THE EFFECT OF SELECTIVE ß1-BLOCKADE ON EMG SIGNAL CHARACTERISTICS DURING PROGRESSIVE ENDURANCE EXERCISE

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ABSTRACT

Aim: This study analysed the effect of selective ß1-blockade on neuromuscular recruitment characteristics during progressive endurance exercise. Methods: Ten healthy subjects ingested a selective ß1-blocker, acebutolol (200mg b.d.), for 7 days (for one of two cycling trials), with a 10-day wash out period between trials. On the last day of acebutolol ingestion subjects performed three successive 15 min rides at 30%, 50% and 70% of their peak power output and then cycled at increasing (15 $W.min^{-1}$) work rates to exhaustion. Force output, heart rate, submaximal VO_2, rate of perceived exertion (RPE), electromyographic (EMG) data and blood lactate was captured during the cycling activity.

Results: Peak work rate (270 ± 111 W vs 197 ± 75 W, CON vs BETA, $P < 0.01$), time to exhaustion (49.7 ± 23.2 min vs 40.3 ± 23.7 min, CON vs BETA, $P < 0.05$) and heart rate (mean, for the full ride 135.5 ± 38.3 $b.min^{-1}$ vs 111.5 ± 30.0 $b.min^{-1}$ CON vs BETA, $P < 0.05$) were significantly lower for the group who ingested ß1-blockade (BETA) compared to the control group (CON). Although not significant, submaximal VO_2 was reduced in BETA during the ride, while RPE was significantly higher during the ride for BETA ($P < 0.01$). Mean integrated electromyography (IEMG) was higher in the BETA group although these differences were not significant. Mean power frequency values (MPFS) of the BETA group showed a significant ($P < 0.05$) shift to the upper end of the spectrum in comparison to the control group. Lactate values (11.7 ± 3.5 $mmol.l^{-1}$ vs 7.1 ± 4.1 $mmol.l^{-1}$ CON vs BETA) were significantly lower ($P < 0.05$) at exhaustion in BETA.

Conclusions: Significant reductions in cycling performance were found when subjects ingested ß1-blockers. This study has shown significant shifts to the upper end of the EMG frequency spectrum after ß1-blocker ingestion, which could be caused by a change in neuromuscular recruitment strategy to compensate for the impaired maximal exercise capacity.

Key words: ß1-blockade; fatigue; integrated electromyography (IEMG), mean power frequency spectrum (MPFS).

INTRODUCTION

Individuals receiving β-adrenergic receptor blocking drugs often complain of muscle fatigue. Both non-selective β_1- + β_2-blockers and selective β_1-blockers reduce most individuals' capacity to exercise {769}{770}{771}. Even when β-blockers possess intrinsic sympathomimetic (β_1-agonist) activity (ISA), to limit the reduction in cardiac output, there is no improvement in exercise tolerance {40}{772}. A failure of β-blockers with ISA to improve sub-maximal exercise tolerance {77}{50}{773}{777} suggests that β-blockade does not accelerate fatigue simply by reducing the supply of O_2 to the active muscles. Beta-blockade either increases {774}{775} or has no effect on plasma lactate accumulation during exercise {769}{50}{770}. Beta-blockade also does not increase muscle glycogenolysis {779}{77} Plasma [glucose] during exercise is either decreased {50}{775}{776}{771} or unaffected by β-blockade {234}{777}. Only the mobilisation of non-esterified fatty acids (NEFA) is consistently decreased by β-blockade {777}{50}{780}{781}. However, whether lower plasma [glucose] or [NEFA] is involved in the reduced exercise endurance capacity during β-blockade is open to question. Intravenous infusion studies have shown that reversal of the decreases in circulating [glucose] and [NEFA] with β-blockade do not improve exercise capacity {781}{776}.

Since changes in metabolism do not readily explain the impaired sub-maximal exercise capacity during β-blockade, other potential causes of early fatigue have to be considered. One possibility is that β-blockade may affect muscle recruitment activity from the central pathways of control. In cycle

exercise the integrated electromyographic (IEMG) activity is known to increase with increased exercise intensity {185}. During continual heavy work at a constant load, an increase in IEMG is observed and is interpreted as a sign of muscle contraction failure {46}. More information detailing the motor unit action potentials can be gained by studying the mean power frequency spectrum (MPFS).

