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Effect of mental fatigue on induced tremor in human knee extensors.

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Key words: mental fatigue, tremor, stretch reflex, loop gain, spring load.

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Abstract

In this study, the effects of mental fatigue on mechanically induced tremor at both a low (3–6 Hz) and high (8–12 Hz) frequency were investigated. The two distinct tremor frequencies were evoked using two springs of different stiffness, during 20 s sustained contractions of the knee extensor muscles at 30% maximum voluntary contraction (MVC) before and after 100 min of a mental fatigue task, in 12 healthy (29 ± 3.7 years) participants. Mental fatigue resulted in a 6.9% decrease in MVC and in a 9.4% decrease in the amplitude of the agonist muscle EMG during sustained 30% MVC contractions in the induced high frequency only. Following the mental fatigue task, the coefficient of variation and standard deviation of the force signal decreased at 8–12 Hz induced tremor by 31.7% and 35.2% respectively, but not at 3–6 Hz induced tremor. Similarly, the maximum value and area underneath the peak in the power spectrum of the force signal decreased by 55.5% and 53.1% respectively in the 8–12 Hz range only. In conclusion, mental fatigue decreased mechanically induced 8–12 Hz tremor and had no effect on induced 3–6 Hz tremor. We suggest that the reduction could be attributed to the decreased activation of the agonist muscles.

Introduction

Mental fatigue is a psychobiological condition that arises due to prolonged periods of cognitive activity [Boksem and Tops, 2008], and can be characterized by feelings of “tiredness” and “reduced propensity for expending energy”. These changes can be attributed to alterations in motor cortical activity with little influence on peripheral mechanisms [Boksem et al., 2005; Marcora et al., 2009; Tartaglia et al., 2008]. Muscle tremor, either physiological, pathological or mechanically induced, is a complex phenomenon that can be affected by both peripheral mechanisms and activities in several areas of the central nervous system including the motor cortex (central factors) [Deuschl et al. 2001], for this reason it might be affected by mental fatigue [Slack et al. 2009] and, in this regard, we postulate that a form of tremor mainly related to peripheral factors, should be less influenced by mental fatigue than a form of tremor mainly related to central factors.

Various studies have shown that self maintaining force fluctuations (hereafter referred to as instability) can be revealed when contracting against a compliant load, such as a spring, and can be attributed to instability of the stretch reflex pathway [Durbaba et al., 2005; Joyce and Rack, 1974; Lippold, 1970; Matthews and Muir, 1980]. Also, modelling and experimental studies have shown that the frequency of oscillation of the instability is linked to whether the short (spinal) or long (transcortical) latency pathway of the stretch reflex is predominantly activated [Brown et al., 1982; De Serres et al., 2002; Durbaba et al. 2005, 2013; Lippold, 1970; Matthews and Muir, 1980; Stein and Oguztörel, 1976]. Predominant activation via the short latency pathway leads to 8-12 Hz tremor, whilst via

the long latency pathway tremor occurs at 3-6 Hz. It is reasonable to postulate that these forms of tremor, being generated by instability around different neuronal loops (either central or peripheral), would respond differently to a stimulus such as mental fatigue which is known to affect an area through which only the central component of the stretch reflex is routed [Mrachacz-Kersting et al., 2006; Taylor et al., 1995].

The purpose of the present study, is to explore the effects of a mental fatigue task on both 8-12 Hz and 3-6 Hz tremor, induced mechanically using springs of different stiffnesses during a knee extension task. We hypothesised that mental fatigue would cause greater changes in the instability at 3-6 Hz, generated by the long latency (transcortical) stretch reflex component, than in the instability at 8-12 Hz, generated by the short latency (spinal) stretch reflex component.

Methods

Participants

Twelve male individuals (29 ± 3.7 years) with no history of neurological disorder participated in the experiment. The study complied with the latest version of the Declaration of Helsinki and received approval from the Human Research Ethics Committee at University College Dublin. All individuals gave written informed consent prior to participation in the study.

