Influence of Antenatal Physical Exercise on Heart Rate Variability and QT Variability

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Short title: Exercise, HRV and QT

Keywords: Heart rate variability, QT variability, Pregnancy, Exercise, Arrhythmias, Autonomic nervous system

Abstract

Objective: We sought to characterise the influence of an antenatal exercise programme on ECG-derived cardiac variables.

Methods: Fifity-one healthy pregnant women were recruited and randomly assigned (2x2x2 design) to an exercise group or a control group. Exercising groups attended weekly classes from the 20th week of pregnancy onwards. Cardiovascular assessments (heart rate variabiliy (HRV), QT, and the QT variability index (QTVI)) were performed at 12-16, 26-28, 34-36 weeks and 12 weeks following birth, during supine rest and exercise conditions.

Results: Advancing gestation was associated with an increased maternal heart rate ($p=0.001$), shorter QT interval ($p=0.003$), diminished HRV ($p=0.002$) and increased QTVI ($p=0.002$). Each of these changes was reversed within 12 weeks postpartum ($p<0.004$). The Exercise group displayed exaggerated changes for all variables (except QT) but only during supine rest in the third trimester ($p<0.029$).

Conclusion: Advancing gestation is associated with a shift in HRV/QTVI towards values that have been associated with an elevated risk of arrhythmia. A 20-week exercise programme undertaken between mid and late pregnancy exaggerated these changes during rest in the third trimester of pregnancy.

1. Introduction

Most [1,2,3] but not all [4] studies have reported that cardiac parasympathetic activity estimated from heart rate variability (HRV) is diminished during the mid-to-late stages of healthy uncomplicated pregnancy. In the non-pregnant population, a diminished parasympathetic tone and/or an elevated sympathetic tone (as occurs in some forms of cardiovascular pathology), has been associated with an elevated risk of arrhythmia and sudden death [5]. It might therefore be suggested that a similar risk exists in mid-to-late pregnancy. Conversely, aerobic exercise training promotes a parasympathetic-dominant state in the non-pregnant population [6], and is generally associated with a reduced risk of cardiac events. However there has been no consistent evidence of a similar change in cardaic autonomic activity during pregnancy, with reports of both reduced [7] and increased [8] parasympathetic activity following exercise training.

Previous studies of this type have focussed on changes in HRV following an antenatal exercise programme and few have considered the potential influence of exercise on the electrocardiographic QT interval. QT reflects the duration of ventricular depolarisation and repolarisation within the cardiac cycle and it is strongly influenced by chronotropic influences such as hormone and electrolyte concentrations [9]. QT is reduced during the second-half of pregnancy, along with an increasing heart rate [10]. Furthermore, the QT variability index (QTVI; [11]) can be used to estimate the relative variability of QT and heart rate. QTVI has been interpreted as an index of elevated risk for ventricular arrhythmic events in the general population [12] but it has not yet been quantified during pregnancy.

The aim of the present study was therefore to characterise the influence of regular physical activity on HRV, QT and QTVI during advancing gestation.

2. Method

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 (1) through direct contact at the antenatal clinic (during the 12-week dating scan or via telephone), (2) via response to posters placed in the antenatal clinic, local GP surgeries, sports centres and antenatal exercise classes, (3) through advertisements placed on the Health Board website and in local newspapers, and (4) via emails sent to university and hospital staff. Exclusion criteria were: a history of cardiovascular or chronic respiratory problems, sleep apnoea, or central/peripheral nervous system disorder. Recruited participants were provided with details about the study and were given one week to consider whether they wished to take part. Individuals who wanted to participate 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

Using a 2x2x2 design (Figure 1) participants were randomly assigned to one of three groups: (1) a control group, members of which did not undertake a formal exercise programme, (2) a land-based exercise group, and (3) a water-based exercise group. Participants were asked a series of questions to determine the group to which they were to be assigned. At each stage they had the option to say answer ‘no’ and were free to choose the group to which they preferred to belong.

