IETI Transactions on Ergonomics and Safety

http://ieti.net/TES

2023, Volume 7, Issue 2, 18-33, DOI: 10.6722/TES.202312_7(2).0003

DORSOLATERAL PREFRONTAL CORTEX ACTIVITY IS NOT CORRELATED WITH PERIPHERAL FATIGUE, UNDER PROVOKED ISCHEMIA OF THE EXTENSOR DIGITORUM DURING TYPING

Philip Gallardo[1, a], Panagiota Karanika[1,b], Panagiota Danou[1,c] and Panagiotis V. Tsaklis[1,2,3,d]

[1]Department of Physical Education and Sport Science, ErgoMech-Lab, University of Thessaly, Trikala, Hellas

[2]Department Molecular Medicine and Surgery, Growth and Metabolism, Karolinska Institute, Solna, Sweden

[3]Center of Orthopaedics and Regenerative Medicine (C.O.RE.) / (C.I.R.I.) - Aristotle University Thessaloniki, Hellas

[a]pgallardo@uth.gr, [b]pkaranik@uth.gr, [c]giotadanou91@hotmail.com, [d]tsaklis@uth.gr

Abstract Emerging data suggest that the DLPFC is involved in several psychological and physiological processes during execution of movements, and is highly active during fatiguing muscular activity. However, it is unclear if DLPFC activity is related to peripheral fatigue developed in ischemic conditions. Thus, the purpose of this study was to evaluate the correlation between DLPFC activity and developed peripheral fatigue under provoked ischemia of the ED muscle in a repeated computer typing test. Root mean square (RMS) amplitude for the ED, total hemoglobin (tHb) concentration and the difference between oxyhemoglobin and deoxyhemoglobin (Hb_{diff}) of the DLPFC were measured and used for comparative and correlational analysis. The novel finding was that both the DLPFC activity and peripheral fatigue increased during the repeated typing test ($p<0.05$), but these changes were not correlated with each other. However, it remains to be elucidated if the duration of the typing test has a mediating effect, as we observed no plateau or drop in neither the mean DLPFC tHb or Hb_{diff} concentrations during the typing test. Having a greater understanding where and how muscle fatigue is regulated during computer typing, may help us find better strategies to prevent overuse injuries and musculoskeletal pain in the general adult's population, as more people are becoming more dependent on computers for work and in their leisure time. Hence, future studies should therefore replicate this study with a longer test duration, but also include a variety of computer tasks, to simulate how computers are used in practice among different populations.

Keywords: Muscle fatigue; electromyography; near infrared spectroscopy; musculoskeletal pain; computer typing.

1. INTRODUCTION

The prefrontal cortex (PFC) is usually associated with its key role in executive functioning, such as decision making, problem-solving, planning, and suppressing impulsive behavior [1, 2]. However, a growing body of evidence suggest that the PFC is also involved with several psychological and physiological processes during execution of movements [2–4]. One region of the PFC that has attracted a great amount of research interest lately is the dorsal lateral prefrontal cortex (DLPFC) [2, 5]. The DLPFC is one of the most recent evolved parts of the human brain [2] and has been found to play a central role for goal-driven attention [6], novelty-seeking [6], and motor planning (i.e., movement planning for achieving a goal [7, 8].

http://ieti.net/TES

2023, Volume 7, Issue 2, 18-33, DOI: 10.6722/TES.202312_7(2).0003

It is located around the anterior mid-frontal gyrus (Brodmann area 46) [8, 9] and through its functional neural network, the DLPFC is connected to various subcortical regions, including the basal ganglia [2], hippocampus [2], and thalamus [1, 2], allowing the DLPFC to effectively received sensory input, communicate with these regions and regulate their activity according to situational demands [2]. During exhaustive and fatiguing muscular activity, the primary motor cortex (M1), supplementary motor areas (SMA) and DLPFC has been shown to be highly active [1–3]. This higher activity in the M1 and SMA during exercise has been attributed to increased motor output [3, 9], as a means to compensate for fatiguing muscles, through increasing voluntary force [10]. Conversely, the activity of the DLPFC has been related to the level of internal motivation during fatiguing muscular activity [9, 11].

However, findings from neurophysiological [4, 8] and neuroimaging studies [9, 12] also suggest that the DLPFC may be involved in regulating muscle fatigue via a facilitation and inhibition system in the central nervous system (CNS), that alters the motor output from the motor cortex (i.e., M1, SMA and other motor-related areas) to the peripheral system [4]. The sensory feedback from muscle nociceptive (groups III and IV) afferents has been proposed to attenuate the descending motor output from the motor cortex during fatiguing muscular activity [10]. The group III/IV muscle afferents have been shown to be stimulated by the buildup of intramuscular metabolites [13], which at sufficiently high levels leads to muscle fatigue [13], via for instance compromising the excitation–contraction coupling mechanism in the muscle [14], and simultaneously limiting descending motor drive to the muscle, via inhibiting spinal motoneuronal output [13]. Generally, muscle fatigue can be defined as the failure to maintain a specified force output or work rate during muscular activity [15], and has indirectly been measured with electromyography (EMG)/surface electromyography (sEMG) [16] and near infrared spectroscopy (NIRS)/functional near infrared spectroscopy (fNIRS) [17], due to their convenient non-invasive methodology. The root mean square (RMS) values from the EMG amplitude (i.e., myoelectric activity) and frequency domain variables, such as median frequency and mean power frequency (MPF), are commonly used to examine muscle fatigue from the recorded EMG signal [18]. Similarly, hemodynamic variables, such as total hemoglobin (tHb), oxygenated-Hb (O_2Hb), deoxy-Hb (HHb) and the difference between O_2Hb and HHb (Hb_{diff}) from the NIRS signal are considered acceptable surrogates for brain activity [3, 19, 20], as brain activity is highly dependent on the supply of oxygen [1].

Traditionally, muscle fatigue has also been divided into two component, peripheral and central fatigue [9, 17], with peripheral fatigue referring to the biochemical and metabolic changes within working muscles leading to reduced force/power output [15], and central fatigue representing a progressive reduction in voluntary activation or descending motor drive to the muscles [15]. Since central fatigue and brain activity is highly sensitive to low brain oxygenation, monitoring changes in cerebral oxygenation has been performed to improve our understanding of the fatiguing process during exercise [1, 3]. For example, a recent NIRS study by Kojma and co-workers [3] observed that the concentration of O_2Hb and THb increased in the PFC, SMA and M1, but the increase in each hemoglobin level in the PFC during an incremental exercise was faster than the motor-related areas, suggesting that the PFC may be more involved in regulating performance and muscle fatigue during the early phase of exercise. Moreover, while there is emerging evidence that the DLPFC is related to a facilitation and inhibition system in the CNS during fatiguing muscular activity [4, 8, 9, 12] and peripheral muscle fatigue is regulated from the motor cortex [15], via the sensory feedback from group III/IV afferents [10], it is unclear if this central regulation of peripheral fatigue is correlated with the activity of the DLPFC. Common methods to activate and investigate the group III/IV muscle afferents, include inducing localized muscle pain via ischaemia, systematic chemical injections, or the use of hypertonic saline injections [15]. However, findings from *in vivo* studies conducted in mice [15] and in humans [13, 15] suggest that one subtype

IETI Transactions on Ergonomics and Safety

http://ieti.net/TES

2023, Volume 7, Issue 2, 18-33, DOI: 10.6722/TES.202312_7(2).0003

of metabosensitive group III/IV muscle afferents, called metabonociceptors, only respond to very high (painful) levels of intramuscular metabolites seen in ischemic conditions[13, 15], or following hypertonic saline infusions [15].

