ALTERATIONS OF RESPONSES TO TRANSCRANIAL MAGNETIC STIMULATION DURING REPEATED ISOMETRIC CONTRACTIONS

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Abstract:

Ten healthy male students (age 22.1±2.3 years), without neurological disorders, volunteered for the study. Muscle fatigue of the first dorsal interosseus muscle was studied during repeated isometric voluntary contractions until exhaustion. Transcranial magnetic stimulation was used to elicit motor-evoked potentials and mechanical responses in the exercised muscle. The averages of 6 responses were analyzed pre-exercise, every 25 contractions during the exercise and during the recovery phase. The average of isometric contractions until the fatiguing of a subject was 175 repetitions. During the protocol, amplitudes of mechanical as well as electrophysiological responses changed significantly ($P<.001$ and $P<.002$, respectively). A potentiation of the electrophysiological responses was prominent only at the beginning of the task while twitch force remained increased until the final fatiguing. Both measures were depressed after the task termination. However, diminishment of electromyographic responses remained more prominent. During the recovery phase twitch force fully recovered, while electrophysiological potentials remained depressed ($P<.05$). During and after the fatiguing task, modulations of mechanical and electrophysiological responses to transcranial magnetic stimulation were not parallel. Additional qualitative analysis of the electrophysiological responses revealed a systematic shift from biphasic responses in pre-tests to polyphasically shaped ones during the fatigue and recovery phase. This phenomenon could indicate a shift from monosynaptic to oligosynaptic corticospinal projections which could namely cause temporally different recruitment of the motor units. The modulatory mechanism is most probably of supraspinal origin while F wave as a measure of peripheral excitability did not show significant modifications through the experiment.

Key words: *central fatigue, brain stimulation, motor-evoked potentials, twitch*

REAKTIONSÄNDERUNGEN AUF TRANSKRANIALE MAGNETISCHE STIMULATION WÄHREND WIEDERHOLTEN ISOMETRISCHEN KONTRAKTIONEN

Zusammenfassung:

10 gesunde Studenten (im Alter 22.1±2.3 Jahre) ohne neurologische Störungen nahmen an der Studie freiwillig teil. Die Ermüdung des ersten dorsalen zwischen den Knochen liegenden Muskels wurde während wiederholten isometrischen freiwilligen Kontraktionen bis zur Erschöpfung untersucht. Die transkraniale magnetische Stimulation wurde angewandt, um motorisch-provozierte Potenziale und mechanische Reaktionen im betreffenden Muskel zu bekommen. Die durchschnittlichen Werte von 6 Reaktionen wurden vor der Übung analysiert, nach jeder 25sten Kontraktion, sowie während der Übung und während der Erholungsphase. Die durchschnittlichen isometrischen Kontraktionen bis zur Ermüdung des Probanden betrugen 175 Wiederholungen. Im Laufe des Protokolls änderten sich wesentlich die Amplituden der mechanischen und der elektrophysiologischen Reaktionen ($P<.001$ und $P<.002$). Die Potentiation von elektrophysiologischen Reaktionen war nur am Anfang der Aufgabe zu merken, während die erhöhte Reaktionskraft bis zur endgültigen Erschöpfung blieb. Die beiden Werte nahmen nach der Aufgabe ab. Die Abnahme der elektromyographischen Reaktionen war aber auffälliger. Während der Erholungsphase wurde die Reaktionskraft völlig zurückgewonnen, aber die elektrophysiologischen Potenziale blieben niedrig ($P<.05$). Während und nach der Aufgabe waren die Modulationen von mechanischen and elektrophysiologischen Reaktionen auf transkraniale magnetische Stimulation nicht parallel. Eine zusätzliche Qualitätsanalyse elektrophysiologischer Reaktionen brachte zum Vorschein eine systematische Änderung von biphasischen Reaktionen vor den Tests zu polyphasischen Reaktionen während der Ermüdungs- und Erholungsphase. Dieses Phänomen könnte auf die Änderung von monosynaptischen zu oligosynaptischen kortikospinalen

Projektionen hindeuten, was nämlich zur Folge eine zeitlich verschiedene Rekrutierung motorischer Einheiten haben könnte. Der Modulatormechanismus ist höchstwahrscheinlich supraspinalen Ursprungs, während die F Welle, als eine Größe der peripheren Erregbarkeit, keine wesentlichen Modifikationen während des Experiments aufzeigte.

