Down |
| Control | | | | | | | | | |
| T1 | 11.6 ± 1.0 | 11.2 ± 1.1 | 10.9 ± 1.0 | 8.5 ± 0.7 | 8.6 ± 0.8 | 7.5 ± 0.7 | -3.1 ± 0.8 | -2.6 ± 1.4 | -3.3 ± 0.7 |
| T2 | 10.4 ± 0.7 | 10.5 ± 0.8 | 9.5 ± 0.8 | 7.6 ± 0.7 | 7.9 ± 0.8 | 7.2 ± 1.2 | -2.8 ± 0.8 | -2.6 ± 0.9 | -2.4 ± 1.2 |
| T3 | 10.7 ± 1.4 | 11.6 ± 1.7 | 9.5 ± 0.8 | 9.0 ± 1.2 | 10.6 ± 1.4 | 5.9 ± 0.9 | -1.8 ± 1.1 | -1.1 ± 1.7 | -3.6 ± 0.6 |
| PP | 14.8 ± 1.4 | 14.8 ± 1.6 | 13.9 ± 1.2 | 9.1 ± 0.8 | 10.1 ± 1.0 | 7.5 ± 0.8 | -5.7 ± 1.0 | -4.7 ± 1.3 | -6.4 ± 0.9 |
| Exercise | | | | | | | | | |
| T1 | 9.6 ± 1.1 | 10.1 ± 1.3 | 8.0 ± 1.1 | 7.7 ± 0.8 | 9.1 ± 1.2 | 6.0 ± 0.6 | -1.9 ± 0.7 | -1.0 ± 1.0 | -2.0 ± 1.0 |
| T2 | 9.6 ± 1.0 | 10.0 ± 1.1 | 8.7 ± 1.0 | 6.8 ± 0.6 | 7.2 ± 0.7 | 6.1 ± 0.8 | -2.8 ± 0.8 | -2.8 ± 1.0 | -2.6 ± 1.1 |
| T3 | 6.1 ± 0.8* | 6.2 ± 0.8* | 6.0 ± 1.0* | 6.6 ± 1.2 | 7.1 ± 1.6 | 4.5 ± 0.9 | 0.5 ± 1.0 | 0.9 ± 1.5 | -1.5 ± 0.6 |
| PP | 14.1 ± 0.9 | 14.5 ± 1.1 | 13.5 ± 1.2 | 8.2 ± 0.7 | 8.5 ± 0.9 | 7.7 ± 0.9 | -5.9 ± 1.3 | -6.0 ± 1.5 | -5.9 ± 1.5 |
| BRS_{BTB} (ms·mmHg ⁻¹) | | | | | | | | | |
| | Mean | Up | Down | Mean | Up | Down | Mean | Up | Down |
| Control | | | | | | | | | |
| T1 | 20.3 ± 1.5 | 20.4 ± 1.4 | 20.8 ± 2.4 | 11.4 ± 1.3 | 11.0 ± 1.7 | 12.2 ± 1.5 | -9.0 ± 1.4 | -9.4 ± 1.7 | -8.6 ± 2.2 |
| T2 | 17.6 ± 1.3 | 18.2 ± 1.5 | 17.7 ± 1.6 | 9.6 ± 0.9 | 9.6 ± 1.2 | 9.2 ± 1.1 | -8.0 ± 1.3 | -8.6 ± 1.8 | -8.5 ± 1.6 |
| T3 | 17.0 ± 1.3 | 17.1 ± 1.5 | 17.0 ± 1.6 | 9.8 ± 1.1 | 10.6 ± 1.6 | 8.7 ± 1.1 | -7.1 ± 1.4 | -6.5 ± 1.8 | -8.3 ± 1.8 |
| PP | 18.7 ± 1.9 | 19.5 ± 1.4 | 17.3 ± 1.4 | 11.3 ± 0.9 | 11.4 ± 1.4 | 11.0 ± 1.2 | -7.4 ± 1.2 | -8.1 ± 1.6 | -6.3 ± 1.6 |
| Exercise | | | | | | | | | |
| T1 | 19.0 ± 1.4 | 16.7 ± 1.8 | 21.0 ± 2.4 | 7.1 ± 0.8 | 8.3 ± 0.9 | 6.3 ± 1.2 | -11.9 ± 1.3 | 8.4 ± 1.9 | -14.7 ± 2.0 |
| T2 | 13.5 ± 1.3 | 15.4 ± 2.4 | 13.0 ± 1.5* | 5.6 ± 0.8* | 6.4 ± 1.1 | 4.9 ± 0.7* | -7.8 ± 1.5 | 9.0 ± 2.2 | -8.1 ± 1.8 |
| T3 | 13.0 ± 1.6 | 13.4 ± 2.3 | 12.3 ± 1.1* | 6.6 ± 0.9 | 7.5 ± 1.3 | 5.5 ± 0.9* | -6.5 ± 1.8 | 5.9 ± 2.6 | -6.8 ± 1.2 |
| PP | 20.9 ± 1.6 | 20.2 ± 1.8 | 21.6 ± 2.2 | 13.1 ± 2.6 | 15.8 ± 3.7 | 9.8 ± 2.1 | -7.7 ± 3.3 | 4.3 ± 4.7 | -11.8 ± 2.8 |