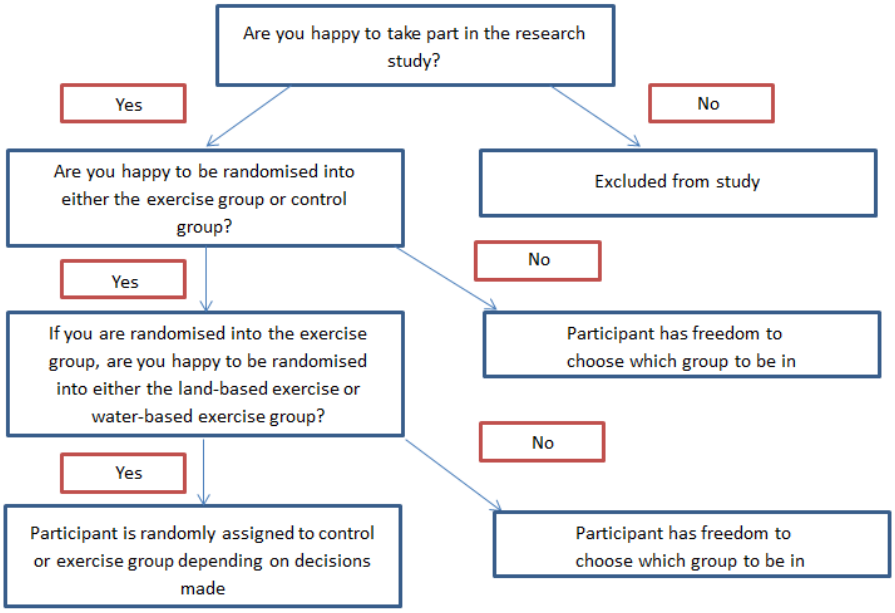

Figure 1. Flow diagram showing the principle of the 2x2x2 randomised design

2.3 Exercise programmes

Participants assigned to the exercise groups started their specific exercise programmes 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 on land and in the water were of similar intensities, assessed via heart rate response. This was continually monitored using heart rate monitors (Polar FT1 Heart Rate Monitor, Polar Electro, Finland) and the BORG 'rating of perceived exertion' scale [13].

Land 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 Cycle, Beny Sports Co. UK Ltd., 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 antenatal aerobic exercise suggested by the Royal College of Obstetrics and Gynaecology [14]. Water-based exercise classes consisted of a 10-minute warm-up followed by 30-minutes of light-to-moderate intensity

'aquanatal' activities such as marching or jogging with various arm actions, weekly throughout pregnancy.

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 the end of the three trimesters of pregnancy (T1, T2, T3) and also at 12-weeks postpartum (PP). Participants were asked to refrain from drinking tea, coffee, alcohol or eating a heavy meal within two hours prior to assessment and to not exercise within 24 hours prior to assessment. Participants also completed a Pregnancy Physical Activity Questionnaire (PPAQ) [15] during each of the three antenatal measurement sessions to monitor changes in physical fitness during pregnancy.

2.4.1 Experimental protocol: Participants were first asked to lie in a 45^{o} reclined-supine position for six minutes, and then to stand for six minutes. Participants then performed a light stepping exercise for six minutes, using the Nintendo Wii games console and 'balance board' platform (to provide a visual stimulus for exercise). This was followed by a six-minute seated recovery period.

2.4.2 Physiological variables quantified: 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) and QTe interval (Q wave onset to T wave end) were measured automatically by the Pathfinder system. HRV was quantified according to the European Society of Cardiology's Task Force Guidelines [16] on heart rate variability: (1) RMSSD (the square root of the mean squared differences of successive RR intervals) and (2) SDRR (standard deviation of the RR intervals). QTVI was calculated according to the equation:

$$QTVI = Log_{10}[(QTv/QTm^2)/(RRv/RRm^2)]$$

where QTv and RRv are the variabilities of QT and RR, respectively, and QTm and RRm are the mean values of these parameters for each defined period.