Noteworthy, the forearm muscles have in computer workers been reported to be predispose to localized muscle pain [21] and overuse injuries [22], and this has suggested to be related to muscle ischemia, due to prolonged periods of repetitive contractions during computer typing [23]. The extensor digitorum (ED) muscle of the forearm has commonly been studied during simulated computer work [24, 25], as it is been reported to be more susceptible to muscle fatigue than other forearm muscles during repetitive typing [26], and may also be prone to musculoskeletal pain in the adult population [27], as more people are becoming dependent on computers for work [28] and in their leisure time [27]. Furthermore, using blood flow occlusion, to acutely induce muscle ischemia, has also been found to be an effective method for rapidly developing peripheral and central fatigue [18]. For example, a study by Broxterman and colleagues [18] found that blood flow occlusion exacerbated the development of both peripheral and central fatigue, with notably lower median frequency of the right flexor digitorum superficialis, during the first two minutes of a handgrip test to exhaustion, compared to a control trial. However, the activity in DLPFC and ED muscle was not examined in this study, leaving an uncertainty if the exacerbated peripheral and central fatigue observed in ischemic conditions is correlated with the activity of the DLPFC during computer typing.

Therefore, the aim of this study was to evaluate the correlation between DLPFC activity and developed peripheral fatigue under provoked ischemia of the ED in a repeated computer typing test. Three hypotheses were proposed: 1) the mean RMS amplitude of ED will differ between the start and end of the typing test, 2) the mean DLPFC tHb and Hb_{diff} concentrations will be different between the three selected time points (0-20sec, 100-120sec, 120-140sec), and 3) the rate of change (Δ) in RMS of the ED (ΔRMS_{ED}) and mean power frequency of the ED (ΔMPF_{ED}) will be correlated, and changes in these EMG parameters will also be correlated with the changes in tHb of the DLPFC (ΔtHb_{DLPFC}) during typing with sphygmomanometer (occlusion) cuffs.

2. MATERIALS AND METHODS

2.1. Ethical Approval

All experimental protocols and procedures followed the principles of the Declaration of Helsinki and were approved by the Bioethics committee, Department of Physical Education and Sports Science, University of Thessaly.

2.2. Subjects

Healthy adult subjects (male = 3; female = 7, mean ± SD; age 30.2±2.8; body mass index 22.35± 3.35) volunteered to participate in this study after providing a written consent and completing a pre-test medical questionnaire. Additionally, the subjects were also given an oral and written explanation of the testing procedures. The subjects were free from musculoskeletal problems, had no pathological condition, were non-smokers, non-heavy drinkers and were not taking any drugs.

IETI Transactions on Ergonomics and Safety

http://ieti.net/TES

2023, Volume 7, Issue 2, 18-33, DOI: 10.6722/TES.202312_7(2).0003

Table 1. Characteristics of the subjects

Characteristics	(Value)
Age (years)	30.2 ± 2.8
Height (cm)	1.70 ± 7.0
Weight (kg)	66.6 + 14.4

Note: SD = Standard Deviation

2.3. Experimental Procedures

Subjects were instructed to refrain from any caffeinated beverages for at least 12h before the experimental testing. The experiment and the measurements lasted two days and were carried out at the Laboratory of Biomechanics and Ergonomics, ErgoMech Lab – DPESS / Physical Education and Sport Science, of University of Thessaly. One day prior to the initial testing, the subjects visited the laboratory for demonstration and familiarization of the testing procedures. The ambient temperature and relative humidity of the laboratory were maintained at 22-24°C and of 50-55%, respectively. For this study, a height adjustable office chair was used, and all subjects came into the laboratory individually. The height of the chair was adjusted to form a 90° angle with the subjects' forearm on the desk, when they were sitting on the chair. Afterwards, the subjects were instructed to repeatedly type the "A" button on keyboard of a laptop placed on the desk using only the middle finger of the right hand, and keeping their forearm stationary on the desk (see Figure 1).

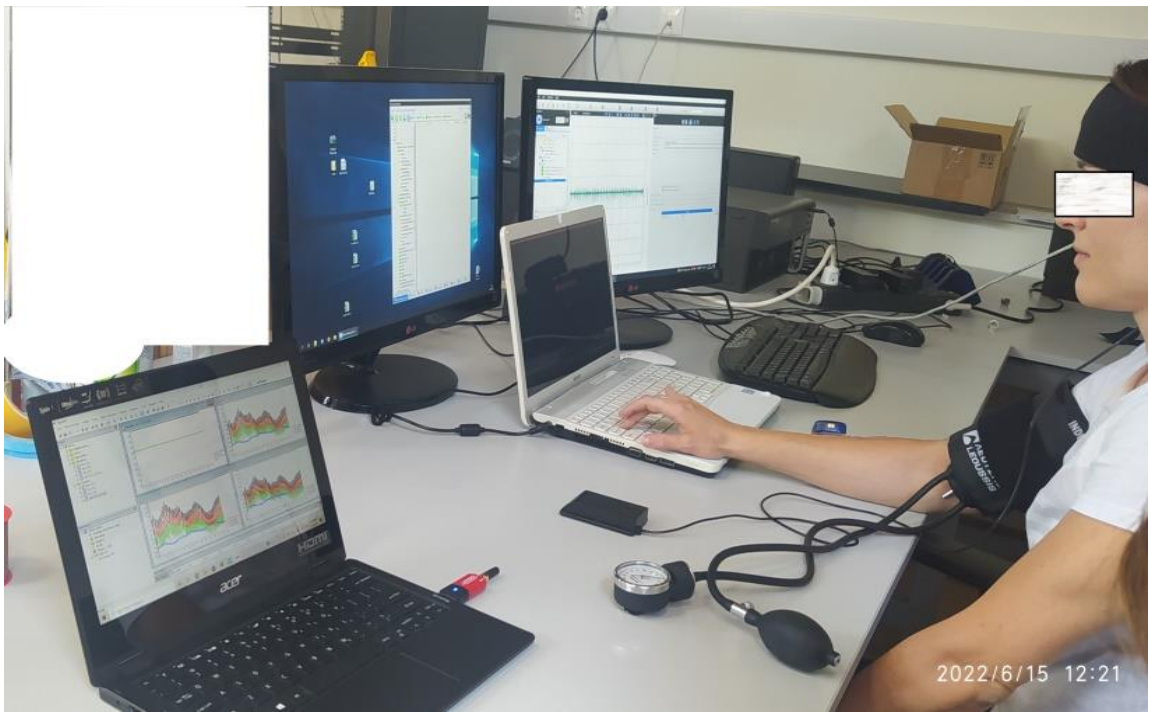

Figure 1. Collection and recording of EMG and fNIRS data during the repeated typing test.