Schlüsselwörter: *zentrale Ermüdung, Gehirnstimulation, motorisch provozierte Potenziale, Zucken.*

Introduction

Fatigue of the motor system is characterized by a decrease in force generated by the neuromuscular system during sustained or repeated muscle activity. It can be divided into peripheral and central fatigue. A contribution to fatigue coming from mechanisms proximal to the neuromuscular junction is known as central fatigue and vice versa (Gandevia, 2001). During the last fifteen years transcranial magnetic stimulation (TMS) has been used by some investigators concerning the corticospinal mechanisms of fatigue. Reports are in disagreement about the modification of motor-evoked potentials (MEP) during and after a prolonged muscular activity (Taylor & Gandevia, 2001). This inconsistency most likely derives from the very different types of experimental protocols employed in these studies (Rollnik, Schubert, Albrecht, Wohlfarth, & Dengler, 2000; Löscher & Nordlund, 2002; Taylor, Petersen, Butler, & Gandevia, 2000). The increasing body of literature relating to central fatigue has been devoted to the identification of the underlying physiological mechanisms for MEP modulation (Mazzocchio, Rothwell, Day, & Thompson, 1994; Taylor et al., 2000). This paper should point out the complex nature of the MEPs and subsequent twitch (TW) responses while the neuromuscular system is to be found in a potentiation or depression state.

The present study was therefore designed to investigate the altering of neurophysiological and mechanical responses to TMS during repeated fatiguing isometric contractions. Before and after the exhausting motor task M wave (MW) was analysed as a measure of efferent peripheral excitability. Additionally, in a few subjects only F waves (FW) were measured in order to test the possible effect of spinal excitability changes.

Methods

Experiments were performed on 10 healthy male students (aged 22.1±2.3 years) with no neurological disorders. They volunteered for the study, were highly motivated and had considerable experience in maintaining voluntary contraction. They all gave their full informed consent and the experimental procedure was carried out in consistence with the Tokio-Helsinki declaration.

Muscle contraction and electromyography

Experiments were performed on the first dorsal interosseus muscle (FDI). The subject was lying in a supine position and his right upper extremity was positioned into an isometric brace (Figure 1). The forearm and 3rd, 4th and 5th fingers were firmly fixed and held in a pronated position. The thumb was fixed in a position of 60° radial abduction. The tested 2nd finger was positioned into a channel which had its axis aligned with the metacarpo-phalangeal joint of the 2nd finger (direction for radial/ulnar

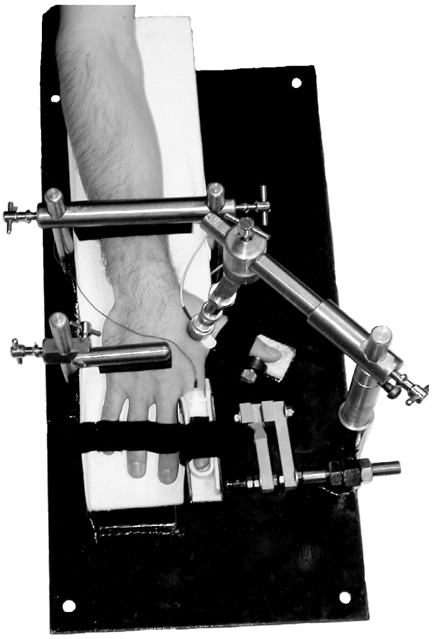

Figure 1. An isometric brace for the second finger of the right hand. Proper fixation of the hand was secured using straps and stiff supports. Torque was detected by the strain gauge mounted at the distal point of the finger while twitch force was captured by the sensor over the muscle belly. The latter was important because of the non-selective nature of responses to TMS. (See the text for details).

abduction). Through the channel, the 2nd finger was attached to a force transducer whose output was displayed on-line on an oscilloscope and fed to a computer. The oscilloscope signal was displayed above the subject in order to provide visual feedback of the sustained muscle tension. When the skin had been prepared, silver/silver chloride surface EMG electrodes were glued over the FDI as described by Ridding and Taylor (2001). An active EMG electrode was placed above the muscle belly, while the reference was attached to the interphalangeal joint of the second finger. Resistance under all electrodes was below 5 kΩ. Data capture was done by Synergy (Oxford Instruments, UK) a system for neurophysiological measurements, whereas later calculations were carried out using the software that we have developed on our own for the purpose of this experiment.

