Effect of gender on P-wave dispersion in asymptomatic populations

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Abstract

Background: Exercise testing is a diagnostic tool for evaluating the induction of stress-induced paroxysmal atrial fibrillation (PAF). Resting P-wave dispersion has been suggested to be greater in males versus females but if used by clinicians, gender difference in response to exercise must be determined. ***Methods:*** Sixteen healthy subjects (n=8 male, age: 21±0.3; n=8 female, age: 23±1.4) performed an incremental exercise test using the Bruce protocol. Electrocardiograms were recorded at rest, end-exercise, 1, 3, and 5 mins recovery. P-waves were measured in each lead with the maximum (P-max) and minimum (P-min) P-wave durations and dispersion calculated. ***Results:*** There was a significant decrease in P-max from rest to end-exercise in males and females [males, 118.3±7.4 (95%CI: 109.7 to 126.8ms) vs. 97.9±6.2 (89.3 to 106.4ms); females, 109.4±4.5 (100.8 to 117.9ms) vs. 94.3±4.6 (85.7 to 102.8ms); p=0.001 (5.7 to 29.8ms)]. Similarly, for P-min [males, 65.6±5.6 (57.4 to 73.9ms) vs. 50.8±2.7 (42.5 to 59.0ms); females, 58.4±3.3 (50.1 to 66.6ms) vs. 45.6±2.7 (37.4 to 53.9ms); p=0.01 (2.2 to 25.4ms)]. Irrespective of gender there was limited change in P-wave dispersion in response to exercise. Males had a longer P-max versus females during the protocol [109.6±2.3 (105.8 to 113.4ms) vs. 103.6±1.8 (99.8 to 107.4ms); p=0.03] but this was not stage-specific. There was no gender differences in either P-min (p=0.12) or P-wave dispersion (p=0.64) across the protocol or stage-specific. ***Conclusions:*** Results from this study indicate that in contrast to P-max and P-min, the P-wave dispersion may not be significantly influenced by the sympathetic nervous system in males and females. Therefore, this study suggests males and females should be evaluated in the same way using the P-wave dispersion for predicting the development of stress-induced PAF at rest and during exercise testing protocols.

Key words: P-wave dispersion; Paroxysmal atrial fibrillation; Exercise; Gender

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Introduction

Atrial fibrillation (AF) is the most common arrhythmia observed in the clinical arena [1] and the athletic community[2]. It has been suggested that the overall risk of AF is significantly higher in athletes than for non-athletes and more predominant in males [1, 3]. The pathological mechanisms of AF have not been fully elucidated. One factor possibly contributing to its initiation is stress, both physiological and psychological, due to fluctuations in autonomic nervous system activity [4-6]. This form of AF is often paroxysmal in nature (self-terminating episodes that generally last 7 days or less, most often less than 24 hours) [7] and can be present in the absence of co-morbidities such as obesity, hypertension and cardiovascular disease.

The cheapest and most detailed diagnostic tool for examining the electrical activity of the heart is the electrocardiogram (ECG). A relatively new ECG measurement termed the P-wave dispersion has been shown to be greater in patients with a history of paroxysmal atrial fibrillation (PAF) compared with healthy controls and has been proposed to be a much more sensitive and specific marker for predicting the development of PAF [8-10] compared to the P-wave duration. Indeed, a retrospective study of 42,751 patients showed that those who subsequently went on to develop AF had significantly greater P-wave dispersions compared with those who did not [11].

The P-wave dispersion has been suggested to be greater in young physically active (moderate endurance trained) males compared with females under resting conditions [12]. However this relationship has not been demonstrated during exercise. The clinical exercise test is routinely applied in the clinical arena for assessing the induction of stress-induced PAF [7] and may be a useful tool in cardiac screening for athletes. It is therefore important to establish the P-wave dispersion response to exercise and highlight any gender differences that may exist. Therefore, the aim of this study is to identify changes in P-wave indices in response to exercise with a particular focus on the P-wave dispersion and to highlight any gender differences that may exist.