Experimental design

Participants were requested to attend the laboratory for a single experimental session. They performed a maximal voluntary isometric contraction (MVC) of the knee extensor

muscles followed by two submaximal sustained (20 s) contractions of the same muscle group at 30% MVC (Fig.1A), using two linear springs of different stiffness. After each participant completed a mental fatigue task lasting 100 minutes, the submaximal contractions were repeated at the same force level as pre-fatigue, and the subject's MVC was measured again.

Participants were seated in a rigid chair with their trunk erect, fastened with an abdominal belt, and with a 90° angle at the knee joint. A cuff around the ankle joint was connected through a metal chain to a load cell (Leane International, Parma, Italy) attached to posterior part of the chair frame. The MVC task consisted of three isometric contractions to the maximum exerted by the knee extensors. Contractions were maintained for approximately 3 s with a five-minute rest between attempts. Participants followed their performance on a computer screen and were verbally encouraged to achieve their maximum, in an effort to exceed the previous force value. MVC was calculated as the highest value reached within any single force recording.

Once the MVC value was determined, individuals performed a submaximal contraction with each of the two different springs. The spring was connected in series between the load cell and the chain, appropriately shortened to maintain 90° at the knee joint when the spring was stretched. The order of the contractions was randomized (counterbalanced), with a three-minute interval between each contraction. During these tasks, the participants were provided with visual feedback of their performance and were instructed to maintain the force as close as possible to the visual force target represented by a horizontal cursor placed on the computer screen.

Surface EMG was recorded from the Vastus Lateralis (VL, Fig.1C) and Biceps Femoris (BF, Fig.1B) muscles. Pre-gelled, self-adhesive Ag/AgCl bipolar disc electrodes (Swaromed Universal, Nessler Medizintechnik GmbH, Innsbruck, Austria) were positioned according to the SENIAM guidelines [Freriks et al. 1999] with an inter-electrode distance of 20 mm on carefully prepared skin (shaved, abraded and cleaned with alcohol).

The force and EMG data were collected using the MP 100 EMG system (Biopac Systems, California; 1000 M Ω input impedance and CMRR of 110 dB). The EMG signals were amplified with a gain of 1000 and band-pass filtered from 1–500 Hz. The force signal was amplified with a gain of 100 and low pass filtered at 500 Hz. The force and EMG data were synchronized, sampled at 1 kHz with a 16-bit A/D converter (Biopac Systems, Inc. Goleta, CA, USA) and stored on a PC for later analysis.

INSERT FIGURE 1 ABOUT HERE

Estimating induced tremor frequency

The choice of the spring's stiffness is important since together with the moment of inertia of the limb, it determines the resonant frequency of oscillation of the mechanical system. This in turn will have a strong influence on the frequency at which oscillations due to instability will be expected to occur.

Under compliant contractions, the frequency of oscillation of the induced tremor can be determined by a spring-mass system coupled to elements contributing to the reflex

pathway. Durbaba et al. (2013) recently modeled this for the knee extensors in relation to predominant activation of the short and long latency stretch reflex pathways using the same spring stiffnesses employed in this study: 5.35 Nmm-1 (hereafter referred to as the 'long' spring) and 11.06 Nmm-1 (hereafter referred to as the 'short' spring).

Inducing mental fatigue

The protocol for mental fatigue used in this experiment was based on a switch task paradigm [Lorist et al. 2000]. Briefly, the participant sat in front of a computer where a black cross divided the white screen in four squares. The first stimulus appeared in the top left square and disappeared after either 2500 ms had elapsed or the user responded. After random intervals (150, 600 or 1500 ms) a new stimulus appeared in the top right square and so on clockwise continuously for 100 minutes. Stimuli were letters that could be red or blue and either consonants or vowels. When the stimulus appeared in any of the top squares, the participant was instructed to respond with a right choice (pressing the enter key on the computer keyboard) if it was red and with a left choice (pressing the spacebar on the computer keyboard) if it was blue. When the stimulus appeared in any of the bottom squares, the participant was instructed to respond with a right choice if it was a vowel and with a left choice if it was a consonant. The reaction time, measured as the interval in ms from the stimulus appearance to the individual's response, and the number of errors made by the subject were estimated.