The only experiments to the author's knowledge that has been conducted to study the influence of ß-blockers on the EMG pattern under exercise conditions was Tesch et al. {737} who discovered no differences in IEMG or MPFS during cycling, but did find a decrease in MPFS during ß-Blockade in comparison to the control group. This could be indicative of muscle fatigue or decreased conduction velocity of the nerve fibers {36}{39}. MPFS was calculated by describing data captured at 90 W initial work rate, and all subsequent data was normalised against it. However, this normalisation technique can be questioned as Ebenbichler et al. {220} concluded that MVC is the most reliable form of reference when conducting MPFS analyses. This has to be considered throughout investigation of biological signals in which the electrical and mechanical activities of the recruited motor units are summated {194}. Second, Derman {191} examined IEMG patterns of exercising subjects ingesting ß-blockade and found no difference in MVC but significantly higher IEMG activity in the subjects who ingested ß-blockade. Derman {191} concluded that the higher IEMG was due to additional recruitment of non-fatigued skeletal muscle fibers to maintain the same work rate. However in this study MPFS was not determined. Therefore, the

hypothesis for this study is that during submaximal exercise to exhaustion, ß1-blocker ingestion will result in an altered neuromuscular recruitment pattern, which will be shown by a changed IEMG and MPFS signal. Accordingly, we examined the effects of acebutolol, a selective ß1-blocker with intrinsic sympathetic activity on IEMG and MPFS during successive cycle rides at 30%, 50% and 70% of peak work rate and at fatigue.

METHODS

Subjects

Ten healthy males volunteered for the study, who were physically active on a regular basis. Three subjects were unable to complete due to adverse effects such as headaches, dizziness and nausea whilst ingesting beta blockade. The mean age of the remaining subjects was 26.1 ± 2.1 years (range 23 – 30 years), height 181 ± 9 cm (range 169 – 194 cm), weight 78.6 ± 9.7 kg (range 62 – 94 kg) and percent body fat 14.8 ± 2.7% (range10.6 - 17.7%). The mean lean thigh volume (LTV) was 6492 ± 928cc (range 4629 – 7381cc). All subjects were well informed about possible risks associated with the experiment and gave their informed consent before participation.

Preliminary testing

To determine peak power output (PPO), a modified protocol as described by Hawley and Noakes {146} was used. Subjects performed a 10-minute warm up on an electrically braked cycle ergometer (Lode, Groningen, Netherlands). The starting power output was determined by multiplying the subject's body weight by 2.5 W. The load was subsequently increased every 150s by first 50 W and then 25 W until the subjects were unable to maintain force output or pedalling frequency dropped from 90 to < 50 revolutions. $min.^{-1}$. PPO was defined as the last completed work rate in watts plus the fraction of time spent in the final non-completed work rate multiplied by 25 W.

Tablet ingestion

Following the progressive exercise tests, the subjects ingested acebutolol for one of the two phases of the trial in a random order. The trials took place over one week periods with a 10 day wash out in between trials. Subjects were instructed to consume two 200 mg capsules between 0700 and 0900 h before breakfast for a period of seven days.

Blood sampling

On the last day of each phase the subjects were instructed to report the laboratory. An 18-guage Teflon cannula (Jelco, Johnson and Johnson, Halfway house, South Africa) was positioned in an antecubital vein and connected to a three way stop cock (Uniflex, Mallinckrodt, Hennef-Seig, Germany). This cannula was flushed periodically with 2-3 ml of sterile saline containing heparin (5 IU ml^{-1}) and was used for the collection of venous blood samples (10 ml) at rest and during exercise. Venous blood samples (10ml) were drawn at rest, at the end of each 15 min work rate and at exhaustion. The samples were then divided into aliquots, which were put into an ice-cold tube containing potassium oxalate and sodium fluoride for later determinations of lactate concentrations. The tubes were centrifuged at 3000-x g for 10 minutes at 4ºC immediately after the completion of the trial and the supernatants were stored at -20ºC for later analyses of plasma lactate. Plasma lactate concentrations were measured with spectrophotomeric (Beckman Model 35, Beckman Instruments Inc., Fullerton, Ca, USA) enzymatic assays (Lactate PAP, BioM (rieux, Lyon, France; NEFA half-micro test; Boehringer Manheim, Germany).

Maximal isometric voluntary contraction (MVC)

To normalise EMG recordings during cycling it was first necessary to perform maximal isometric force output testing, which is not affected by ß-blocker ingestion {759}. The strength of the subjects' right knee extensors were measured on an isokinetic dynamometer (Kin-Com Chattanooga Group Inc., USA). Subjects sat on the dynamometer and their hips, thighs and upper bodies were firmly strapped to the seat. In this position their hip angle was at 100° angle of flexion. The right lower leg was then attached to the arm of the dynamometer at a level slightly above the lateral malleolus of the ankle joint and the axis of rotation of the dynamometer arm was aligned with the lateral femoral condyle. The dynamometer arm was then set so that the knee was at a 60° angle from full leg extension. Each subject performed four sub-maximal familiarisation contractions prior to performing two maximal MVC's; the latter of which was used for subsequent analyses. All subjects were encouraged verbally to exert maximal effort during both MVC's.