Transcranial magnetic stimulation

A figure-of-eight coil (9.5 cm external diameter) powered by Magstim 200 stimulator (Magstim Company Ltd, Whitland, UK) was used for the TMS. The coil was held in an optimal position over the left part of the scalp for evoking MEPs in the target muscles of the right hand. The induced current flow was in a posterior-to-anterior direction, which should activate the cortico-spinal tract transsynaptically (Di Lazzaro, Oliviero, Profice, Saturno, Pilato, Insola, Mazzone, Tonali, & Rothwell, 1998). The proper spatial relationship between the coil and the subject's head was secured using a stereotactic pneumatic brace of the author's own production (Figure 2). The intensity of the stimulus was 30% above the motor threshold for the FDI. The threshold was defined as the lowest intensity evoking at least five out of 10 trials of above 100 μV peak-to-peak amplitude. The trials in whose background the EMG activity was present (amplitudes larger than 50 μV) in the 100 ms pre-stimulus time period were rejected off-line. Mechanical responses of the FDI were measured concurrently as a *force: time curve* detected by the force sensor positioned perpendicular over the muscle belly (Figure 1). The argumentation for such a modification of the classical TW was provided by the previous pilot study. It has been based on the fact that TMS is non-selective in its nature (divergent corticospinal control) and hence it is not possible to selectively activate the 2nd finger abductors only. As a result net torque around the joint would have been affected by many other muscular factors and not purely by agonist tension (antagonist activation, activation of proximal muscles, temporal delay, etc.). Stores of 6 responses were constructed for every time point of the experimental. Peak-to-peak amplitudes of the averaged MEPs and peak force of the TW were analyzed.

Figure 2. Maintainance of the head position using a mechanical brace and stereotactic manipulation handle based on pneumatic mechanisms of fixation. By the use of the two technical expedients it was possible to secure a controlled spatial relationship between the brain and a stimulation coil. It is an important issue when concerning the site of stimulation and its potential impact on motor output.

Electrical nerve stimulation

In order to check the appearance of changes in the peripheral neuromuscular factors as a result of fatigue, M waves were measured prior to the beginning of the fatiguing task and immediately after exhaustion. In a relaxed subject the ulnar nerve was stimulated at the wrist using a single supramaximal electrical stimulus (symmetrical, square, biphasic, width 0.2 ms). The strongest response out of three consecutive stimulations was used for further calculations of peak-to-peak amplitudes.

Additionally, F wave of the FDI was measured in four subjects. It is the EMG response of the homonymous muscle, which appears as a result of the antidromic volley after the supramaximal stimulation of the peripheral alpha motoneurone axons. During the first (onset of the task) and the last ten contractions FWs were measured and stores were constructed for further analyses. The amplitude was analyzed. Parameters of electrical stimulation were the same as for MW though stimulation was done at the moment of a voluntary contraction.

Experimental protocol

When summed up, the preparation procedure included EMG electrode placement and positioning of a subject onto a therapeutic table with his head and the right upper extremity properly fixed. Initially, the threshold for TMS was determined and pre-measurements of MWs and MEPs were carried out. Afterwards, the maximal voluntary contraction of the FDI was initially identified by means of the 2nd finger torque. Following that, the subject were asked to proceed with voluntary contractions of 75% of the estimated maximum. Feedback of a dynamometer signal was provided to subjects while performing the task. Then, the subjects repeated cycles of 6 seconds of active contractions and 4-second pauses, alternately. As the force began to fall below the pre-set value, the feedback signal served only as a time sequencer, while the subject tried to perform his best. The task was terminated when the voluntary force had fallen below 60% of the maximum. Hence, the "point of exhaustion" depended on an individual.

TMS-evoked MEPs of FDI were studied during prolonged repeated isometric voluntary contractions. TMS was applied during the rest intervals between two subsequent voluntary contractions (note the marks on the abscissa in Figure 3). The averages of 6 responses were analyzed repeatedly (pre-exercise, every 25 contractions, during the recovery phase). A prolonged effect of fatigue was traced during the recovery phase 3, 5 and 10 minutes after exhaustion.

The peripherally evoked potentials were measured only twice in the four subjects who took part in the subsequent experiment that involved FW measurements. At the beginning of the task and during the additional ten repetitions of muscle contractions, after 60% of the borderline the task could not be accomplished anymore.

Analysis of data

Statistical significances of differences between peak-to-peak amplitudes of MEPs and amplitudes of the concurrently measured TWs elicited during the repeated isometric contractions were estimated using the repeated measures of analysis of variance (ANOVA). As *post-hoc* tests of the two variables and as the main test for the estimate of FW and MW pre/post differences, the Student's *t*-test was used. In order to test potential discrepancies between the behavior of MEPs and TWs the analysis of covariance (ANCOVA) was introduced.