Methods

Subjects

Sixteen healthy participants (n=8 male, age: 21±0.3; n=8 female, age: 23±1.4) were recruited for the study. All participants were healthy at the time of participation and had no history of cardiovascular disease. All participants completed a health screen immediately prior to exercise and gave written informed consent. Exclusion criteria for this study included any person with known cardiovascular conditions, anyone who was outside of the age range 18-40 years and anyone who could not give written informed consent. This study had received ethical approval from the University of Hertfordshire, School of Life Sciences Research Ethics committee that complies with international standards according to the Helsinki Declaration (revised 2008).

Exercise Protocol

Participants were allowed to rest for five minutes before a resting ECG was recorded. Participants followed the clinically used Bruce protocol[13] which consisted of seven three minute stages of differing speed and incline (Table 1), lasting a maximum of 21 minutes. In common with previous research methods, the ECG was analysed at rest, at end exercise, and at 1, 3, and 5 minutes into recovery [9]. The ECG was continually recorded and monitored throughout the protocol. In addition to ECG indices, all participants had their age, gender, maximum exercise time, resting and maximum heart rate, and number of MET's recorded. Cessation of exercise was either due to completion of the protocol or at the participants' request.

Electrocardiogram (ECG)

All 12-lead ECG's were performed adopting the Mason-Liker lead arrangement as per standard clinical practice[8]. ECG's were recorded at a speed of 25mm/s and with a voltage gain of 10mm/mV. The P-wave was measured in each lead across one cardiac cycle and the minimum and maximum P-wave duration from the ECG recorded. The P-wave dispersion, defined as the difference between the maximum and the minimum P-wave duration [8], was then calculated for each individual from ECG's recorded at rest, end exercise, and 1, 3, and 5 minutes recovery. The P-wave was considered to be defined as the distance between the first visible upward departure from the bottom of the baseline to

the point of return to the bottom of the baseline [10]. All ECG's were analysed by the same observer on a computer screen using a cursor in agreement with the work carried out by Dilaveris et al., (1999) who demonstrated this to be the method with the lowest intra and inter-observer error [14].

Statistical Analysis

All data is expressed as mean±standard error of the mean (SEM) with 95% confidence intervals. The effect of gender and exercise on P-wave indices was determined by 2-way ANOVA and Turky post-hoc test performed using SPSS data analysis software. All other variables were analysed using independent t-test. Significance was assumed at P=<0.05.

Results

Participant baseline (resting) characteristics are shown in Table 2. There was no significant difference in age (21±0.3 vs. 23±1.4; p=0.22), heart rate (83±6 vs. 85±5 bpm; p=0.76), maximum P-wave duration [118.3±7.4 (95%CI: 109.7 to 126.8ms) vs. 109.4±4.5 (100.8 to 117.9ms); p=0.32), minimum P-wave duration [65.6±5.6 (57.4 to 73.9ms) vs. 58.4±3.3 (50.1 to 66.6ms); p=0.28] or P-wave dispersion [52.6±4.4 (43.0 to 62.2ms) vs. 53.5±5.0 (43.9 to 63.1ms); p=0.90] between males and females when at rest.

P-wave characteristics measured at rest, at end exercise, and at 1, 3, and 5 minutes recovery for both males and females are shown in Table 3. Despite a trend towards prolonged values in males, at no specific stage of the protocol are there any significant differences between males and females with regards to the maximum and minimum P-wave durations or the P-wave dispersion (Table 3).