Data analysis

All data were imported and analyzed using custom algorithms developed in Matlab (7.8.0.347 R2009a). The force data were digitally low-pass filtered using a fourth order Butterworth filter with cut-off frequency of 15 Hz. For the anisometric sustained contractions, the standard deviation and the coefficient of variation (CoV) of the force were computed as estimates of the tremor amplitude. The power spectral density of each force signal was estimated using Welch's averaged periodogram method with overlapping Hanning windows of duration 3.75 s and 50% overlap (0.267 Hz frequency resolution). The force spectra, were plotted on a linear amplitude scale and the integral of the power was calculated for each participant in the range ± 1 Hz about the tremor frequency, which was identified as the frequency at which the maximum value of the force power spectrum occurred.

The raw EMG signals were digitally high-pass filtered using a fourth order, zero-lag, Butterworth filter, with cut-off frequency at 20 Hz. The root mean square (RMS) value of the EMG data during the last 15 s of the contraction was calculated for both the VL and BF. The level of co-activation was estimated as the ratio of the VL/BF RMS EMG activity.

Mental fatigue was assessed by comparing the mean response time and total number of errors during the first 50 min with the mean response time and total number of errors during the last 50 min of the mental fatigue test.

Statistics

In order to investigate the effects of mental fatigue on the parameters of interest, the percentage changes pre and post the mental fatigue task were compared between the 2 tremor induced conditions using an unpaired Student's t-test (two-tails). To compare MVC and reaction time measures as well as changes pre and post mental fatigue within the tremor conditions, a paired Student's t-test was used. Finally correlation analyses were based on two-tailed Spearman's rho as the CoV and SD data at baseline were not normally distributed. A significant level of $P < 0.05$ was adopted.

Results

Isometric leg extension MVC decreased from 796 ± 150 N to 741 ± 137 N, (-6.9%; $P < 0.01$) after 100 minutes of the continuous mental task.

The mean time from the presentation of the stimulus to the participants' response (reaction time) increased, indicating that volunteers slowed their reaction time during the fatiguing protocol (Fig.2A). Reaction time increased by 4% from 1210 ± 142 ms to 1260 ± 169 ms ($P < 0.05$) (Fig.2B). The average number of errors also increased, although not significantly, from 33.3 ± 23.2 to 39.3 ± 32.6 after mental fatigue.

INSERT FIGURE 2 ABOUT HERE

Figure 3A and 3B show 1 s segments of rectified muscle EMG from a representative participant during two different 20 s sustained contractions when the two springs were used; the corresponding force fluctuation recordings is plotted in panels 3C and 3D.

Visual inspection of the force signals shows that the two springs induced either high (~9 Hz for short spring) or low (~5 Hz for long spring) frequency oscillations. The power spectra plots in panels 3E and 3F confirm the presence of a peak at these frequencies. For this participant, a reduction in the amplitude of the fluctuations around the target value, with no change in frequency of oscillation, is apparent as a consequence of mental fatigue in the case of the higher frequency tremor only.

INSERT FIGURE 3 ABOUT HERE

Similar to that observed in the single participant in Figures 3E and 3F, results from the entire group indicate that mental fatigue led to a decrease in the peak value of the force power spectrum by 55.5% in the 8-12 Hz frequency range ($P = 0.17$) and increased (non-significantly, $P = 0.28$) by 8.3% in the 3-6 Hz frequency range. Similarly, the area around the peak was reduced by 53.1% in the range 8-12 Hz ($P = 0.15$) and unchanged (+ 5.7%; non significantly, $P = 0.32$) in the lower frequency range 3-6 Hz.

The group data confirm this result also in relation to CoV (Fig.4A) and SD showing a significant reduction of 31.7% and of 35.2% respectively ($P < 0.05$) of the raw force during the sustained contractions performed after the mental fatigue task in the 8-12 Hz range only, with no changes in the 3-6 Hz range ($P = 0.53$ for CoV and $P = 0.49$ for SD).