IETI Transactions on Ergonomics and Safety

http://ieti.net/TES

2023, Volume 7, Issue 2, 18-33, DOI: 10.6722/TES.202312_7(2).0003

2.4. Fatigue Protocol and Experimental Measurements

After the described preparation, an analog sphygmomanometer (occlusion) cuff was bandaged around the brachial region of each subject's right arm, with the pump valve closed. The cuff was placed with the aim of rapidly developing a high degree of peripheral muscle fatigue in the ED via occluding brachial artery blood flow and inducing ischemia. The duration of the typing test was set for two minutes, as this has been shown to be adequate to induce both central and peripheral fatigue [16]. The subject was instructed to breathe at a normal pace, to be focused, keep their eyes on open and hold the rest of their body still, and to place the middle finger of their right hand on the "A" button. After inflating the occlusion cuff to a pressure gauge > 33mmHg, the subject was instructed to begin the test.

During the test, DLPFC hemodynamics were monitored continuously with a functional NIRS (fNIRS) device and parallelly, ED activation was monitored with sEMG. The variation in myoelectric activity of ED and DLPFC hemodynamics were quantified during the typing test (0-120s), with an additional quantification of twenty seconds after the test (120-140s) for the DLPFC hemodynamics. Throughout the test there were verbal encouragement towards the participant. At the end of the test, the subjects were instructed to stop typing and stay calm, while the pump valve were simultaneously unscrewed to release the air from the cuff. This recovery period (reperfusion phase) lasted twenty seconds and was conducted to examine the cerebral hemodynamic response pattern during acute ischemia–reperfusion in the forearm, which is a physiological state that has been linked to localized muscle pain [29] and sensitization of group III/IV afferents in mice models [29]. Subsequently, the subject was disconnected from all measuring instruments.

2.5. Electromyography (EMG)

A wireless EMG system (Myon AG, Schwarzenberg, Switzerland) was used to examine the changes in the myoelectric activity of the ED muscle. The skin was prepared, before the electrodes were applied. The sEMG bipolar electrodes were placed on the skin of the right forearm with an interelectrode distance of 20 mm and paralleled to the direction of the muscle fibers, in accordance with previous studies [24, 26]. The EMG signal was than processed and smoothened by band-pass filtering at 10-400 Hz (4^{th} order Butterworth filter). A Fast Fourier Transform (FFT) window analysis was applied to determine the cut off frequencies. Moreover, the FFT was also used to obtain the MPF. The signal amplitude of sEMG was rectified and calculated as RMS values.

Muscle fatigue of the ED was estimated and calculated as the percentage difference in RMS amplitude during the first twenty (RMS_{start}) and last twenty seconds (RMS_{end}) of the typing test. The RMS amplitude growth rate (RMS%) and the frequency drop rate (MPF%) of the ED was also calculated from the same recorded EMG signal. The MPF% was also used to confirm the presence of peripheral muscle fatigue in ED, as changes in EMG frequency domain variables are strongly associated with muscle fiber conduction velocity (MFCV) [30], which in turn has been found to be related to changes in intracellular pH, and consequently peripheral fatigue [31]. Subsequently, these signal calculations were used for statistical analysis.

IETI Transactions on Ergonomics and Safety

http://ieti.net/TES

2023, Volume 7, Issue 2, 18-33, DOI: 10.6722/TES.202312_7(2).0003

2.6. Near-Infrared Spectroscopy (NIRS)

A portable fNIRS system (Portalite, Artinis Medical Solutions, Netherlands) were applied to monitor changes in total hemoglobin (tHb) and the difference between O_2Hb and HHb [Hb_{diff} = O_2Hb –HHb] of the DLPFC. The NIRS probe was placed in the Brodmann 46 region on the right DLPFC (see Perlman and colleagues (2016)), which has been proposed to be more involved in regulating muscle fatigue [9]. Subsequently, the NIRS probe was fixed with adhesive tape and a dark elastic bandage around the head to avoid external light and artifacts. Throughout the test, brain perfusion and myoelectric activity were continuously monitored using both the fNIRS and an sEMG respectively.

In the present study, tHb was used an indicator of DLPFC activity, while the Hb_{diff} (i.e., oxygen supply vs demand) was predominately used as a marker of oxygenation in the DLPFC. This was based on previous findings suggesting that tHb reflects changes in tissue blood volume within the target area [32], and thus could be used to estimate brain activity [19] Conversely, the Hb_{diff} has been shown to be the most sensitive measure of cerebral oxygenation, as it is strongly correlated to mean arterial pressure and cerebral blood flow [20]. Hence, changes in cerebral Hb_{diff} has also been used as an indicator of brain activity during exercise [20].

2.7. Statistical Analysis

The data are presented as means ± standard deviations (SD) unless otherwise stated. The differences between the pre-test and post-test measurements were normally distributed and was checked using the Shapiro–Wilk test. To examine hypothesis 1, a paired t-tests were carried out to compare the mean RMS amplitude of the ED at the beginning (RMS_{start}) and at the end (RMS_{end}) of the typing test. Further, to examine hypothesis 2, a one-way repeated ANOVA was conducted to compare differences in the mean DLPFC tHb and Hb_{diff} concentrations for the three selected time points (0-20sec, 100-120sec, 120-140sec), respectively. If significant differences were detected, LSD was used for post-hoc analysis. In addition, Greenhouse Geisser corrections were used if the assumption of sphericity was not met. Lastly, to examine hypothesis 3, a Pearson correlation coefficient was performed to examine the correlation between the $\Delta RMS_{ED,}$ ΔMPF_{ED}, and ΔtHb_{DLPFC}, respectively. The primary data was analyzed in MATLAB® (R2015b, Mathworks Inc., Natick, MA, USA) and remaining data was analyzed using SPSS ver. 27.0 statistical program for Windows (SPSS Software, IBM Inc., Chicago, IL, USA). The level of significance was set at $p < 0.05$, with a confidence level (C.I.) set at 95%.

3. RESULTS

3.1. Myoelectric Activity and Peripheral Fatigue (Hypothesis 1)

A paired t-test revealed that there was a significant difference in the average RMS amplitude of the ED from the start to the end of the repeated test, $t(9) = -6.083$, $p<.001$. The mean RMS_{start} was significantly lower (M =.172, SD = .050) compared to the mean RMS_{end} (M = .396, SD = .140), mean difference = -.224, 95% CI [-.307, -.140] (see Figure 2). The mean RMS% of the ED increased during the typing test by 53.7%, while the mean MPF% decreased by 56,6% (see Figure 3).