Progressive submaximal exercise

As with the preliminary PPO testing, Lode cycle ergometers were used. After taking a venous blood sample and measures of heart rate at rest, the subjects performed three successive 15 min rides at 30, 50 and 70% of their PPO and subsequently cycled at increasing 15 $W.min^{-1}$ until they could not maintain force (Figure 1). The same ride was performed for both the controls (CON) and the group ingesting ß-blocker (BETA).

Recordings of heart rate and perceived exertion

Heart rate was recorded at rest and then recorded along with rate of perceived exertion (RPE) {782} at 10, 25, 40 minutes and at exhaustion (Figure1).

Submaximal VO_2 testing

During the final 5 minutes of each 15 min work rate and at exhaustion, subjects wore and breathed through a mask connected to an Oxycon Alpha automated gas analyser (Mijnhardt, Netherlands). Before each test, the analyser was calibrated with a Hans Rudolph 5530, 3L syringe (Vacuumed, Ventra, USA) room air and a 5% CO_2: 95% N_2 gas mixture. Analyser outputs were processed by a computer, which calculated one minute ventilation, oxygen consumption and carbon dioxide production values for each breath. Oxygen consumption values were the average of the highest values measured over 60s in the final work rate. VO_2 was then determined by dividing the oxygen consumption value by the body weight of the subject ($ml.kg^{-1}.min^{-1}$).

Electromyographic (EMG) testing

Prior to maximal isometric strength testing on the Kin-Com isokinetic dynamometer, EMG electrodes were attached to the subject's lower limb midway between the superior surface of the patella and the anterior superior iliac crest of the "belly" of the rectus femoris. The overlying skin on the muscles was carefully prepared. Hair was shaved off, the outer layer of epidermal cells abraded, and oil and dirt were removed from the skin with an

alcohol pad. Triode electrodes (Thought Technology USA) were placed on the muscle sites as described above, and linked via a fibre-optic cable to the Flexcomp/DSP EMG apparatus (Thought Technology USA) and host computer. The electrodes were heavily taped down with cotton swabs to minimise sweat-induced interference. The EMG data was filtered with a 50Hz line filter to prevent electrical interference from electrical sources and was automatically anti-aliased by the hardware (Thought Technology USA). Each activity was sampled at a 1984 Hz capture rate for 5-second bouts. Recordings were taken on the second maximal isometric trial and during the cycling trial at 10, 25, 40 minutes and at exhaustion thus yielding a raw signal. MVC EMG data was recorded before both cycle rides to ensure similar normalisation of EMG in both trials. The raw data were divided into 5 x five second epochs. The first epoch included all data collected during the second MVC trial, and the remaining four epochs included data collected on the ride at 10, 25, 40 minutes and at exhaustion.

The EMG signals were full wave rectified, movement artifact removed using a high-pass second order Butterworth filter with a cut off frequency of 15 Hz, then smoothed with a low-pass second order filter with a cut off frequency of 5 Hz. This was performed using MATLAB^{TM} gait analyses software. This integrated data (IEMG) was used for subsequent analyses.

The spectrum of the frequency for each epoch of data collected during the cycle ride was assessed using the raw EMG data by using a fast Fourier transformation algorithm. The analyses for frequency spectrum were

restricted to frequencies of the 5-500 Hz range, due to the EMG signal content consisting mostly of noise when it is outside of this bandwidth. The frequency spectrum from each epoch of data was compared with that derived from the MVC, and the amount of spectral compression was estimated. This technique was performed as described by Lowery et al. {48}, which is a modification of the work of Lo Conte and Merletti {47} and Merletti and Lo Conte {729}. The spectrum of the raw signal of each epoch was obtained and the normalised cumulative power at each frequency was calculated for each epoch. The shift in percentile frequency was then examined (i.e. at 0%...50%...100% of the total cumulative). The percentile shift was then estimated by calculating the mean shift in all percentile frequencies throughout the mid-frequency range (ie. 5-500 Hz). This method has been suggested as a more accurate estimate of spectral compression than median frequency analyses, which uses single value of (50th) percentile frequency {48}. This change in mean percentile frequency (MPFS) data was used for subsequent analyses.