The maximum and minimum P-wave durations significantly decreased at the end of exercise participation in both genders [P-max: males, 118.3±7.4 (109.7 to 126.8ms) vs. 97.9±6.2 (89.3 to 106.4ms); females, 109.4±4.5 (100.8 to 117.9ms) vs. 94.3±4.6 (85.7 to 102.8ms); p=0.001 (5.7 to 29.8ms)]; [P-min: males, 65.6±5.6 (57.4,73.9ms) vs. 50.8±2.7 (42.5 to 59.0ms); females, 58.4±3.3 (50.1 to 66.6ms) vs. 45.6±2.7 (37.4 to 53.9ms); p=0.01 (2.2 to 25.4ms)] (Figures 1 & 2). In males (Figure 1) and females (Figure 2) the values returned back towards baseline measurements within the 5 minute recovery period. When viewed across the whole protocol (Table 4), there was a significant difference in maximum P-wave duration between males and females [109.6±2.3 (105.8 to 113.4ms) vs. 103.6±1.8 (99.8 to 107.4ms); p=0.03]. However, this difference was not stage specific (Table 3). Despite a trend towards males having a longer minimum P-wave duration across the whole protocol compared to females (Table 4), this did not reach significance (p=0.12).

The change in P-wave dispersion at the end of exercise for both males and females is shown in Figure 3. There was no significant change in P-wave dispersion at the end of exercise participation for either gender [males, 52.6±4.4 (43.0 to 62.2ms) vs. 47.1±4.4 (37.5 to 56.7ms); females, 53.5±5.0 (43.9 to 63.1ms) vs. 48.5±6.0 (38.9 to 58.1ms); p=0.81 (-8.3 to 18.8ms)]. There were no gender differences in the P-wave dispersion at any specific protocol stage (Table 3) or across the whole protocol (p=0.64) (Table 4).

The relationship between the three P-wave indices and heart rate is demonstrated in Table 5. The maximum and minimum P-wave duration (Table 5) displayed a limited inverse relationship with heart rate (p-max, r^2=0.24 p=0.00; P-min, r^2=0.18 p=0.00), whereas there was no clear relationship between the P-wave dispersion and heart rate (r^2=0.001 p=0.80).

Discussion

This study aimed to identify changes in P-wave indices in response to exercise with a particular focus on the P-wave dispersion and sought to highlight any gender differences that may exist. The P-wave dispersion is suggested to be a new measurement for identifying those individuals that may be at risk of developing paroxysmal atrial fibrillation (PAF) [8] and may therefore be a useful measure within both the clinical and sports pre-participation screening environments.

For both males and females the maximum and minimum P-wave durations significantly decreased at the end of exercise participation (Figures 1 & 2 respectively). Limited studies have investigated P-wave changes in response to exercise in healthy individuals making a direct comparison hard to determine. However, these results are in agreement with early studies[15] that demonstrated a reduction

in P-wave duration concomitant to an increase in heart rate as a result of exercise participation in healthy individuals.

As an individual takes part in exercise there is a greater predominance in sympathetic nervous system activity and a release of catecholamine's [16, 17]. This has a number of effects. (1) An increase in the rate of discharge of pacemaker action potentials from the sino-atrial node (sino-atrial node depolarisation) and throughout the rest of the atria[18], (2) a faster rate of repolarisation of the sino-atrial node[18], and (3) an increase in action potential conduction velocity through the cardiac muscle fibres, all of which culminating in the elevation of heart rate. It is suggested this physiological response may account for the reduced P-wave durations observed in this study. This is further supported by the relationship between heart rate and maximum and minimum P-wave duration found in this study (P-max, r^2=0.24 p=0.00; P-min, r^2=0.18 p=0.00) (Table 5). Although an inverse relationship existed it was limited, suggesting the presence of other influencing factors acting on atrial conduction, such as the size of the atria [19]. However, a number of more recent studies comparing P-wave indices in healthy controls and those with cardiac pathology report no significant reduction in maximum and minimum P-wave durations in response to exercise within the healthy control groups [9, 20]. Barutcu and colleagues studied P-wave indices changes in response to exercise in patients with isolated myocardial bridging and healthy controls and reported that for healthy controls there was no significant difference in maximum and minimum P-wave duration at rest and at the end of exercise participation (P-max: 113±9ms vs. 115±8ms; P-min: 68±11ms vs. 68±11ms; p=>0.05).