2.5 Statistical analysis

Normality of the data was assessed using the Kolmogorov-Smirnof test. Repeated measures ANOVA assessed the influence of main factors 'Pregnancy Stage' (within-group repeated measure) and 'Exercise Group' (between-group measure) on the physiological variables, as well as the Stage x Group interaction. 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, otherwise Sphericity was assumed. Post-hoc analysis was carried out with Bonferroni correction to identify the locations of significant 'difference effects' as appropriate. Independent samples t-tests were also used to assess between group differences at each of the four measurement occasions. Statistical significance was accepted as $p<0.05$. Effect sizes were quantified as partial eta squared (η^2). All data are presented as Mean ± SEM (standard error of the mean) and all error bars in the figures represent SEM.

3. Results

3.1 Participant Characteristics

Fifity-one women completed all four antenatal assessments, at mean gestational ages of 15.1 ± 1.9 weeks, 25.5 ± 1.2 weeks, 34.6 ± 1.4 weeks and at 13.4 ± 1.7 weeks postpartum. Mean BMI values (Initial Assessment/Late Pregnancy for Control vs. Exercise groups) were 24.8 ± 0.7 / 28.4 ± 0.8 $kg \cdot m^{-2}$ vs. 26.4 ± 1.3 / 30.0 ± 1.5 $kg \cdot m^{-2}$. Participant characteristics and pregnancy outcomes are displayed in Table 1. Data from the water-based exercise class were excluded from the final analysis because only a small number of these participants completed the study (n=4). In the following, 'Exercise Group' therefore refers specifically to those participants who took part in the land-based exercise.

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 ($kg \cdot m^{-2}$)				
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 ($kg \cdot m^{-2}$)				
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
Planned Pregnancy				
Yes	30	85.7	5	31.3
No	3	8.6	9	56.3
Unknown	2	5.7	2	12.5
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
Gestational Age at Birth (Weeks)				
37-40	8	22.9	6	37.5
>40	27	77.1	10	62.5
Method of Delivery				
Vaginal	28	80	11	68.8
Caesarean Section	7	20	5	31.2
Complications				
Breech	0	0	1	0
Prolonged Rupture	0	0	1	0
Low Platelets	1	0	0	0
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
APGAR Score				
1 minute	9	4-9	9	4-9
5 minutes	10	8-10	10	9-10
10 minutes	10	8-10	10	9-10
Initial Fitness Status[2] ($MET\text{-}h \cdot week^{-1}$)				
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 Physiological variables

Table 2 shows the values for each of the QT and heart rate variability indices during the Supine (rest) and Exercise conditions for the control and exercise groups. ANOVA revealed a significant interaction effect between Pregnancy Stage and Exercise Group for each of the HRV variables in the supine posture only ($p<0.05$), indicating group-dependent trends with advancing gestation in this condition. On average (across all stages of pregnancy) Exercise Group did not influence any of the measured variables. Each of the measured HRV and QT variables was dependent on Pregnancy Stage (all $p<0.0005$). Significant pairwise (between-stage) and Group differences are noted in Table 3.

Table 2. QT and heart rate variability indices (Mean ± SEM) during Supine (rest) and Exercise conditions.

* Significant differences from control values at equivalent antenatal/postpartum stages.

Variable	Control Group				Exercise Group			
	T1	T2	T3	PP	T1	T2	T3	PP
Supine								
RR (ms)	748 ± 13	695 ± 14	678 ± 13	813 ± 19	737 ± 25	702 ± 18	638 ± 18	855 ± 27
QT (ms)	350 ± 4	340 ± 3	334 ± 3	364 ± 4	344 ± 6	337 ± 5	326 ± 4	369 ± 9
QTVI	-0.92 ± 0.05	-0.74 ± 0.06	-0.76 ± 0.05	-1.12 ± 0.05	-0.84 ± 0.08	-0.66 ± 0.08	-0.55 ± 0.07*	-1.14 ± 0.06
RMSSD (ms)	31.5 ± 2.7	21.7 ± 1.8	22.8 ± 2.7	45.3 ± 5.4	26.3 ± 2.9	21.9 ± 2.9	14.4 ± 1.8*	42.8 ± 2.8
SDRR (ms)	45.6 ± 2.9	37.5 ± 2.0	42.4 ± 3.2	63.5 ± 4.2	41.4 ± 4.2	39.8 ± 4.3	31.4 ± 2.6*	61.8 ± 3.4
Exercise								
RR (ms)	627 ± 13	614 ± 13	598 ± 10	680 ± 14	637 ± 19	630 ± 14	593 ± 18	735 ± 23*
QT (ms)	337 ± 4	330 ± 4	329 ± 4	347 ± 4	340 ± 6	338 ± 3	331 ± 4	361 ± 7
QTVI	-0.43 ± 0.05	-0.34 ± 0.05	-0.49 ± 0.05	-0.60 ± 0.05	-0.38 ± 0.05	-0.33 ± 0.04	-0.39 ± 0.10	-0.60 ± 0.04
RMSSD (ms)	20.3 ± 2.0	17.0 ± 1.2	18.1 ± 1.4	24.2 ± 2.0	17.2 ± 1.5	16.5 ± 1.9	14.8 ± 1.5	26.7 ± 3.0
SDRR (ms)	40.3 ± 3.2	36.2 ± 2.2	43.4 ± 3.4	49.0 ± 3.2	37.0 ± 2.6	37.9 ± 3.8	36.5 ± 3.2	52.9 ± 4.6