Results

The main results are presented in Figures 3 and 4. The average number of isometric contractions up to fatiguing of a subject was 175 repetitions (maximum 225 reps, minimum 110 reps). During the protocol MEP amplitude and TW force changed significantly ($p<.001$ and $p<.002$, respectively). The results of the *post hoc t*-tests are presented in the graph (Figure 3). Thus, filled shapes (squares - MEP, circles - TW) indicate statistically significant modulations of responses related to the introductory measurements. It can be noticed that MEPs are augmented at the very beginning and then they significantly decrease from the 25th repetition on. At first, this phenomenon is very steep and afterwards it progresses moderately, so that MEPs' amplitudes are significantly attenuated (to 60% of the control value captured before the onset of the task) at the point of exhaustion. Ten minutes after the termination of the task, the reduced MEPs had not recovered completely ($P<.01$). However, the restorative tendency could be identified. The mechanical responses to TMS behaved in a different way. The amplitudes of TWs were enlarged at the onset of the exercise and remained such until the very end of it. Any significant depression of the mechanical responses could not be seen

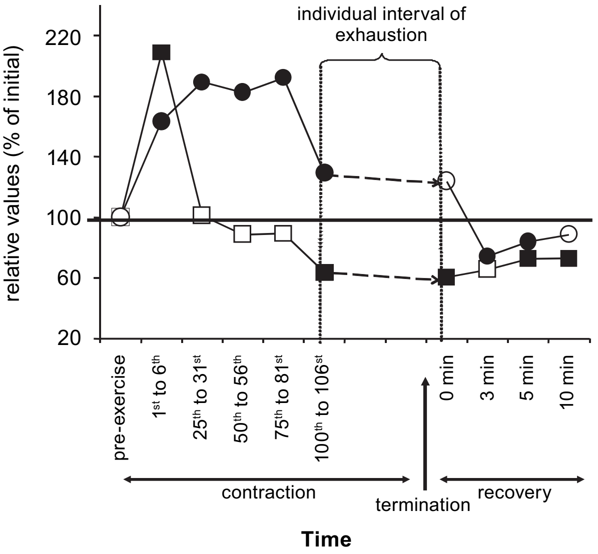

Figure 3. Average amplitudes of MEP (squares) and TW (circles) responses to TMS at different time intervals. Statistically significant modifications, relative to introductory measurements, are presented as filled in shapes (p<.05).

earlier than three minutes after exhaustion. In this late phase of recovery, mechanical and physiological parameters behaved similarly. To infer, both measures related to TMS evoked responses which were depressed at the end of the fatiguing exercise. However, MEP diminishment remained more prominent. During the recovery phase TW fully recovered in its amplitude, while MEP remained depressed. These differences between the measures were confirmed by ANCOVA as well.

The amplitude of the MW in FDI, elicited by the wrist ulnar nerve stimulation after a prolonged repeated isometric fatiguing voluntary contraction, did not differ significantly from the same stimulation applied before this exhausting protocol (Figure 4). The values remained actually unchanged and the variability of the results was low. Although additional control measurements were performed in four subjects only, FWs showed no systematically behavioral patterns among the subjects. Intra-individual variability among single responses was very high at the same test point.

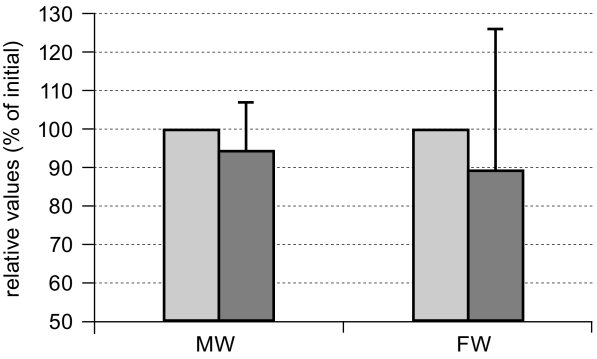

Figure 4. Results for the MW and FW measurements expressed in relative terms. Both peripherally evoked responses were measured before (MW) or at the very beginning (FW) of the onset of the repeated isometric contractions (light gray columns), and immediately after exhaustion had taken place (dark gray columns). No pre-/post- differences were estimated. Attention should be paid to the ordinate scale starting at 50%.