IETI Transactions on Ergonomics and Safety

http://ieti.net/TES

2023, Volume 7, Issue 2, 18-33, DOI: 10.6722/TES.202312_7(2).0003

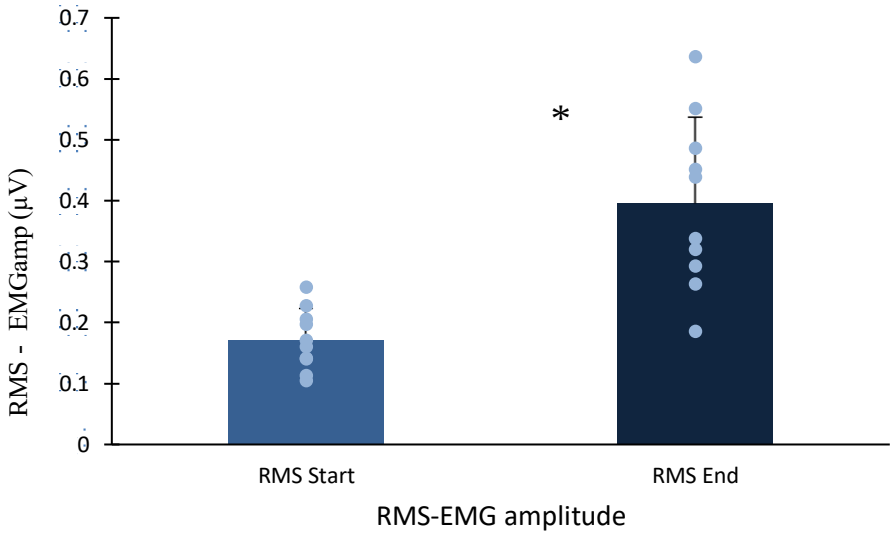

Figure 2. Bar graph (with subject data points) of the mean differences in the myoelectric response between the first and last twenty seconds of the typing test. * = p<.001 compared to the first twenty seconds of the test.

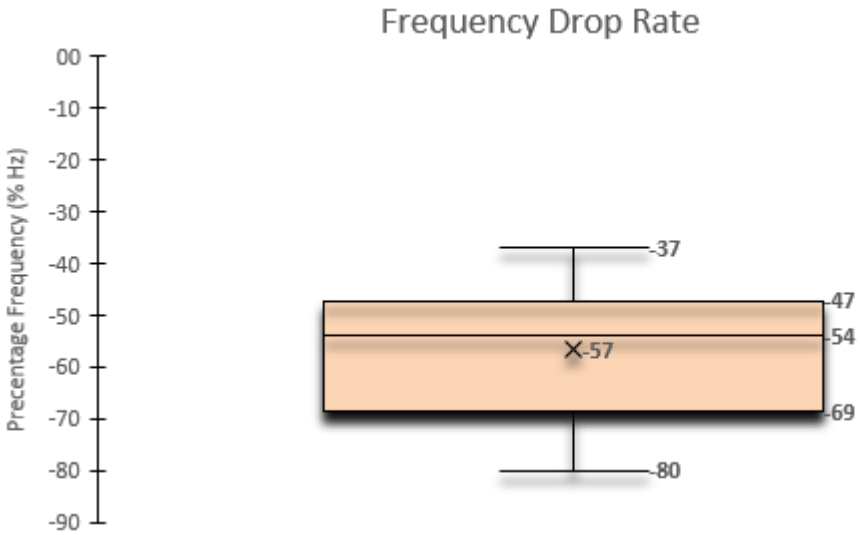

Figure 3. Descriptive statistical characteristics of the frequency drop rate (MPF%) of the ED, calculated from the recorded EMG signals (0-20sec, 100-120sec).

3.2. Cerebral Hemodynamics (Hypothesis 2)

3.2.1. Changes in DLPFC tHb (brain activity)

A one-way repeated ANOVA test determined that mean DLPFC tHb concentration differed statistically significantly between all-time points, F(2,18)=9.598, p<.001. Post hoc analysis revealed that the tHb concentration was significantly higher in the last twenty seconds of the typing test (M =2.031, SD = 1.060) compared to the first twenty seconds (M =.811, SD = .25), mean difference = 1.221, 95% CI [.379, 2.063], p

IETI Transactions on Ergonomics and Safety

http://ieti.net/TES

2023, Volume 7, Issue 2, 18-33, DOI: 10.6722/TES.202312_7(2).0003

= .010, and twenty seconds after the test (M = 1.812, SD = .989), mean difference = .214, 95% CI [.123, .305], p <.001. Additionally, the tHb concentration was significantly higher twenty seconds after the typing test, compared to the first twenty seconds of the test, mean difference = 1.007, 95% CI [.205, 1.808], p =.019. The above results are presented in Figure 4.

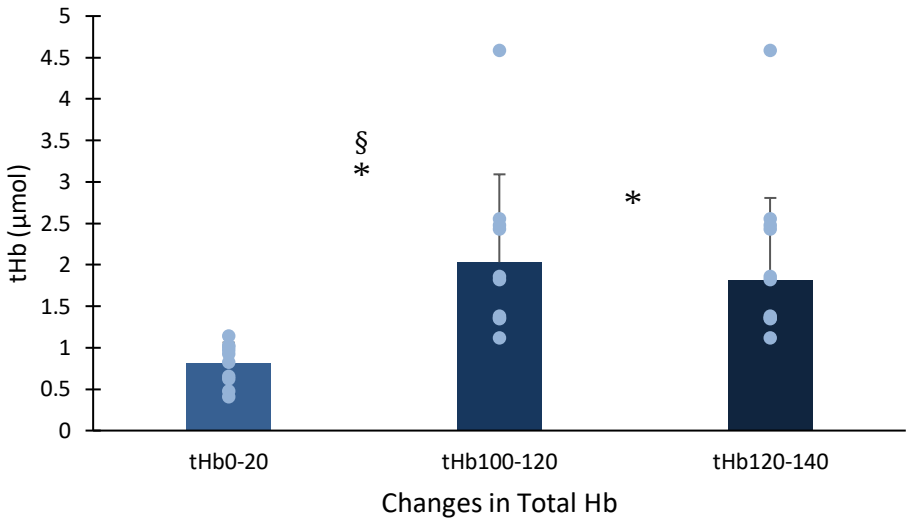

Figure 4. Bar graph (with subject data points) of the mean differences in the tHb response pattern during the test, with cuff-induced ischemia (tHb0-20, tHb100-120) and during acute ischemia–reperfusion (tHb100-120, tHb120-140). * = p<.05 compared to tHb0-20; § = p<.05 compared to tHb120-140.

3.2.2. Changes in DLPFC Hb_{diff} (Cerebral Oxygenation)

A one-way repeated ANOVA test showed that mean DLPFC Hb_{diff} concentration differed statistically significantly between the time points, F(2,18)=22.382, p<.001. Post hoc analysis revealed that the Hb_{diff} concentration was significantly lower in the first twenty seconds of the typing test (M =.348, SD = .458) compared to the last twenty seconds (M =2.827, SD = 1.6), -2.479, 95% CI [-3.588, -1.371], p <.001, and twenty seconds after the test (M = 2.758, SD = 1.734), mean difference = -2.410, 95% CI [-3602, -1.219], p <.001. There were no significant differences between the last twenty seconds of the typing test and twenty seconds after the test, mean difference = .069, 95% CI [-.223, .362], p =.605. The results are presented in Figure 5.