INSERT FIGURE 4 ABOUT HERE

Finally, the peak frequency of induced tremor ranged between 7.6 and 9.4 Hz (± 0.70 Hz) and between 5.0 and 6.6 Hz (± 0.73 Hz) when the short and long springs were used, respectively. These values are similar to those obtained by Durbaba et al. (2013) where identical springs were used. In neither of the two conditions did the peak frequency show any significant change following mental fatigue.

Analysis of EMG RMS activity in the VL muscle between the two induced tremor frequencies showed no significant difference either at baseline, post fatigue or between the delta change baseline-post fatigue. Statistical analysis of EMG RMS activity in the VL muscle within the two induced tremor frequencies showed a 10.6% reduction (group mean) in EMG RMS amplitude ($P < 0.05$) within the 8-12 Hz frequency range, whilst

within the lower frequency range, the mean reduction of 6.2% in EMG RMS amplitude did not reach significance ($P=0.09$, Fig.4B). No changes in antagonist muscle activation or in estimated co-activation were observed in either of the tremor conditions examined. A positive correlations was observed between the relative tremor reduction (using the CoV as an index of tremor amplitude) and the baseline tremor CoV (Fig.5A) and SD (Fig.5B) ($P < 0.01$). No significant correlation was observed between the relative reduction in MVC (Fig.5C) or EMG amplitude (Fig.5D) and relative tremor reduction.

INSERT FIGURE 5 ABOUT HERE

Discussion

The aim of this study was to investigate the effects of mental fatigue on induced instability in both the 3-6 and 8-12 Hz frequency ranges. Mental fatigue improved force steadiness within the 8-12 Hz frequency band with no change in the amplitude of fluctuations at 3-6 Hz.

Reaction time and MVC

As expected, during the mental fatigue task, the reaction time increased (~4%). Similar results (~4.4% increment) were obtained in another study where the same mental fatigue protocol was used [Lorist et al. 2000].

MVC decreased as a consequence of mental fatigue. It is well known that both peripheral and central fatigue can reduce maximal voluntary force [for review see Gandevia 2001] and it has been suggested by an early study [Mosso 1904, cited by Gandevia 2001] that a prolonged mental task could induce central fatigue. Unfortunately, since these early observations, no other studies have been conducted on the topic and the effects of mental fatigue on muscle performance remained under-investigated. Recently a paper by Marcora et al. (2009) confirmed that 90 minutes of mental fatigue caused a reduction in physical performance, in which the effect was attributed to decreased exercise tolerance rather than to a physiological alteration. Further evidence in support of the hypothesis that muscle performance is not compromised by cognitive efforts can be found in studies on sleep deprivation, which is known to induce mental fatigue [Akerstedt et al. 2004]. Symons et al. (1988), for instance, demonstrated that sleep deprivation does not affect MVC, with a similar result reported as a consequence of partial sleep loss [Bambaeichi et

al. 2005]. In six other sleep deprivation studies reviewed by Martin (1986), only one study reported of a single case of MVC reduction. Therefore, although the effects of mental fatigue on MVC have not been directly investigated before, existing related literature would appear to be contrary to the findings observed in the present study. A possible explanation might be found in the decrease of vigor and feelings of activation, two known effects caused by mental fatigue [Lorist et al. 2000 and 2009, Marcora et al. 2008]. These elements suggest that individuals may be demotivated in repeating the MVC task after completing the mental fatigue protocol and this might account for the observed reduction in MVC in the present study. Indeed, it has been previously demonstrated that individuals described as "not motivated" were unable to generate a sufficient central command during a knee extension task with a consequent force decline [Bigland-Ritchie et al. 1986].