ANOVA indicated that there was a significant interaction effect between Pregnancy Stage and Exercise Group (p<0.007) for BRS_{SEQM} and BRS_{SEQUIP} in the supine state (i.e. the trend in

these variables with advancing gestation was group-dependent). On average (across all stages of pregnancy) Exercise Group did not influence any of the measured variables. Pregnancy Stage influenced both the Supine ($p < 0.0005$) and Δ ($0.0005 < p < 0.037$) values of BRS_{SEQ} but influenced the Standing values of only $BRS_{SEQDOWN}$. Significant pairwise (between-stage) and Group differences are noted in Table 5.

Table 5. Influence of gestation and exercise on BRS

| Variable | Change with advancing gestation? | Antenatal/Postpartum change? | Exercise influence? |
|-----------------|----------------------------------|-----------------------------------------------------|--------------------------------------------------------------------|
| $BRS_{SEQMEAN}$ | ↓ $p < 0.014$ (Supine only) | ↑ $p < 0.001$ (Supine) ↑ $p < 0.02$ (Δ) | ↓ $p = 0.006$ (Supine only, T3) |
| BRS_{SEQUP} | No | No | ↓ $p = 0.002$ (Supine only, T3) |
| $BRS_{SEQDOWN}$ | No | No | ↓ $p = 0.034$ (Supine only, T3) |
| $BRS_{BTBMEAN}$ | ↓ $p < 0.025$ (Supine only) | ↑ $p < 0.019$ (Supine) ↑ $p < 0.03$ (Standing) | ↓ $p = 0.004$ (Standing only, T2) |
| BRS_{BTBUP} | No | No | No |
| $BRS_{BTBDOWN}$ | No | No | ↓ $p < 0.032$ (Supine, T2, T3) ↓ $p < 0.046$ (Standing, T2, T3) |

ANOVA indicated that there was a significant interaction effect between Pregnancy Stage and Exercise Group only for $BRS_{BTBDOWN}$ in the Supine state ($p = 0.022$). On average (across all stages of pregnancy) Exercise Group influenced $BRS_{BTBMEAN}$ and $BRS_{BTBDOWN}$ during Standing ($p < 0.001$). Pregnancy Stage influenced the Supine ($0.0005 < p < 0.031$) and Standing ($0.001 < p < 0.037$) values of each BRS_{BTB} measure but did not influence Δ values. Significant pairwise (between-stage) and Group differences are noted in Table 5.

4. Discussion

Baroreceptor sensitivity was diminished during mid-to-late pregnancy in all women, but this was true only for mean BRS and only when measured during the supine posture. Postnatal increases in BRS were again observed for mean BRS only, irrespective of posture. Women in the exercise group had the lowest BRS values. The ‘sequence’ and ‘beat-to-beat’ BRS indices were generally in very good agreement, but there were some differences regarding the influence of exercise training: training-induced BRS_{BTB} reductions occurred sooner (second trimester) than BRS_{SEQ} changes (third trimester) and BRS_{BTB} changes alone were independent of posture.