Table 3. Influence of gestation and exercise on the QT and HRV indices

Variable	Change with advancing gestation?	Antenatal/Postpartum change?	Exercise influence?
QT	⇩ $p=0.003$ (Supine only)	⇧ $p=0.004$	No
QTVI	⇧ $p=0.002$ (Supine only)	⇩ $p<5\times10^{-4}$	⇧ $p=0.028$ (Supine, T3)
RR	⇩ $p=0.001$	⇧ $p<5\times10^{-4}$	⇧ $p<5\times10^{-4}$ (Exercise, PP)
RMSSD	⇩ $p=0.002$ (Supine only)	⇧ $p<5\times10^{-4}$	⇩ $p=0.029$ (Supine, T3)
SDRR	No	⇧ $p<5\times10^{-4}$	⇩ $p=0.029$ (Supine, T3)

4. Discussion

In line with most previous studies [1-3] we found that HRV (RMSSD, SDNN) is reduced with advancing gestation. In addition, we have demonstrated that the assessment of gestational changes in HRV is dependent on physiological state (resting versus exercise conditions). Our data were obtained from a healthy population of women, and so presumably the physiological changes that they reflect define 'desirable' changes during advancing gestation. Thus it appears that healthy pregnancy is associated with a decline in cardiac parasympathetic tone as pregnancy progresses, with an elevated cardiac sympathetic tone during the later stages of pregnancy. We extended previous observations by demonstrating that regular physical exercise during pregnancy causes additional changes in HRV and QT during the later stages of pregnancy: women who had undertaken our exercise programme showed further reductions in supine values of RMSSD, SDRR and QTVI. Antenatal physical exercise therefore influences both heart rate variability and ventricular repolarisation during normal pregnancy.

It is well known that exercise conditioning promotes a parasympathetic-dominant state in the non-pregnant population [6] but there has been less consistent evidence of a similar response during pregnancy. We found that the pregnancy-associated reduction in RMSSD was exaggerated (further reduced) in an exercise-trained group of pregnant women. In contrast, Stutzman et al. [7] previously reported that exercise conditioning attenuated the decline in parasympathetic activity (measured using HF power) with advancing gestation. These authors used a low-intensity walking exercise programme, with both normal-weight and over-weight pregnant women walking three times each week from the 20th week of gestation. Paynter et al. [8] reported greater values for pNN50 (an alternative surrogate measure of parasympathetic control) and a trend towards an increased SDNN (a marker of sympathetic control) in pregnant women who exercised regularly (>30 minutes, three times per week) compared to a control group. These results suggest that exercise conditioning enhances overall HRV (reflecting combined sympathetic and parasympathetic activity), in contrast to our findings. Different exercise training programmes (type and duration) might explain the disparity between these studies. Interestingly the 'normal' decline in parasympathetic activity associated with advancing pregnancy behaves in a similar manner to the normal response when a healthy individual undertakes an acute bout of exercise. We

might therefore speculate that pregnancy is a state of persistent physiological stress on the body and that perhaps the cardiovascular adaptations of pregnancy are responding to a state of 'training' in preparation for the physical demands of labour. The greater reduction in parasympathetic activity that we observed with exercise conditioning might further enhance the body's ability to endure the physical demands of labour. Arrhythmias are more likely to occur during a state of increased sympathetic tone or of reduced parasympathetic tone (as occurs in cardiac disease; [17,18]). Therefore, although pregnancy is not a pathological state, the changes in HRV that we observed might be expected to increase the risk of an arrhythmogenic event in pregnant women.