3.3. Relationship Between EMG and Cerebral Hemodynamic Responses (Hypothesis 3)

The Pearson correlation coefficient revealed that there was no relationship between the ΔRMS_{ED}, the ΔMPF_{ED}, and the ΔtHb_{DLPFC} respectively during the typing test with occlusion cuffs (p> .05). Specifically, the ΔRMS_{ED} had no correlation with ΔMPF_{ED} (r=.168, p=.643), and ΔtHb_{DLPFC} (r=.316, p=.374). Further, the ΔMPF_{ED} had no correlation with ΔtHb_{DLPFC} (r=.-379, p=.280).

IETI Transactions on Ergonomics and Safety

http://ieti.net/TES

2023, Volume 7, Issue 2, 18-33, DOI: 10.6722/TES.202312_7(2).0003

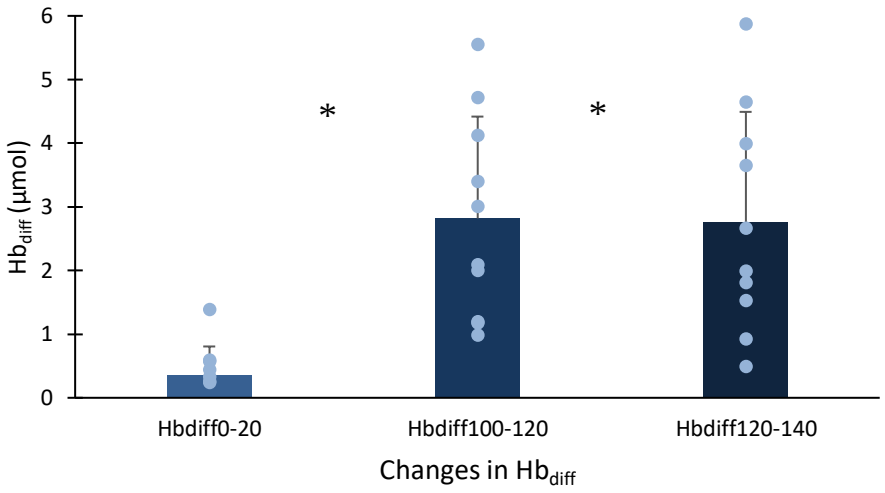

Figure 5. Bar graph (with subject data points) of the mean differences in the Hb_{diff} response pattern during the test, with cuff-induced ischemia (Hb_{diff}0-20, Hb_{diff}100-120) and during acute ischemia–reperfusion (Hb_{diff}100-120, Hb_{diff}120-140). * = p<.001 compared to Hb_{diff}0-20.

4. DISCUSSION

The purpose of this study was to evaluate the correlation between DLPFC activity and developed peripheral fatigue under provoked ischemia of the ED muscle in a repeated computer typing test. The main findings were that myoelectric activity of the ED muscle increased from the start to the end of the typing test with occlusion cuffs, and there was a concomitant drop in MPF (see figure 2-3), confirming the presence of peripheral fatigue. In addition, the concentration of tHb and Hb_{diff} was significantly higher in the DLPFC during the typing test (see figure 4-5), indicating an increased brain activity. However, a drop was seen in the tHb concentration immediately after the typing test, compared to the last twenty seconds during the test, inferring a decreased DLPFC activity after the typing test (reperfusion phase of the ED). Additionally, no correlation was observed between the rate of change in EMG parameters (ΔRMS_{ED} and ΔMPF_{ED}) and ΔtHb_{DLPFC} during typing with occlusion, indicating that central regulation of peripheral fatigue, via the sensory feedback from group III/IV afferents, may not be correlated with fluctuations in DLPFC activity.

4.1. Hypothesis 1: Electromyographic Activity During Typing

The findings support hypothesis 1, with differences in mean RMS amplitude of ED from the start to the end of the typing test. The mean RMS_{end} amplitude of the ED was significantly higher compared to the mean RMS_{start} (see figure 2), and there was also a notable decline in the MPF% of the ED during the typing test with occlusion cuffs (see figure 3). Specifically, the RMS% increased on average by 53.7%, while the MPF% of the ED decreased on average by 56,6%. This infers that the repetitive contractions from the typing test with occlusion upregulated motor unit activity (i.e., increased recruitment of additional motor units and firing rate) [33, 34] and decreased muscle fiber conduction velocity [30] of the ED muscle, confirming the presence of peripheral muscle fatigue [31]. This is in line with previous studies, reporting an increase in myoelectric activity of the ED muscle during simulated computer work [24, 25], a decline in MPF during repetitive

contractions [35], and that blood flow occlusion is an effective method for rapidly developing peripheral muscle fatigue [18].

4.2. Hypothesis 2: Cerebral Hemodynamic Responses During Typing

The findings partially confirmed hypothesis 2, with significant differences in mean DLPFC tHb and Hb_{diff} concentrations between the three selected time points (0-20sec, 100-120sec, 120-140sec). A significant increase in the mean tHb and Hb_{diff} concentrations was noted between the first two selected time points (0-20sec, 100-120sec), but also between the first and last time point (0-20sec, 120-140sec) respectively (see figures 4-5), which supports the hypothesis. However, no differences were observed for the Hb_{diff} concentration between the second and the third time point (Hb_{diff}100-120, Hb_{diff}120-140) (see figures 5), while the tHb concentration dropped significantly in the last time point (tHb120-140) compared to the second time point (tHb100-120) (see figures 4), which rejects the hypothesis.

These findings suggests that the DLPFC activity was elevated during the typing test itself (0-20sec, 100-120sec), presumably via an increased cerebral blood volume [32], cerebral oxygenation and greater cerebral blood flow [20], but it also suggests that the cerebral blood volume in the DLPFC acutely decreased after the typing test (Hb_{diff}100-120, Hb_{diff}120-140), inferring a reduced DLPFC activity [19]. This supports previous findings suggesting that PFC cerebral blood volume and activity of different PFC regions tends to increase during exercise from low to moderate intensity [1, 20], up to maximal intensity [3], but then rapidly decrease during the recovery period after maximal intensity exercise [1]. This has been attributed to a reduction in oxygenation (reflected by higher increase HHb, relative tHb and O_2Hb) during near maximal exercise intensities in the PFC [1]. This may therefore explain the observed decline in DLPFC tHb concentration between the last time point, compared to the second time point in the present study (tHb120-140, tHb100-120, see figure 4).

Furthermore, there was no change in the Hb_{diff} concentration after the typing test, compared to the last twenty seconds during the test (Hb_{diff}100-120, Hb_{diff}120-140, see figure 5), inferring that the cerebral blood flow and oxygenation in the in the DLPFC was higher after the test. Based on previous work, this could be interpreted as the DLPFC activity remained greater after the typing test, as a higher cerebral blood flow and oxygenation reflects increased brain activity [1, 20, 32]. However, it has been proposed that Hb_{diff} may predominantly be a good indicator of oxygenation when the tHb concentration is stable over time, as it seems to reflects cerebral blood flow better in these conditions [32].