Statistical Analyses

A two-way ANOVA for repeated measures was used to evaluate statistical significance of all the variables measured. A Scheffe's post hoc test was used to detect differences over time and between groups. Single comparisons between treatments were analysed with a paired Students t-test using two-tailed values of P. Significance was accepted at $P \leq 0.05$. All data are expressed as means $\pm$ SD.

RESULTS

Significantly lower values ($P < 0.05$) during the cycle ride were found in BETA compared to CON for maximum power output (P_{WATT}) ($P < 0.01$) and time to exhaustion (TIME) in BETA (Table 1).

Heart rate increased significantly less ($P < 0.05$) (Figure 2) for BETA in comparison to CON and both groups responded similarly over time. Mean heart rate for the total ride was 111.5 $\pm$ 30.0 $b.min^{-1}$ for BETA and 135.5 $\pm$ 38.3 $b.min^{-1}$ for CON. In BETA the reduced heart rate was accompanied by a trend for lower submaximal VO_2 values with both groups increasing significantly over time ($P < 0.05$) (Figure 3). Mean submaximal VO_2 values for the duration for the ride were 32.0 $\pm$ 8.3 $ml.kg^{-1}.min^{-1}$ for BETA and 38.1 $\pm$ 9.6 $ml.kg^{-1}.min^{-1}$ for CON.

RPE was significantly greater for BETA than CON ($P < 0.01$) (Figure 4) and mean RPE values for the total ride were 6.1 $\pm$ 3.6 for BETA and 4.7 $\pm$ 3.6 CON.

IEMG values showed a trend to increase by 34.7, 30.2, 44.1 and 64.4% at 10, 25, 40 min and exhaustion respectively for BETA in comparison to CON. The BETA group also showed a large standard deviation for IEMG data at exhaustion (Figure 5). The mean IEMG for the total ride was 56.9 $\pm$ 25.4 % for BETA and 29.4 $\pm$ 4.0 % for CON. There was a significant ($P < 0.05$) shift to the upper portion of MPFS in BETA with a mean of 1.15 $\pm$ 0.03 in comparison

to a shift to the lower portion of MPFS in CON, which showed an average of 0.78 $\pm$ 0.07 for the total ride (Figure 6).

Lactate concentrations were significantly less for BETA in comparison to CON (7.1 $\pm$ 4.1 mmol.l^{-1} BETA; 11.7 $\pm$ 3.5 mmol.l^{-1} CON) at exhaustion (Figure 7) ($P < 0.01$).

DISCUSSION

The results of this study indicate that ß-blockade significantly effects neuromuscular recruitment activity during submaximal exercise. Maximal exercise capacity was reduced by ingestion of selective ß-1 blockade, as reported by most investigators {40}{27}. The impaired maximal exercise capacity may reduce heart rate and VO_2 as is shown in this study. It is also well documented that an increased perception of effort will reduce exercise performance in healthy individuals who have ingested ß-blocker {35}{760}, which is shown in this study by an increase in RPE for BETA. It is has been proposed that this increase in perception of effort results from an inability of healthy individuals to compensate for the decrease in heart rate by increasing stroke volume as it is has been maximised as an adaptation effect of exercise training {32}. These changes in RPE may also be related to neuromuscular recruitment differences as shown in this study.

IEMG data firstly showed similar results to Derman et al. {191}, where IEMG tended to increase in subjects who ingested ß-blockade. This could be due to a central mechanism projecting increased neural output due to the reduced maximal exercise capacity. Moritani and Yoshitake {59} showed a linear increase for IEMG/VO_2 in normal subjects. However the BETA group had a significantly lower VO_2, yet IEMG was higher. This would indicate that there is a higher neural input to compensate for the reduced $VO_{2.}$ Another possibility is that there was a higher recruitment of non-fatigued muscle fibres {191}, when subjects were on ß-blocker.

The large standard deviations for final force output and IEMG activity in the BETA group show that certain subjects are more vulnerable to reduced exercise tolerance when ingesting ß-blockade. This finding is supported by Derman {191} who showed that not all the subjects' performance capacities were equally affected following the ingestion of ß-blockade.