Our observation of diminished BRS with advancing pregnancy is consistent with previous studies that have reported reductions in BRS of up to 50% by late pregnancy [2-4]. Blake et al. [2] have previously observed that, despite a reduction in supine BRS during pregnancy, the response to orthostatic challenge (standing up) remains intact. This was confirmed in the present study: BRS_{Δ} was not influenced by gestational age. Furthermore, although exercise training reduced BRS it did not alter BRS_{Δ} . Our study therefore confirms that the BRS response to orthostatic challenge remains intact throughout pregnancy despite reductions in steady-state values.

HR increased with advancing pregnancy, in agreement with previous studies [3,14-16]. We additionally showed that the supine-to-standing HR response was diminished in pregnancy and that exercise training did not affect HR. We also observed a reduction in both supine and standing high-frequency HRV (HF_n , a surrogate measure of cardiac parasympathetic activity) as pregnancy progressed. Reductions in HRV during pregnancy have been reported previously [5,17,18], although there have been few longitudinal reports of HRV trends. Previous studies have also shown that reduced cardiac parasympathetic activity is associated with lower baroreceptor sensitivity [19]. We have additionally shown that exercise training in pregnancy further reduces HRV and (by implication) parasympathetic cardiac control. Our results contrast with Stutzman et al. [8], who suggested that exercise conditioning attenuates the decline in parasympathetic activity during advancing gestation, and with Paynter et al. [20] who reported that exercise increases parasympathetic activity. Differences in the modes, frequencies and duration of exercise will all have had some impact on our various studies, and this highlights the need for further investigation. It is worthy of comment that reduced parasympathetic activity is associated with poor outcome in myocardial infarction [21,22] and hypertensive patients [23]. In contrast, here the reduction in parasympathetic activity is associated with a 'healthy' population of women. It could be suggested that a reduction in parasympathetic activity provides a desirable physiological state during pregnancy; perhaps it is a safety mechanism, with a more dominant sympathetic tone conferring a preparedness to counter stress during labour.

Our antenatal exercise programme involved weekly classes that were led or supervised by a qualified midwife. A team including a consultant obstetrician/gynaecologist, senior midwife and other clinicians and academics designed the format of the exercise classes. Our aim in

this regard was to provide an exercise regime that would be well-tolerated and enjoyable for participants, but which also involved sufficient effort to afford a realistic expectation of cardiovascular 'training'. We decided on an exercise protocol that involved recumbent cycling at an intensity that allowed each individual to cycle for up to 15 minutes within the RCOG-recommended heart rate zone for aerobic exercise during pregnancy [9]. Stretching, toning and pelvic floor exercises were included in order to maximise the clinical benefits of attending the classes. The 37% overall attrition rate observed here is low compared with other longitudinal cardiovascular studies in pregnancy [24], suggesting that the study protocol was well-tolerated by our participants.

4.1 Limitations

Future work needs to assess the impact on BRS of the frequency and intensity of exercise. Repetition of our study with a range of different exercise programmes would build on our understanding of training-induced BRS adaptations. Participants in our study completed weekly exercise classes, although the American College of Obstetricians and Gynecologists guidelines [25] recommend 30 minutes of physical activity on most (and preferably all) days of the week during pregnancy. Supervision of this level of exercise would have been unrealistically time-consuming in our study. It would be useful to determine whether more frequent exercise classes would be acceptable to pregnant women and indeed whether this is important with regard to physiological adaptation.

5. Conclusion

In conclusion, taking part in weekly antenatal exercise further reduces heart rate variability and baroreceptor sensitivity by late pregnancy. The reduction in parasympathetic activity and increased sympathetic tone seen in the exercising group could be advantageous for mothers, acting as a 'safety mechanism' to counteract the increased systemic stresses of pregnancy. This autonomic shift is also a possible explanation for the simultaneous reduction in baroreceptor function, which triggers a parasympathetic response within its negative feedback loop. Further studies are needed to explore the influence of exercise

training on this mechanism, and to assess whether different exercise modalities have consistent influences on cardiac autonomic control and baroreceptor function.

Declaration of Interest

The authors report no conflicts of interest. The authors alone are responsible for the content and writing of the paper. R Carpenter received a NISCHR (Welsh Government National Institute for Social Care and Health Research) PhD studentship, and The Cooperative Pharmacy (UK) provided financial support for project consumables.

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