Tremor amplitude

Since mental fatigue alters activity in the motor cortex [Tartaglia et al. 2008, Boksem et al. 2005] and does not influence peripheral mechanisms [Marcora et al. 2009], our original hypothesis was that the instability at 3-6 Hz, generated by the stretch reflex central component, should be more affected by mental fatigue, than the instability at 8-12 Hz generated by the stretch reflex peripheral component. However, in the present study a decrease in tremor was observed at 8-12 Hz and not at 3-6 Hz.

A first explanation of this result could be that the magnitude of the stretch reflex response might not be the main factor influencing the amplitude of the instability induced by it. In fact, although the presence of muscle spindles is necessary to generate instability

[Durbaba et al. 2005], in order to obtain an optimal resonance, the delay around the feedback loop [Lippold 1970] and the inertia of the oscillating part [Halliday et al. 1956] are also of primary importance. These last two components (inertia of the system and delay around the feedback loop) might be more relevant in terms of effects on tremor amplitude with the stretch reflex response only acting as a pacemaker ensuring the timing for optimal entrainment. On the other hand, in the present study no shifts in tremor frequency were detected (Fig.3C,D,E,F), suggesting that mental fatigue does not influence the speed within the neurological transmission related to muscle tremor, at least in a way appreciable with the adopted tremor frequency measurements. The result is also indicative that the system dynamics (total stiffness and inertia of the system) have not changed.

Previous studies have shown that induced tremor increases as the level of muscle activity increases [Joyce and Rack, 1974; Manini et al., 2005; Matthews and Muir, 1980]. Thus the observed reduction in tremor cannot be related to the reduction in MVC. Indeed, due to the protocol used in this study, one might have expected the tremor amplitude to have increased as the post-fatigue submaximal contractions were performed at a relatively higher level of MVC than pre-fatigue (group average 32% of the post-fatigue MVC value). Moreover, no significant correlation was observed between relative MVC reduction and relative tremor reduction (Fig.5C).

An alternative possible explanation for the reduction in tremor amplitude could be associated with corticomuscular coupling. Although it has been shown that oscillations of the motor cortex are usually not synchronized with similar activity of the spinal motoneuron pool in the 8-12 Hz band in healthy humans [Conway et al. 1995], 8-12 Hz

cortico-muscular coherence has been shown in pathological conditions in which tremor is the major symptom [Raethjen et al. 2007, Hellwig et al. 2000, Timmermann et al. 2003]. One possibility is that by provoking oscillations resembling a pathological state, we induced corticomuscular coupling which was then weakened by mental fatigue. In this case, the observed differences between the two frequency ranges could be explained on the basis that both Parkinsonian tremor and voluntary hand movements in healthy individuals at 3-6 Hz result in significant corticomuscular coherence at 8-12 Hz (Timmermann et al. 2003, Pollok et al. 2004). This suggests that corticomuscular coherence could predominantly, if not exclusively, be induced at 8-12 Hz, regardless the actual displacement frequency.

In an early study on sleep deprivation [Eagles et al. 1953], a reduction of tremor was observed and attributed to muscle relaxation. Similarly, we cannot exclude muscle relaxation as another potential explanation of tremor reduction basing our assumption only on the lack of correlation between EMG reduction and relative tremor reduction. Indeed, although the reduction in EMG and tremor were uncorrelated, this might just be due variations between subjects and nonlinearity in the force EMG relationship (Fig. 5D).

EMG

In the present study, we observed a reduction of EMG activity after mental fatigue within the 8-12 Hz frequency band only (Fig. 4B). This result can be explained on the consideration that EMG amplitude is consistent with the reduction in tremor at the same frequency. This is to be expected as they are just electrical and mechanical manifestations of the same thing i.e. motor unit activity. However it is important to reiterate that in the

group there were no differences in EMG between the two induced tremor frequencies at baseline, post fatigue and between the delta changes. Therefore, mental fatigue could have reduced EMG RMS in a way not distinguishable between the two experimental conditions. The reason why this result was not observed specifically in the 3-6 Hz range might be attributed to the size of the sample. In this case, the observed reduction of EMG activity could possibly be ascribed to decreased excitability of the motor cortex provoked by the fatiguing protocol [Tartaglia et al. 2008]. Indeed reduced activity in this cortical area has been reported to decrease background EMG [Ferber et al. 1992, Taylor et al. 1995].