There was a significant shift to the upper portion of MPFS in BETA, which indicates an increase in firing rate to recruit more motor units {763} in response to the reduced exercise capacity. {484}{485}{63}{480}. This shift towards the upper portion of MPFS could have been caused by an increase in muscle fiber conduction velocity (MFCV) {186} from an up regulation in central command {697}{313}. This change in central command may be an attempt to recruit more type II muscle fibers as ß-blockade will cause the impairment of type I fibers during cycling {37}, resulting in a greater use of type II fibers which have a lower fatigue threshold. Furthermore, this finding is supported by Kupa et al {165}, who showed that the greater proportion of type II muscle fibers would result in a shift to the upper end of the spectrum. This is due to type II fibers having a greater maximum rate of repolarization and depolarisation compared to type I fibers and indeed produce an action potential that has a lesser duration {166}. Action potentials that have a shorter duration, contribute high frequency components to the EMG spectrum that produce a greater value of MPFS {165}. This increased use of type II fibers, which have a lower fatigue threshold may have also been a factor in the early termination of exercise in BETA.

However, it is also possible that the difference in MPFS could be from muscle changes. First, it has been suggested that the decline in MPFS is as a result of increased lactate concentrations causing a lowering of pH {104} and a consequent reduction in MFCV {105}{63}{106}{107}. In this study, lactate concentrations were significantly less for BETA, which does suggest a possible cause for the difference in MPFS. Conversely, it has also been shown in McArdle's disease patients that MPFS declined during MVC, in the absence of any lactate and MFCV changes, therefore suggesting that factors other than increasing lactate would influence MFCV {111}. The change in MPFS could also be from an increase in muscle temperature in BETA, as the reduced cardiovascular capacity will be requiring a higher amount of effort to sustain the same given workload as CON. Bigland-Ritchie {186} showed that by heating a muscle it would increase conduction velocity and therefore produce a shift to the upper portion of MPFS.

Blood lactate concentrations were lower in the BETA group at fatigue, which is supported by some investigators {183}{34}. However, other studies show conflicting results {32}. In our study, BETA subjects fatigued at lower power outputs, which will inevitably cause a decrease in absolute lactate values. Therefore, reduced lactate may be caused simply by reduced cycling intensity at fatigue.

In conclusion this study supports earlier studies that selective ß1-blockade will limit prolonged exercise endurance. Furthermore, this study has shown that

subjects who have ingested ß-blockers have altered EMG frequency spectrum, which could result from a change in the neuromuscular recruitment strategy in an attempt to generate more power to compensate for the reduction in exercise capacity.

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TABLES

Table 1. Peak watts (PWATT) reached at the point of cycling exhaustion and time taken to reach exhaustion (TIME) for both control (CON) and subjects who have ingested ß-blocker (BETA).

	CON	BETA
PWATT	270.8 ± 111.6 **	197.45 ± 75.7
TIME	49.7 ± 23.2 *	40.33 ± 23.7

All values are mean ± SD

**-P < 0.01 PWATT CON vs BETA

*-P < 0.05 TIME CON vs BETA

FIGURES

Figure 1. Progressive cycle exercise test protocol. Rate of perceived exertion (RPE), electromyography (EMG), heart rate (HR) and VO_2 were all recorded at 10, 25, 40 minutes and at exhaustion during the ride.

Figure 2. Heart rate values captured at rest, 10, 25, 40 mins and exhaustion during the cycle ride for the ß-blocker group (BETA) and the control group (CON) (*P < 0.05 group effect).

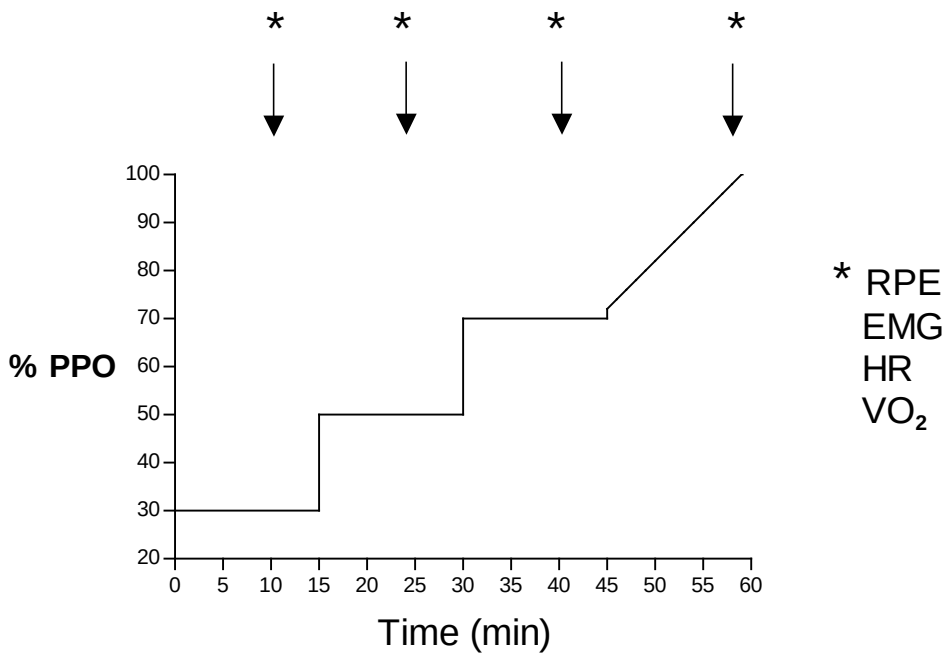
Figure 3. VO_2 values captured at 10, 25, 40 mins and exhaustion ride for the ß-blocker group (BETA) and the control group (CON) during the cycle ride (*P < 0.05 increase for both groups over time).