Since, the tHb concentration fluctuated during the last twenty seconds of the test, compared to after the typing test, this signifies that the Hb_{diff} concentration may not have been the best representative of DLPFC oxygenation in the present study, and evaluating the O_2Hb concentration may have instead yielded slightly more accurate results. In addition, O_2Hb are also more frequently used as an indicator of PFC oxygenation [3, 32]. Although, there also NIRS findings indicating the Hb_{diff} concentration can detect differences in DLPFC oxygenation not observed by O_2Hb alone, specifically during intense muscular effort [1], which justifies the use of the Hb_{diff} concentration to estimate DLPFC oxygenation in this study. This therefore demonstrates that the discrepancy in findings between different studies could partially be attributed to the hemodynamic parameter used to assess brain activity, as tHb, Hb_{diff}, and O_2Hb have all been used as a surrogate for brain activity during fatiguing muscular activity [1, 19, 20].

IETI Transactions on Ergonomics and Safety

http://ieti.net/TES

2023, Volume 7, Issue 2, 18-33, DOI: 10.6722/TES.202312_7(2).0003

4.3. Hypothesis 3: Correlation Between Electromyographic Responses and Cerebral Hemodynamic Responses During Typing

The findings do not support hypothesis 3, with ΔRMS_{ED} and ΔMPF_{ED} being correlated, and these EMG parameters being correlated with ΔtHb_{DLPFC} during typing with occlusion cuffs. Specifically, this study found no correlation between ΔRMS_{ED} and ΔMPF_{ED}, nor any correlation between ΔRMS_{ED} and ΔtHb_{DLPFC} , or ΔMPF_{ED} and ΔtHb_{DLPFC}. These findings suggest that the increases in RMS amplitude of ED muscle and decreases in MPF, during typing in ischemic conditions were not correlated.

Based on previous EMG research, these findings are not totally unreasonable [36], as conflicting results have frequently been reported in regards to the correlation between the EMG amplitude and MPF [33, 36]. Since there is a strong correlation between RMS amplitude and muscle force [33], many studies have instead examined the correlation between changes in muscle force and MPF [33, 36], and found an positive correlation [37], no differences [38, 39] and a negative correlation [33]. Several reasons have been proposed to explain these inconsistencies, including inter-individual differences in muscle fiber-type proportions, [40], electrode size and configuration [33], thickness of the skinfold [33, 38] and the epoch length used for signal analysis [41], which may inadvertently explain the lack of correlations between the ΔRMS_{ED} and ΔMPF_{ED} in the present study.

Additionally, there is also growing evidence that performing repetitive contractions with blood flow occlusion may independently alter the EMG response pattern [18]. For instance, a study by Broxterman et al. and co-workers (2015) compared the effect of repetitive hand grip contractions to exhaustion with or without blood flow occlusion and examined the corresponding EMG response in each condition. The author found that the RMS amplitude of the flexor digitorum superficialis increased similarly in both conditions, but the drop in median frequency was exacerbated during the first two minutes of the repetitive test in the occluded condition. Hence, there is a possibility that the ΔMPF_{ED} dropped too severe and quick in the present study for it to be correlated with ΔRMS_{ED}

This proposition is further supported by experimental findings showing that the ED muscle is more susceptible to muscle fatigue, compared to the flexor digitorum superficialis during repetitive typing [26], hence we can speculate that the repetitive typing test with occlusion cuffs in the present study may have exacerbated the drop in ΔMPF_{ED}. Moreover, we also found that neither the increase in ΔRMS_{ED} nor the decrease in ΔMPF_{ED}, were correlated with elevated concentrations in ΔtHb_{DLPFC} in the present study. This implies that the central regulation of voluntary performance and peripheral fatigue, related to the sensory feedback from group III/IV afferents, may not be correlated with fluctuations in DLPFC activity.

Based on previous neuroimaging and NIRS research, this may in part be explained by differences in duration protocol [3, 34], the intensity [1, 3] and the type of contractions [34] used in different studies. For instance, a neuroimaging study by Liu and colleagues [34] compared the neural activity of different cortical areas during sustained and repetitive (intermittent) hand grip contractions at submaximal intensities. The authors found that the activity of the PFC increased and remained stable only after two minutes in the sustained condition, while it increased and started decline only after 10 min in the repetitive condition. Noteworthy, the authors also observed a concomitant increase in the activity of M1, as the activity of PFC dropped in the repetitive condition. Thus, this signifies that the lack of correlation between the ΔRMS_{ED} and the ΔtHb_{DLPFC}, or the ΔMPF_{ED} and the ΔtHb_{DLPFC}, in the present study may be related to the short duration of the typing test.

http://ieti.net/TES

2023, Volume 7, Issue 2, 18-33, DOI: 10.6722/TES.202312_7(2).0003

Moreover, there is also growing evidence that the DLPFC may be more sensitive to exercise intensity compared to other PFC regions [1] and brain areas [42]. For example, a NIRS study by Tempest and co-workers [1] noted that the activity of all PFC regions increased from below ventilatory threshold to the ventilatory threshold (i.e., low to moderate intensity), but the activity only started to decline in dorsal regions of the PFC (including the DLPFC) at the respiratory compensation point (near maximal exercise intensity). Intriuingly, the authors showed that the changes in tHb and O_2Hb in the dorsal regions of the PFC reached a plateau and remained stable from the compensation point to the end of exercise, while the Hb_{diff} concentration started to decrease.

As we observed no plateau or drop in neither the mean DLPFC tHb or Hb_{diff} concentrations during the typing test (see figure 4-5), this further strengthens the proposition that the duration of typing test may have been too short in this study for a reduced DLPFC activity to be observed, but also to correlate with the regulation of peripheral fatigue, via the sensory feedback from the group III/IV afferents. Additionally, the inherent limitations with using fNIRS for studying cerebral hemodynamics (e.g., inter-individual differences in skull thickness [43] and the interference from scalp-hemodynamics [44]) and using sEMG for assessing muscle function and fatigue (e.g. inter-individual differences in muscle architecture and morphology [33, 40] and the susceptibility to signal artifacts [45]) could also have contributed to the lack of correlations between the sEMG parameters and the DLPFC tHb concentration in this study.

However, other researchers have speculated that the afferent signal from reduced PFC oxygenation may also influence central motor output during intense muscular effort [46], via impacting the decision to stop exercising [47]. Although this has only been proposed to be one of many afferent signals influencing motor output during fatiguing muscular activity [46]. Therefore, the present findings may simply signify that the DLPFC are not involved in regulating peripheral muscle fatigue via the group III/IV afferent feedback. To the best of our knowledge, this is the first study that have examined the correlation between DLPFC activity and peripheral muscle fatigue in provoked ischemic conditions during a repetitive typing test. Although no correlation was observed between any measure, an increased involvement of the DLPFC was seen during the typing test (see figure 4-5).

Hence, this study may nevertheless provide new insight in neurophysiological research, pain science and ergonomics. However, as DLPFC activation has been linked with mental fatigue [48], cognitive ability [49], subjective perceived effort [5], and internal motivation [9, 48], more research is certainly needed to understand how these factor might influence DLPFC activity during repetitive computer typing, in addition to how they may relate to the development of muscle fatigue in ischemic conditions.