The P-wave dispersion (Figure 3) reported no significant change for either gender after exercise participation (males, 52.6±4.4 vs. 47.1±4.4ms; females, 53.5±5.0 vs. 48.5±6.0 ms; p=0.81) (Figure 3). This finding is in agreement with Barutcu et al. (2009) who reported no significant difference in P-wave dispersion between rest and exercise in their healthy control group (45±11 vs. 48±15ms; p=>0.05) [20]. Additionally, the P-wave dispersion in the current study observed a limited relationship with heart rate (r^2=0.001 p=0.80) (Table 5) suggesting that the P-wave dispersion, in contrast with the P-wave duration, is relatively unaffected by changes in sympathetic nervous activity. If the P-wave dispersion is shown to be more than or just as sensitive as the P-wave duration then the requirement for exercise testing for assessing PAF risk could be removed, making patient assessment less time consuming and thus a more useful tool for the clinician. More research into the sensitivity of the P-wave dispersion and larger trials are thus warranted.

More importantly, in the whole protocol, males had a significantly longer maximum P-wave duration compared with females (p=0.03) (Table 4) but this difference could not be seen at any specific stage of the protocol (Table 3). Limited research using exercise has been conducted in determining gender differences in P-wave indices. For example, a previous study by Yildiz and colleagues (2008) studied P-wave duration and related factors in endurance trained students. They determined that males had a significantly longer maximum P-wave duration compared with females when in a resting state (112.79±16.07 vs. 109.86±12.70ms, p=0.02) [12]. However, this study did not investigate if this finding continued in response to exercise. Therefore, the current study demonstrates that despite a trend towards prolonged values in males, there is no significant difference in maximum P-wave duration at the end of participation of exercise between males and females (p=0.65) (Table 3).

There was no gender difference in the whole protocol with minimum P-wave duration (p=0.12) or P-wave dispersion (p=0.64) (Table 4), or at any specific stage of the protocol (Table 3). These results differ from the work of Yildiz et al. (2008) who reported a significant difference between males and females at rest for minimum P-wave duration (54.17±12.88 vs. 57.17±11.39ms; p=0.005) and P-wave dispersion (58.56±16.24 vs. 52.76±12.57ms) respectively [12]. However, Yildiz and colleagues (2008) did not investigate these characteristics beyond resting conditions. Therefore, the results of the current study (Table 3 & 4) indicate that there are no significant differences in minimum P-wave duration and P-wave dispersion between males and females after the participation of exercise. However, the trend towards prolonged P-wave duration observed in this study and the statistically significant difference reported by Yildiz et al. (2008) may support the suggestion that females may have a more dominant parasympathetic influence on heart rate control [21] but this requires further investigation.

There were a number of limitations that may have influenced the results of the current study. Firstly, it has been shown that the size of the left atrium can alter the duration and dispersion of the P-wave in healthy individuals [19]. However, due to no echocardiography equipment being available, atrial size could not be determined in this study. Additionally, it is well documented that increased body mass

index (BMI) is associated with the development of atrial fibrillation [22] and that subjects with increased BMI have increased P-wave dispersion, which can be reduced upon decreasing body weight [23]. As BMI and atrial size was not taken into account in this study it cannot be confirmed that no additional influences on P-wave duration and dispersion was taking place. Secondly, it is suggested that a limitation of the present work is the relatively small sample size. However, this often reflects the time taken for exercise stress tests in a study of this nature.