Figure 4. Rate of perceived exertion values captured at 10, 25, 40 mins and exhaustion ride for the ß-blocker group (BETA) and the control group (CON) during the cycle ride (*P < 0.01 main effect).

Figure 5. Mean IEMG values a normalised as a % of MVC for both BETA and CONTROL, taken at 10, 25, 40 min and exhaustion.

Figure 6. MPFS values normalised against MVC for both BETA and CON, taken at 10, 25, 40 mins and exhaustion. (*-P < 0.05 group effect).

Figure 7. Lactate samples taken at rest, at 15 minutes during the ride and at exhaustion in both CON and BETA groups. (**P < 0.01 CON vs BETA main effect)



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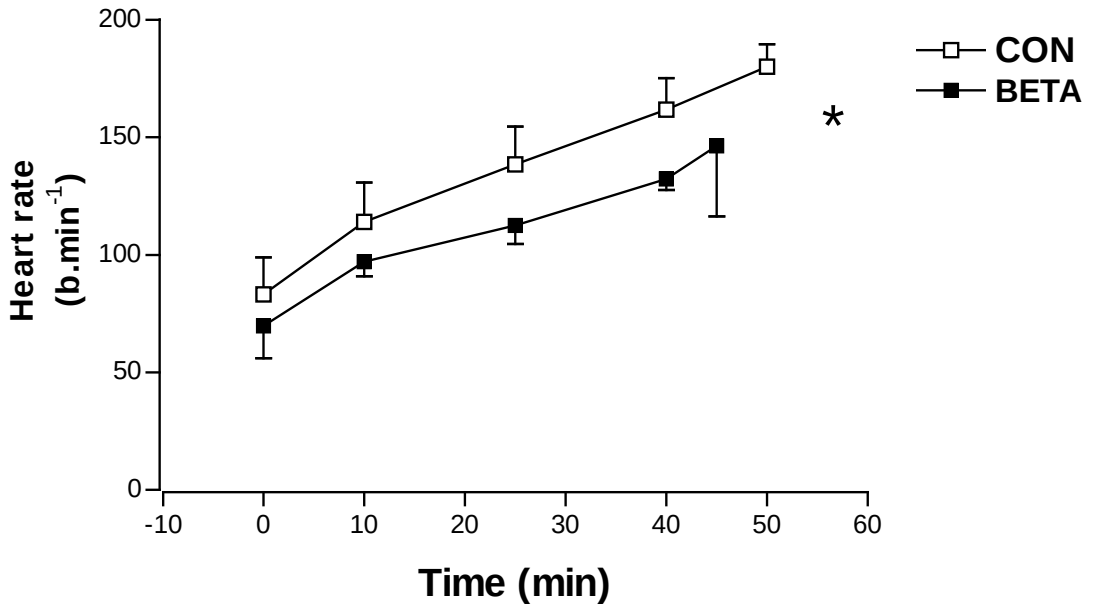
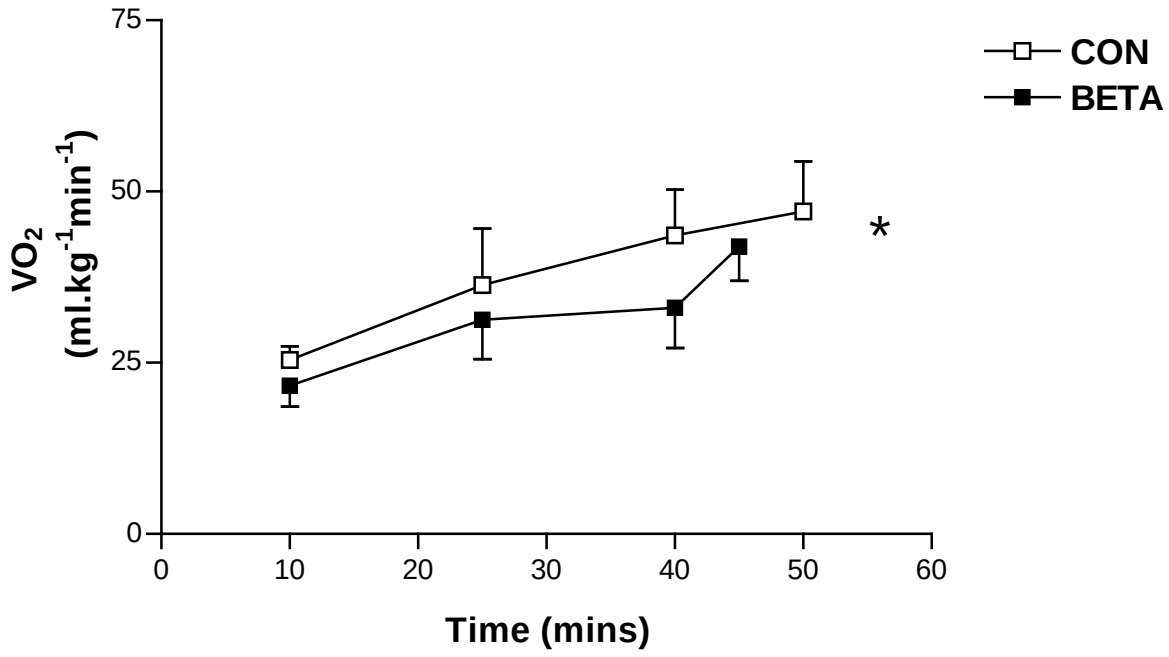