Study limitations

A limitation of this study is the lack of a control condition where the volunteers sat quietly for 100 minutes with no mental fatigue task administered, as it cannot be excluded that this alone could have affected knee extension function. Moreover, a direct measurement of cortical activity would have clarified whether or not cortico-muscular coherence in the 8-12 Hz band can be elicited by inducing tremor.

Conclusions

In conclusion, it was demonstrated that appropriate spring loads can generate tremor at frequencies associated with instability around both the short and long loop reflexes.

Mental fatigue induced a marked reduction in mechanically induced tremor at 8-12 Hz with no effect on tremor at 3-6 Hz. A possible explanation is that the use of the spring

induced cortico-muscular coupling in the 8-12 Hz frequency band which was reduced by mental fatigue.

Acknowledgements

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Figure 1: Sustained anisometric contraction. Representative data from a single subject: **A**, Force output at 30% MVC. **B**, Surface EMG from the antagonist biceps femoris muscle. **C**, Surface EMG from the agonist vastus lateralis muscle.

Figure 2: Reaction time

A: Reaction times of the first (grey triangles) and last (black circles) 50 minutes of mental fatigue task are presented for each participant.

B: Group average reaction time during the first (grey bar) and last (black bar) 50 minutes of mental fatigue. Paired student t-test $*P \leq 0.05$

Figure 3: Representative effects of mental fatigue on induced tremor.

Panels A,B,C,D,E,F show data from one representative volunteer. Data using the 11.06 N.mm⁻¹ spring are in the left hand column and data using the 5.35 N.mm⁻¹ spring are on the right. A and B: 1 s sample of rectified EMG of VL activity (EMG has been full-wave rectified and resampled at 125 Hz for clearer graphic visualization); black area corresponds to pre-fatigue condition only, white to post-fatigue only and grey to common pre and post-fatigue. C and D: 1 s sample of the raw force extracted from a 20 s sustained contraction (mean background level removed); grey line corresponds to pre-fatigue condition, black to post-fatigue. E and F: Force power spectrum; grey line correspond to pre-fatigue condition, black to post-fatigue.

Figure 4: Effects of mental fatigue on tremor and EMG.

The histograms represent the mean and standard deviation for the whole sample (n = 12).

Panel A: CoV of the force, dark grey bars refer to pre-fatigue condition, light grey bar to post-fatigue; B: Agonist EMG RMS amplitude, dark grey bars refer to pre-fatigue, light grey bar to post-fatigue. *P ≤ 0.05.

Figure 5: Correlation graphs.

Each point represents a single participant. All data refer to the 8-12 Hz condition. The top two graphs show the correlated relative reductions and baseline values of: A, Force CoV and B, Force SD. In the bottom two graphs the correlation between the relative reduction in tremor and C, relative MVC reduction and D, relative EMG reduction are presented.