In conclusion, this study indicates that the P-wave response after exercise participation is similar for both males and females, suggesting that changes in atrial conduction in response to exercise are the same for both genders. It may indicate that the P-wave dispersion, unlike the P-wave duration, may not be significantly influenced by changes in sympathetic activity. In addition, there is no significant difference in P-wave duration or dispersion between males and females at rest or after participation in the incremental exercise test. This indicates that both males and females should be evaluated in the same way using P-wave dispersion in predicting the development of stress-induced paroxysmal atrial fibrillation during clinical exercise testing. Further studies with greater sample sizes are clearly warranted to further the results of this study and to identify ‘normal’ and ‘abnormal’ reference ranges, in terms of P-wave dispersion values during and after exercise. Furthermore, it is suggested that, future work should investigate other factors that affect cardiovascular risk, such as age and ethnicity and how they may influence P-wave indices.

Table 1: Timings and intervals of the full Bruce protocol

Stage	Speed (km/h)	Gradient (%)	Time (min)
1	2.7	10	3
2	4.0	12	3
3	5.5	14	3
4	6.6	16	3
5	8.0	18	3
6	8.9	20	3
7	9.7	22	3

kilometers per hour (km/h); minutes (min)

Table 2: Participants baseline characteristics

	Male Subjects (n = 8)	**Female Subjects (n = 8)**	**p value**
Age	21 ± 0.3	23 ± 1.4	0.22
Heart rate (beats/min)	83 ± 6	85 ± 5	0.76
P-Max wave duration (ms)	118.3 ± 7.4	109.4 ± 4.5	0.32
P-Min wave duration (ms)	65.6 ± 5.6	58.4 ± 3.3	0.28
P-wave dispersion (ms)	52.6 ± 4.4	53.5 ± 5.0	0.90

beats per minute (beats/min); milliseconds (ms); significance assumed if $p<0.05$

Table 3: Male and female P-wave indices at each stage of the protocol (mean±SEM)

	Male Subjects n= 8	Female Subjects n= 8	p value
Exercise Duration	13.0 ± 0.8	11.1 ± 0.7	0.12
MET Value	14.9 ± 0.4	14.0 ± 0.2	0.08
Rest			
Heart rate (beats/min)	83 ± 6	85 ± 5	0.76
P-max wave duration (ms)	118.3±7.4	109.4 ± 4.5	0.32
P-min wave duration (ms)	65.6 ± 5.6	58.4 ± 3.3	0.28
P-wave dispersion (ms)	52.6 ± 4.4	53.5 ± 5.0	0.90
End Exercise			
Heart rate (beats/min)	176 ± 2	177 ± 4	0.71
P-max wave duration (ms)	97.9 ± 6.2	94.3 ± 4.6	0.65
P-min wave duration (ms)	50.8 ± 4.5	45.6 ± 2.7	0.35
P-wave dispersion (ms)	47.1 ± 4.4	48.5 ± 6.0	0.86
1 Minute Recovery			
Heart rate (beats/min)	139 ± 6	141 ± 6	0.77
P-max wave duration (ms)	106.1 ± 3.1	100.5 ± 1.6	0.13
P-min wave duration (ms)	65.0 ± 3.5	61.5 ± 2.7	0.44
P-wave dispersion (ms)	41.1 ± 3.5	39.0 ± 4.0	0.69
3 Minute Recovery			
Heart rate (beats/min)	115 ± 5	116 ± 5	0.93
P-max wave duration (ms)	112.3 ± 2.8	106.0 ± 2.1	0.09
P-min wave duration (ms)	69.1 ± 4.3	66.3 ± 4.8	0.66
P-wave dispersion (ms)	43.3 ± 4.7	39.8 ± 4.8	0.61
5 Minute Recovery			
Heart rate (beats/min)	105 ± 5	107 ± 4	0.83
P-max wave duration (ms)	113.4 ± 2.4	107.9 ± 4.4	0.29
P-min wave duration (ms)	65.8 ± 4.2	64.1 ± 4.9	0.80
P-wave dispersion (ms)	47.6 ± 3.0	43.8 ± 7.2	0.63

Minutes (min); beats per minute (beats/min); milliseconds (ms); Significance assumed if $p<0.05$