Figure 2. Heart rate values captured at rest, 10, 25, 40 mins and exhaustion during the cycle ride for the ß-blocker group (BETA) and the control group (CON) (*P < 0.05 group effect).



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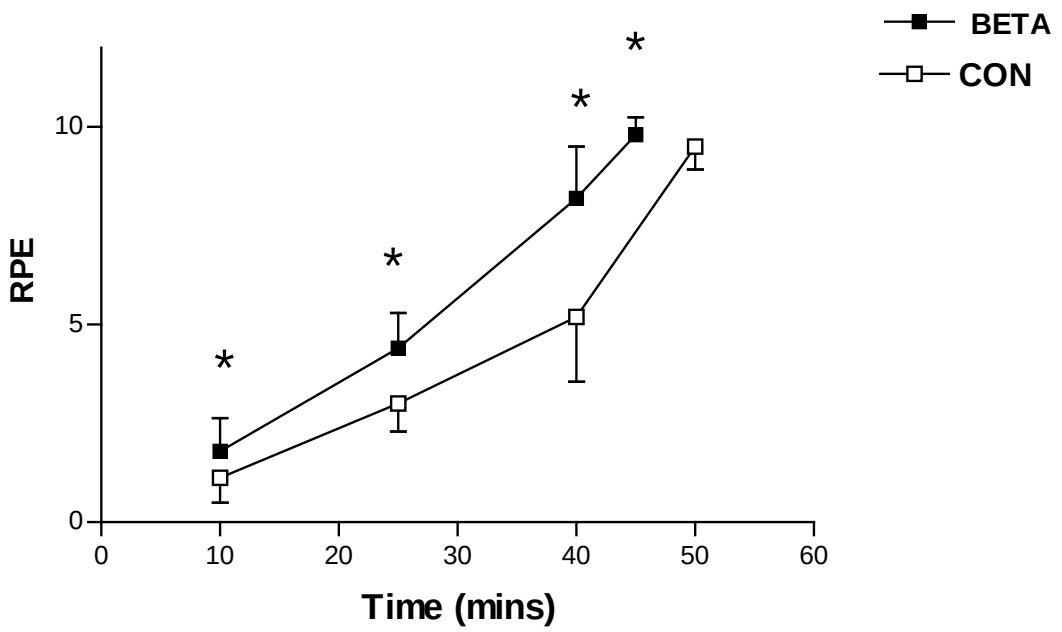


Figure 4. Rate of perceived exertion values captured at 10, 25, 40 mins and exhaustion ride for the ß-blocker group (BETA) and the control group (CON) during the cycle ride (*P < 0.01 main effect).