Discussion and conclusion

While repetitively performing 6-second isometric contractions of the FDI that were separated by short 4-second pauses, initial enhancement of responses to TMS took place. As the subject proceeded with the exercise, mechanical and electrophysiological evoked responses started to behave in a strikingly different way. Therefore, during and after the fatiguing task, the modulations of the MEP and TW evoked by TMS were not parallel. The MEP depression was not strictly mirrored in TW. However, 3 and 5 minutes after the fatigue point, both responses were significantly depressed. Peripheral efferent and spinal mechanisms seemed not to be affected during the exhaustive exercise.

It was already demonstrated by Balbi and associates (Balbi, Perretti, Sannino, Marcantonio & Santoro, 2002) that MEP elicited by TMS increased soon after a non-exhaustive voluntary contraction of the target muscle. They showed that maximal facilitation of the response was provoked by the shortest and strongest muscle contraction. The results of the present study are consistent with these observations, namely, obvious initial facilitation of the responses was observed during the first contractions. Many possible underlying mechanisms for the MEP augmentation could be taken into account. Theoretically, the site of increased facilitation could be peripheral or central as well as afferent or efferent.

Most studies dealing with post-contraction facilitation of the MEPs propose cortical mechanisms as responsible for the introduced phenomenon. In their investigation, Mazzochio and associates (1994) concluded that tonic voluntary contraction of the target muscle decreased the threshold of indirect activation (trans-synaptic recruitment) of corticospinal neurones, but not for direct stimulation of their axons. Supportively, Ridding, Taylor and Rothwell (1995) discussed the voluntary drive reducing the excitability of inhibitory circuits in cortical areas that project to the active muscle. However, a high incidence of an enhanced muscle spindle discharge after the voluntary contraction suggests that more peripheral factors such as muscle "history" should be taken into account when interpreting changes in modulations of corticospinal excitability (Wilson, Gandevia, & Burke, 1995). Nevertheless, when FWs during the first 10 voluntary contractions were compared to the subsequent FWs, no obvious tendency of change was present. But, it should be remembered that the fluctuations of FWs were rather high. Such analysis of non-averaged data might thus be questionable.

Besides all the above-mentioned mechanisms, the mechanical response to TMS additionally depends on the mechanical status of the muscle-skeletal system. Thus, the captured response is an integrated event comprising corticospinal excitability, functioning of the excitation-contraction coupling at the periphery, and finally initial stiffness of the muscle. The latter would be normally sustained at a relatively high level throughout the voluntary task, thus serving as a basis for the higher TW force. Although MEPs returned to the control values after the first 25 contractions, TW amplitudes remained significantly above the initial level. There are two main potential reasons for the discrepancies observed. First, because of the increased muscle stiffness lower activation of the muscle tissue could result in relatively constant mechanical responses. Second, temporal desynchronization of the input volleys acting onto the spinal motoneurons would possibly cause polyphasic evoked responses detected by surface EMG (an effect of volume conduction), hence the smaller peak-to-peak amplitude of the MEPs.

After a subject had fatigued, depression of responses took place. These changes were statistically significant and were more prominent in MEP than in TW. At the end of the exercise there was a 40% average reduction in the MEP amplitude according to the control values, while, on the other hand, TW was not yet attenuated at that moment. However, from the 3rd minute of the recovery phase on, both responses to TMS behaved in a similar way. Taylor, Buttler, Allen, and Gandevia (1996) suggested decreased intracortical facilitation and increased intracortical inhibition after the fatiguing task. In the experiment being discussed here FW as a peripheral measure was not modulated as a result of fatiguing exercise, although elicited at the two intervals of the highest MEP alterations. It is very difficult to evoke H reflex in the intrinsic hand muscles. Even if there are methodological problems of comparing FW and HW while they are not equally sensitive to changes in motoneuronal excitability (Hultborn & Nielsen, 1995, 1996), FW is frequently used as a valid measure for this purpose in the intrinsic hand muscles such as FDI. Nevertheless, the results of our experiment are consistent with other studies probing H reflexes during the fatiguing task in other than the intrinsic hand muscles (Ljubisavljevic, Milanovic, Radovanovic, Vukcevic, Kostic, & Anastasijevic, 1996). If summed up, it seems very likely that the actual site responsible for the modulation of the EMG responses to TMS while exercising were supraspinal centres. In the context of peripheral mechanisms possibly, at least in part, responsible for MEP modulations changes in axonal excitability of alpha motoneurones should be additionally considered (Burke, Kiernan, & Bostock, 2001; Chan, Lin, Pierrot-Deseilligny, & Burke, 2002). As MW measured at the two most extreme points (means of MEP and TW changes) showed no significant alterations, it can be concluded that efferent peripheral excitability was not influential.