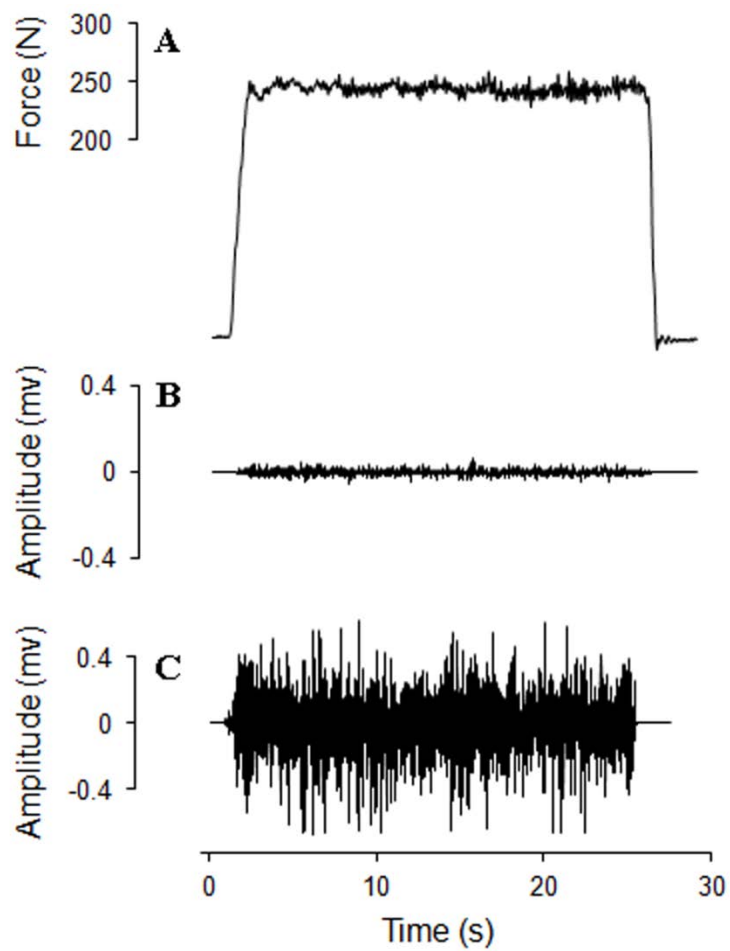


Figure 2.

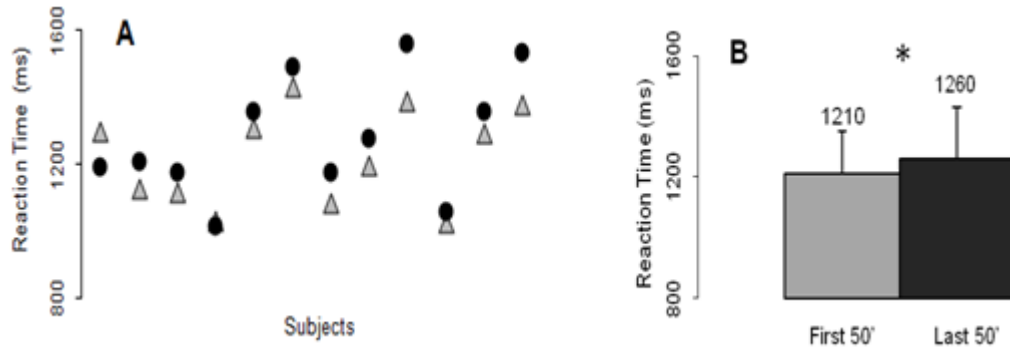


Figure 3.