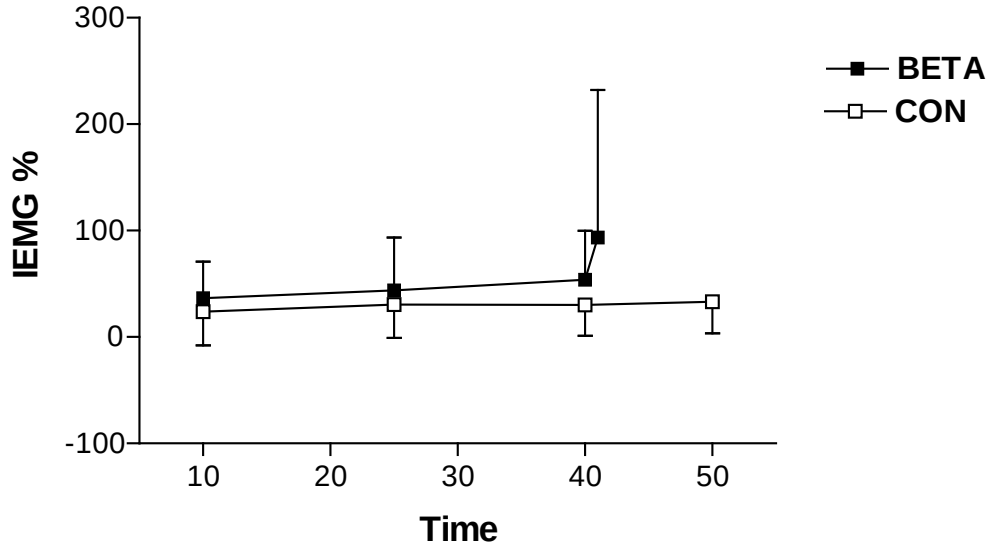


Figure 5. Mean IEMG values a normalised as a % of MVC for both BETA and CONTROL, taken at 10, 25, 40 min and exhaustion.

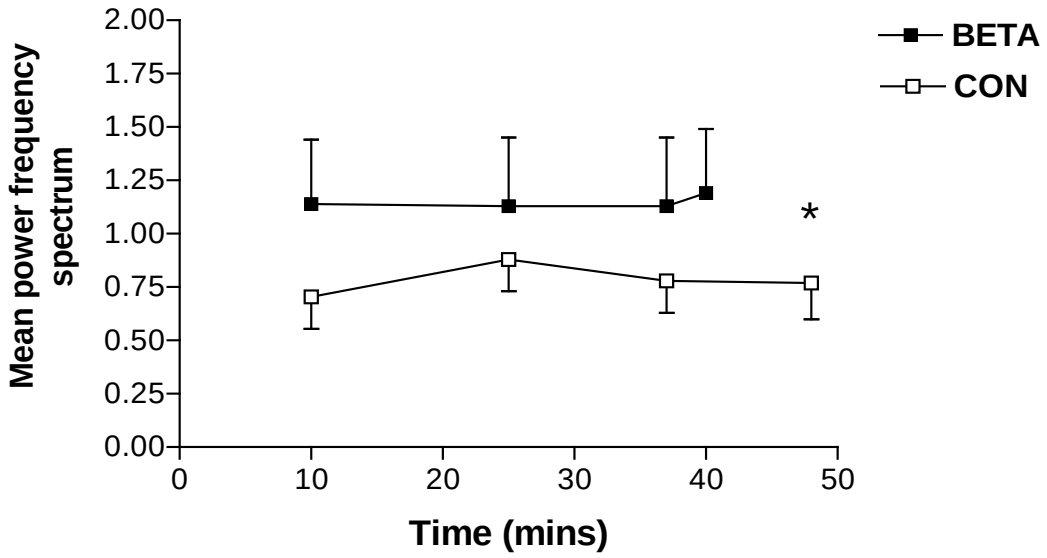
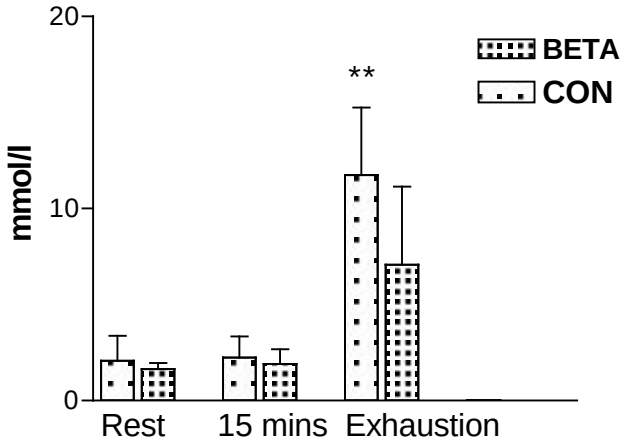


Figure 6. MPFS values normalised against MVC for both BETA and CON, taken at 10, 25, 40 mins and exhaustion. (*-P < 0.05 group effect).



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