4.4. Limitations and Future Recommendations

Three key limitations must be considered when interpreting the findings in this study. Firstly, we had no control trial in this study (repeated typing test without occlusion cuffs). This makes it difficult to formulate an unambiguous conclusion regarding the correlation between DLPFC activity and peripheral fatigue during transient muscle ischemia, as the DLPFC could be confounded by several psychological and physiological processes. Secondly, we only measure the right side of the DLPFC, and thus it remains unclear how repeated typing with occlusion cuffs affects the whole DLPFC. However, as the right DLPFC have been found to be more involved during fatiguing muscular effort, this probably had a minor effect on our findings. Thirdly, no

psychological parameters were examined, which leaves an uncertainty of how these factors may have influenced the EMG and cerebral hemodynamic response in the present study. While the purpose of this study was to evaluate the correlation between DLPFC activity and developed peripheral fatigue under provoked ischemia of the ED muscle, we can't dismiss the possibility that the motivational levels (or other psychological factors) of the subjects may have influenced the DLPFC activity during the typing test, since we had no control trial.

Furthermore, future studies should also investigate how the DLPFC activity is related to mental fatigue and cognitive ability during simulated computer work, as the present findings suggest that the activity of DLPFC are increased during repetitive computer typing. Although it has been recommended to break up prolonged sedentary time at least every 60 minutes [50], it is unclear if taking several smaller breaks can also help to maintain a higher mean level of DLPFC activity in computer workers. Based on previous reports [51], knowing this may potentially save employers and companies billions of dollars each year, by helping their employees to maintain a higher average cognitive ability, and consequently improving their productivity at work.

5. CONCLUSION

The present study supports previous findings suggesting an increased involvement of the DLPFC during fatiguing muscular activity. However, this study also indicates that central regulation of peripheral fatigue, via the sensory feedback from group III/IV afferents, may not be reflected by fluctuations in DLPFC activity. Moreover, it remains to be elucidated if the duration of the repetitive typing has a mediating effect, as we observed no plateau or drop in neither the mean DLPFC tHb or Hb_{diff} concentrations during the typing test. Having a greater understanding where and how muscle fatigue is regulated in the body, may help us find better strategies for managing and preventing musculoskeletal pain in the general adult population, as a growing number of people are becoming more dependent on computer for work and in their leisure time. Future studies should therefore replicate this study with a longer test duration, but also include different computer tasks, to simulate how computers are used in practice among different populations.

References

[1] Tempest GD, Eston RG, Parfitt G., 2014, Prefrontal cortex haemodynamics and affective responses during exercise: a multi-channel near infrared spectroscopy study, *PLoS One*, 9: e95924.

[2] Bigliassi M, Filho E., 2022, Functional significance of the dorsolateral prefrontal cortex during exhaustive exercise. *Biol Psychol*, 175, 108442.

[3] Kojima S, Morishita S, Hotta K, et al. 2022, Temporal changes in cortical oxygenation in the motor-related areas and bilateral prefrontal cortex based on exercise intensity and respiratory metabolism during incremental exercise in male subjects: A near-Infrared spectroscopy study, *Front Physiol*, 13, 794473.

[4] Vila-Villar A, Naya-Fernández M, Madrid A, et al., 2022, Exploring the role of the left DLPFC in fatigue during unresisted rhythmic movements, *Psychophysiology*, 59, e14078.

[5] Angius L, Santarnecchi E, Pascual-Leone A, et al., 2019, Transcranial Direct Current Stimulation over the Left Dorsolateral Prefrontal Cortex Improves Inhibitory Control and Endurance Performance in Healthy Individuals, *Neuroscience*, 419, 34–45.

[6] Jones DT, Graff-Radford J., 2021, Executive Dysfunction and the Prefrontal Cortex, *Continuum (Minneap Minn)*, 27, 1586–1601.

[7] Caplan D., 2006, Why Is Broca'S Area Involved in Syntax? *Cortex*, 42, 469–471.
[8] Hasan A, Galea JM, Casula EP, et al., 2013, Muscle and timing-specific functional connectivity between the dorsolateral prefrontal cortex and the primary motor cortex, *J Cogn Neurosci*, 25, 558–570.
[9] Tanaka M, Ishii A, Watanabe Y., 2016, Roles of the right dorsolateral prefrontal cortex during physical fatigue: a magnetoencephalographic study, *Fatigue: Biomedicine, Health & Behavior*, 4, 146–157.
[10] Amann M., 2012, Significance of Group III and IV muscle afferents for the endurance exercising human, *Clin Exp Pharmacol Physiol*, 39, 831–835.
[11] Robertson CV, Marino FE., 2016, A role for the prefrontal cortex in exercise tolerance and termination, *J Appl Physiol (1985)*, 120, 464–466.
[12] Rowe JB., 2004, The Prefrontal Cortex shows Context-specific Changes in Effective Connectivity to Motor or Visual Cortex during the Selection of Action or Colour, *Cerebral Cortex*, 15, 85–95.
[13] Pollak KA, Swenson JD, Vanhaitsma TA, et al., 2014, Exogenously applied muscle metabolites synergistically evoke sensations of muscle fatigue and pain in human subjects: Synergistic metabolites evoke muscle pain and fatigue, *Experimental Physiology*, 99, 368–380.
[14] Blain GM, Mangum TS, Sidhu SK, et al., 2016, Group III/IV muscle afferents limit the intramuscular metabolic perturbation during whole body exercise in humans: Muscle afferents limit metabolic perturbation, *J Physiol*, 594, 5303–5315.
[15] Taylor JL, Amann M, Duchateau J, et al., 2016, Neural Contributions to Muscle Fatigue: From the Brain to the Muscle and Back Again, *Medicine & Science in Sports & Exercise*, 48, 2294–2306.
[16] Schillings ML, Hoefsloot W, Stegeman DF, et al., 2003, Relative contributions of central and peripheral factors to fatigue during a maximal sustained effort, *Eur J Appl Physiol*, 90, 562–568.
[17] Urquhart EL, Wanniarachchi H, Wang X, et al., 2019, Mapping cortical network effects of fatigue during a handgrip task by functional near-infrared spectroscopy in physically active and inactive subjects, *Neurophoton*, 6(4):045011. doi: 10.1117/1.NPh.6.4.045011.
[18] Broxterman RM, Craig JC, Smith JR, et al., 2015, Influence of blood flow occlusion on the development of peripheral and central fatigue during small muscle mass handgrip exercise, *J Physiol*, 593, 4043–4054.
[19] Krieger SN, Streicher MN, Trampel R, et al., 2012, Cerebral blood volume changes during brain activation, *J Cereb Blood Flow Metab*, 32, 1618–1631.
[20] Moriarty T, Bourbeau K, Bellovary B, et al., 2019, Exercise Intensity Influences Prefrontal Cortex Oxygenation during Cognitive Testing, *Behavioral Sciences*, 9(8):83. doi: 10.3390/bs9080083.
[21] Kaliniene G, Ustinaviciene R, Skemiene L, et al., 2016, Associations between musculoskeletal pain and work-related factors among public service sector computer workers in Kaunas County, Lithuania, *BMC Musculoskelet Disord*, 17(1):420. doi: 10.1186/s12891-016-1281-7.
[22] Green RA, Briggs CA., 1989, Effect of overuse injury and the importance of training on the use of adjustable workstations by keyboard operators, *J Occup Med*, 31, 557–562.
[23] Murphy B, Dawson N., 2002, The effects of repetitive contractions and ischemia on the ability to discriminate intramuscular sensation, *Somatosensory & Motor Research*, *1*9, 191–197.
[24] Birch L, Juul-Kristensen B, Jensen C, et al., 2000, Acute response to precision, time pressure and mental demand during simulated computer work, *Scand J Work Environ Health*, 26, 299–305.
[25] Blangsted AK, Hansen K, Jensen C., 2003, Muscle activity during computer-based office work in relation to self-reported job demands and gender, *Eur J Appl Physiol*, 89, 352–358.
[26] Lin M-I, Liang H-W, Lin K-H, et al., 2004, Electromyographical assessment on muscular fatigue—an elaboration upon repetitive typing activity, *Journal of Electromyography and Kinesiology*,14, 661–669.
[27] Gustafsson E, Johnson PW, Hagberg M., Thumb postures and physical loads during mobile phone use – A comparison of young adults with and without musculoskeletal symptoms, *Journal of Electromyography and Kinesiology*, 2010, 20, 127–135.
[28] Quemelo PRV, Vieira ER., 2013, Biomechanics and performance when using a standard and a vertical computer mouse, *Ergonomics*, 56, 1336–1344.