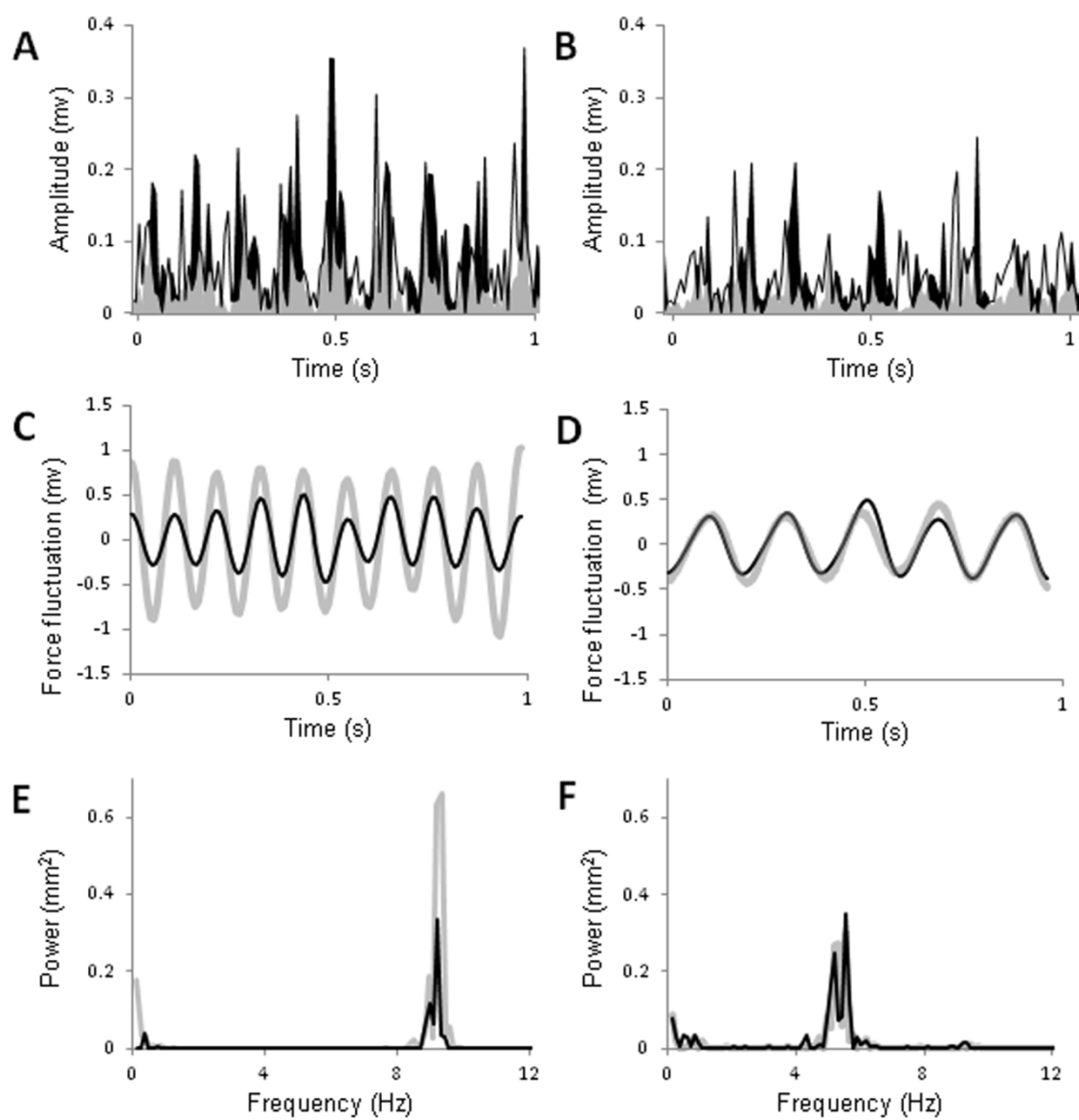


Figure 4.

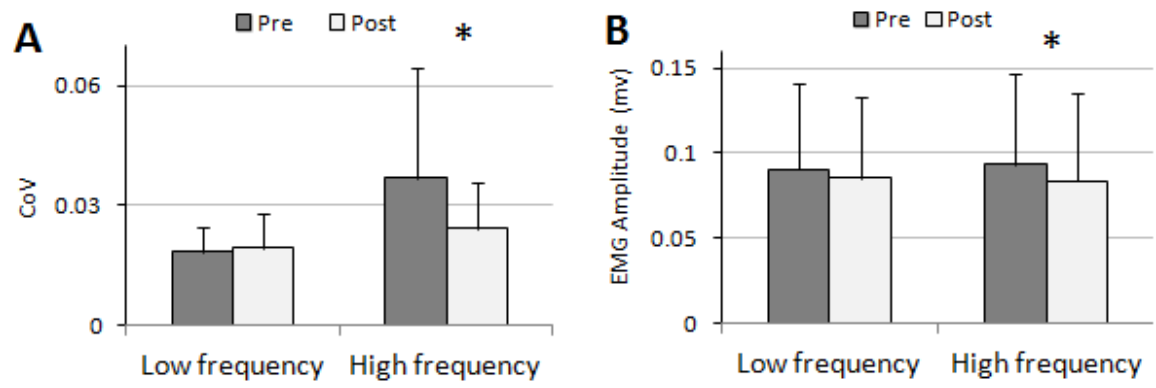


Figure 5.