Table 4: Male and female P-wave indices across the whole protocol (Mean±SEM; 95%CI)

P-wave Indie	Male (n=8)	Female (n=8)	p-value
P-Max (ms)	109.6 ± 2.3 (105.8 to 113.4)	103.6 ± 1.8 (99.8 to 107.4)	0.03
P-Min (ms)	63.3 ± 2.1 (59.6 to 66.9)	59.2 ± 2.0 (55.5 to 62.9)	0.12
P-Disp (ms)	46.4 ± 1.8 (42.0 to 50.7)	44.9 ± 2.5 (40.6 to 49.2)	0.64

Milliseconds (ms); Significance assumed if $p<0.05$

Table 5: Relationship of P-wave indices and heart rate.

P-wave Indie	r	r^2	p-value
P-Max duration	- 0.49	0.24	0.00
P-Min duration	- 0.42	0.18	0.00
P-wave dispersion	- 0.03	0.00	0.80

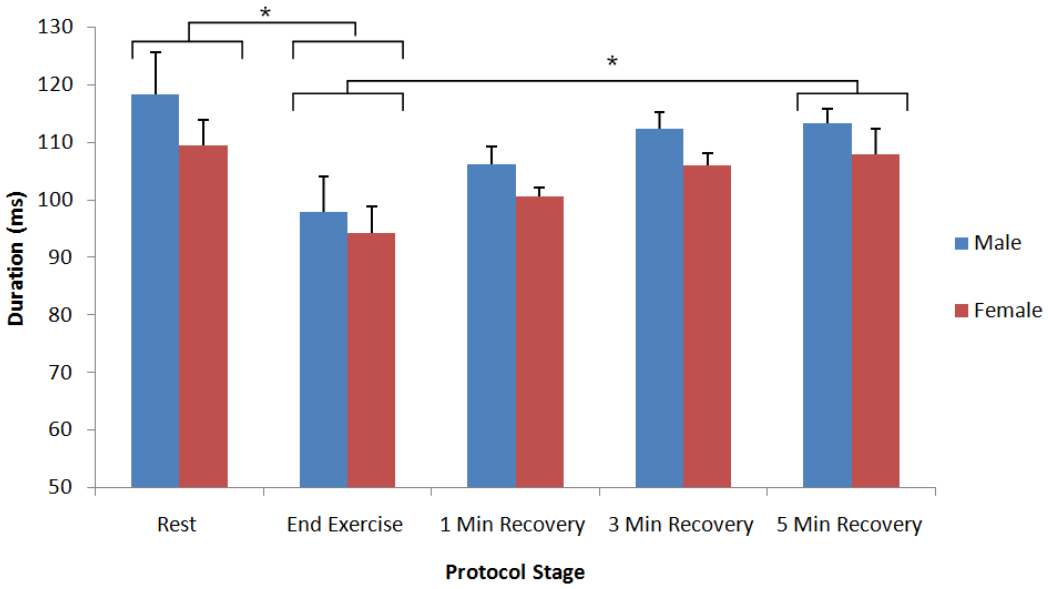

Figure 1: Mean±SEM of maximum P-wave duration for males and females at rest, end exercise and 1, 3, and 5 minute's recovery (* = $p<0.05$).