Our observed reduction in QT interval with advancing gestation is consistent with that reported by Baumert et al. [10], who found that QT interval was shortened by the second-half of pregnancy in comparison to non-pregnant controls. However, our study is the first to demonstrate longitudinal (within-subject) changes in the QT interval. We also showed that QT interval is altered as early as the 15th week of gestation by comparing T1 and postpartum values. The QT interval was not influenced by antenatal exercise, in contrast to a previous report that exercise training in non-pregnant women elicits a shortened HR-corrected QT compared with sedentary women [19].

QTVI describes the relative magnitude of temporal variability in myocardial repolarisation and depolarisation [11] and allows the HR-dependent and HR-independent changes in the QT interval to be characterised [20]. An increase in QTVI has generally been associated with a greater susceptibility to ventricular arrhythmias and sudden death [11,21]. We hypothesised that QTVI could be used as another indicator for determining the risk of arrhythmogenic activity in pregnant women, for example using the previously noted value of 0.1 as a discriminator for higher risk of arrhythmogenic events [22]. Our results showed that supine QTVI values became less negative with advancing gestation, and the lowest values were observed in the postpartum period. Healthy non-pregnant individuals typically have a QTVI value of around -1 or lower at rest: Dobson et al. [23] reported a mean resting QTVI of -1.34 in 173 healthy volunteers (unpublished data), which is similar to our mean postpartum value of -1.1 (which does not appear to return to pre-pregnancy values within 12 weeks postpartum). We noted QTVI values increasing from -0.9 to -0.6 in the supine resting position between the first and third trimesters, with some values as high as -0.3

during exercise. Antenatal exercise further increased QTVI during late pregnancy (supine and metronomic breathing states), reaching a value as high as -0.4. These changes in QTVI further emphasise the contribution of antenatal exercise to parasympathetic dominance during late pregnancy. Therefore, QTVI moves towards apparently less favourable values throughout pregnancy and antenatal exercise magnifies this change – and this might initially be seen as a deleterious effect. However, as noted earlier, these changes occurred in healthy pregnant women and so we interpret the observed influence of exercise as an enhancement of the normal or expected change in QTVI.

Limitations

We did not perform any direct haematological assessments in this study. However, individual medical and obstetric notes showed no recorded abnormalities of any of the major haematological indices (although one woman had a low platelet count) and so the likelihood of haematological status influencing our results was low. Neuromodulator (catecholamines, acetylcholine) levels were not measured in the study and were not available from medical notes, so our estimates of cardiac autonomic control could not be verified biochemically. Neither did we carry out direct assessment of cardio-respiratory (aerobic) conditioning, and whilst maximal oxygen uptake assessment would have been useful in this regard it is unlikely that this would have been acceptable to participants.

Our study assessed physiological responses to land-based exercise only (owing to recruitment and retention difficulties) and it will be important to assess how different exercise modalities influence our findings. Participants in the present study only completed weekly exercise classes, despite current recommendations suggesting more frequent exercise. Future work should therefore also consider whether the frequency and intensity of exercise are important factors in modifying antenatal/postpartum cardiac adaptations. Ideally we would have liked to compare our results to a population of women who experienced ventricular arrhythmias during their pregnancy, to examine possible relationships between arrhythmia incidence and HRV/QT variables.

Conclusion

Advancing gestation is associated with increasing maternal heart rate, shorter QT interval, diminished parasympathetic activity and increased QT variability (QTVI). Each of these changes is reversed within 12 weeks postpartum. Women who took part in our exercise programme displayed exaggerated changes for all variables (except QT) during supine rest in the third trimester. The supine resting condition during late pregnancy is therefore characterised by HRV/QT properties that are associated with an increased risk of arrhythmia.

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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