2023, Volume 7, Issue 2, 18-33, DOI: 10.6722/TES.202312_7(2).0003

[29] Ross JL, Queme LF, Lamb JE, et al., 2018, Interleukin 1β inhibition contributes to the antinociceptive effects of voluntary exercise on ischemia/reperfusion-induced hypersensitivity, *Pain,* 159, 380–392.

[30] Boccia G, Dardanello D, Tarperi C, et al., 2017, Decrease of muscle fiber conduction velocity correlates with strength loss after an endurance run, *Physiol Meas,* 38, 233–240.

[31] Beretta-Piccoli M, D'Antona G, Barbero M, et al., 2015, Evaluation of Central and Peripheral Fatigue in the Quadriceps Using Fractal Dimension and Conduction Velocity in Young Females, *PLoS ONE,* 10: e0123921.

[32] Rupp T, Perrey S., 2007, Prefrontal cortex oxygenation and neuromuscular responses to exhaustive exercise, *Eur J Appl Physiol,* 102, 251–251.

[33] Karlsson S, Gerdle B. 2001, Mean frequency and signal amplitude of the surface EMG of the quadriceps muscles increase with increasing torque — a study using the continuous wavelet transform, *Journal of Electromyography and Kinesiology,* 11, 131–140.

[34] Liu JZ, Shan ZY, Zhang LD, et al. 2003, Human brain activation during sustained and intermittent submaximal fatigue muscle contractions: an FMRI study, *J Neurophysiol,* 90, 300–312.

[35] Potvin JR, Bent LR., 1997, A validation of techniques using surface EMG signals from dynamic contractions to quantify muscle fatigue during repetitive tasks, *Journal of Electromyography and Kinesiology,* 7, 131–139.

[36] Roman-Liu D., 2016, The influence of confounding factors on the relationship between muscle contraction level and MF and MPF values of EMG signal: a review, *Int J Occup Saf Ergon,* 22, 77–91.

[37] Thongpanja S, Phinyomark A, Phukpattaranont P, et al., 2013, Mean and Median Frequency of EMG Signal to Determine Muscle Force based on Time-Dependent Power Spectrum, *ElAEE,* 19, 51–56.

[38] Bilodeau M, Arsenault AB, Gravel D, et al., 1990, The influence of an increase in the level of force on the EMG power spectrum of elbow extensors, *Eur J Appl Physiol Occup Physiol,* 1990, 61, 461–466.

[39] Petrofsky J, Laymon M., 2005, Muscle temperature and EMG amplitude and frequency during isometric exercise, *Aviat Space Environ Med,* 76, 1024–1030.

[40] Pincivero DM, Campy RM, Salfetnikov Y, et al., 2001, Influence of contraction intensity, muscle, and gender on median frequency of the quadriceps femoris, *Journal of Applied Physiology,* 90, 804–810.

[41] Keenan KG, Valero-Cuevas FJ., 2008, Epoch length to accurately estimate the amplitude of interference EMG is likely the result of unavoidable amplitude cancellation, *Biomed Signal Process Control,* 3, 154–162.

[42] Fontes EB, Bortolotti H, Grandjean Da Costa K, et al., 2020, Modulation of cortical and subcortical brain areas at low and high exercise intensities, *Br J Sports Med,* 54, 110–115.

[43] Antonakakis M, Schrader S, Aydin U, et al., 2020, Inter-Subject Variability of Skull Conductivity and Thickness in Calibrated Realistic Head Models, *NeuroImage,* 223, 117353.

[44] Sato T, Nambu I, Takeda K, et al., 2016, Reduction of global interference of scalp-hemodynamics in functional near-infrared spectroscopy using short distance probes, *NeuroImage,* 141, 120–132.

[45] Ostensvik T, Belbo H, Veiersted KB., 2019, An automatic pre-processing method to detect and reject signal artifacts from full-shift field-work sEMG recordings of bilateral trapezius activity, *Journal of Electromyography and Kinesiology,* 46, 49–54.

[46] De Wachter J, Proost M, Habay J, et al., 2021, Prefrontal Cortex Oxygenation During Endurance Performance: A Systematic Review of Functional Near-Infrared Spectroscopy Studies, *Front Physiol,* 12: 761232.

[47] Amann M, Romer LM, Subudhi AW, et al., 2007, Severity of arterial hypoxaemia affects the relative contributions of peripheral muscle fatigue to exercise performance in healthy humans, *J Physiol,* 581, 389–403.

[48] Muller T, Apps MAJ., 2019, Motivational fatigue: A neurocognitive framework for the impact of effortful exertion on subsequent motivation, *Neuropsychologia,* 123, 141–151.

[49] Yanagisawa H, Dan I, Tsuzuki D, et al., 2010, Acute moderate exercise elicits increased dorsolateral prefrontal activation and improves cognitive performance with Stroop test, *Neuroimage,* 50, 1702–1710.

2023, Volume 7, Issue 2, 18-33, DOI: 10.6722/TES.202312_7(2).0003

[50] Starkoff BE, Lenz EK., 2015, BREAK IT UP: Improving Health by Breaking Up Continuous Bouts of Sedentary Behavior, *ACSM'S Health & Fitness Journal,* 19, 14–19.

[51] Stewart WF, Ricci JA, Chee E, et al., 2003, Lost Productive Work Time Costs From Health Conditions in the United States: Results From the American Productivity Audit, *Journal of Occupational and Environmental Medicine,* 45, 1234–1246.

[52] Perlman SB, Huppert TJ, Luna B., 2016, Functional Near-Infrared Spectroscopy Evidence for Development of Prefrontal Engagement in Working Memory in Early Through Middle Childhood, *Cereb Cortex,* 26, 2790–2799.