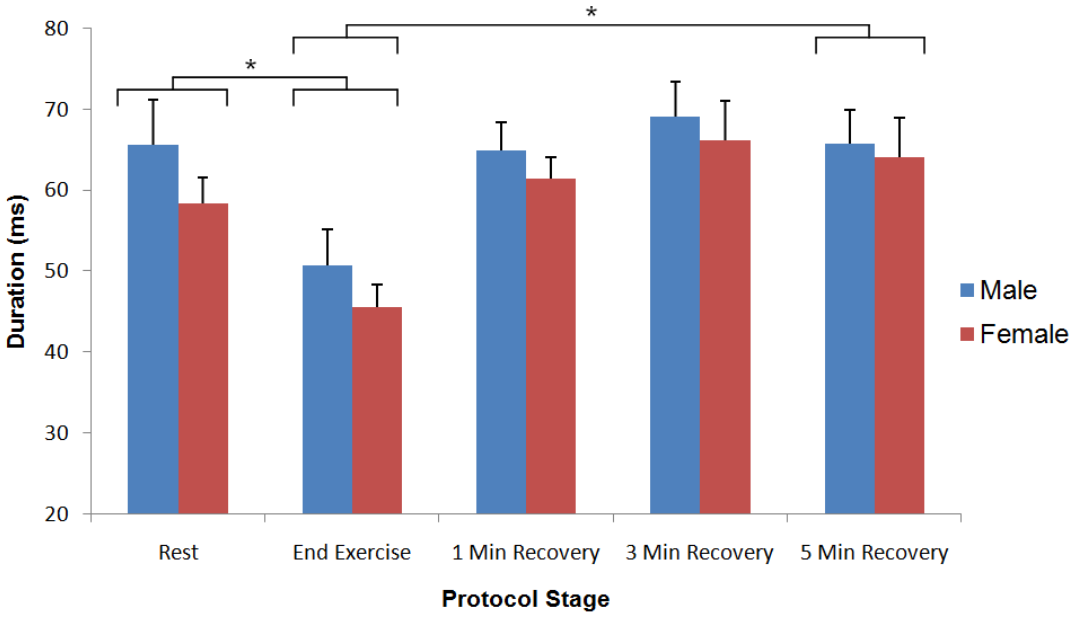

Figure 2: Mean±SEM of minimum P-wave duration for males and females at rest, end exercise and 1, 3, and 5 minute's recovery (* = $p<0.05$).

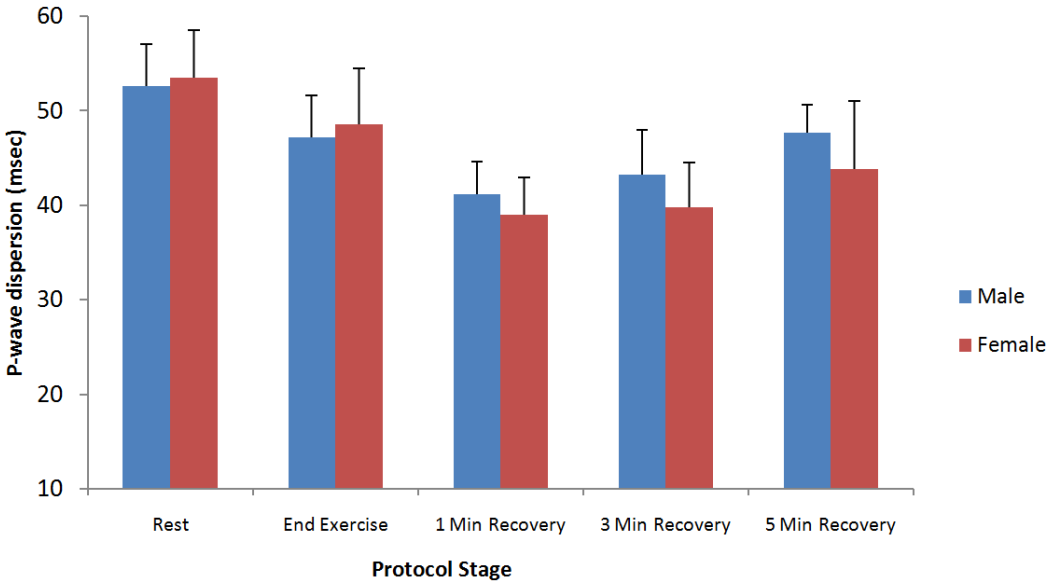

Figure 3: Mean ± SEM of P-wave dispersion for males and females at rest, end exercise and 1, 3, and 5 minutes recovery

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