One of highly important underlying mechanisms for MEP potentiation could be afferent input from the periphery to the central system. Namely, sensory-motor integration is one of the most prominently developing research areas in human neurosciences. If the main concepts of this field are summed up, it can be concluded that there could be no volitional movement unless the sensory input precedes it. Taylor and associates (2000) tested the effect of ischaemia on the modulation of post exercise MEP depression. They showed that ischaemically sensitive group III and IV muscle afferents did not mediate depression of responses to motorcortical stimulation after a fatiguing exercise. On the other hand, gating of signals coming from the large fibre afferents (Ia, II, large cutaneous fibres) is probably one of the most responsible mechanisms, which could strikingly affect the excitability of supraspinal centres (Abbruzzese, Marchese, Buccolieri, Gasparetto, & Trompetto, 2001; Chen, Corwell, & Hallet, 1999; Hirashima & Yokota, 1997; Inghilleri, Berardelli, Cruccu, Manfredi, Priori, & Rothwell, 1995). The role of sensory input for motor control in the fatiguing task has been demonstrated recenly (Rollnik et al., 2000). It showed how, using somatosensory manipulation, a decrease in the central drive can be overcome at the fatigue point.

Finally, the MEP measured with surface electrodes is an integrated response that besides corticospinal excitability depends also on other factors such as spatial and temporal summation of the surface EMG signal. Additional qualitative analysis of the MEPs re-vealed a systematic shift from biphasic res-ponses in the pre-tests to polyphasically shaped ones during the fatigue and recovery phase. This phenomenon could indicate a shift from monosynaptic to oligosynaptic cor-ticospinal projections, which could namely cause temporally different recruitment of the motor units. A group of Pierrot-Deseilligny (Gracies, Meunier, & Pierrot-Deseilligny, 1994; Pauvert, Pierrot-Deseilligny, & Rothwell, 1998) suggested spinal premotoneurons as the modulators of the descending motor commands. Corticospinal fibres are thus able to activate "propriospinal" neurons which act onto the alpha motoneurons. If this circuitry is modulated, it can affect the final output characteristics of the efferent volley and possibly detected MEPs. Any geometrical modifications of the EMG potentials to TMS (as a result of desynchronization) would affect amplitudes of responses, but no changes would be seen in mechanical responses providing the same population of muscle fibres recruited.

To infer, prolonged repetitive isometric voluntary contractions induced initial augmentation and subsequent depression of responses to TMS. Based on the results, peripheral factors can be excluded from having a role in the modulations. Mechanical responses to TMS did not strictly mirror MEPs, moreover, they behaved strikingly differently at some points. Cortical mechanisms are most possibly responsible for the global behavior of the evoked responses. Their level of excitability is very likely highly influenced by the afferent input. Discrepancies between TWs and MEPs could be explained by the modulation of cervical propriospinal system and by the mechanical explanations related to the role of muscle stiffness in TW force production.

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PROMJENE ODGOVORA NA TRANSKRANIJALNU MAGNETSKU STIMULACIJU ZA VRIJEME PONOVLJENIH IZOMETRIČKIH KONTRAKCIJA

Sažetak

Uvod

Posljednjih petnaest godina neki istraživači koriste transkranijalnu magnetsku stimulaciju kako bi istražili kortikospinalne mehanizme umora. Njihovi izvještaji ne slažu se oko modifikacije motoričkih evociranih potencijala za vrijeme i nakon produžene mišićne aktivnosti. Naše je istraživanje stoga osmišljeno kako bi se ispitala promjena neurofizioloških i mehaničkih odgovora na transkranijalnu magnetsku stimulaciju za vrijeme ponavljane iscrpljujuće izometričke kontrakcije. Status perifernih modulatornih mehanizama testiran je valovima M i F.

Metoda

Eksperiment je proveden na deset zdravih studenata (u od dobi od 22±2.3 godine) bez ikakvih neuroloških poremetnji. Mišićni umor prvog dorzalnog interkostalnog mišića proučavao se za vrijeme ponavljane voljne izometričke kontrakcije (ponavljane kontrakcije u trajanju 6 sekundi s pauzom u trajanju 4 sekunde). Ispitanici su ovu aktivnost izvodili sve dok su bili sposobni proizvoditi mišićnu silu veću od 60% njenog početnog maksimuma. Transkranijalna magnetska stimulacija korištena je kako bi se dobio motorički evocirani potencijal i mehanički odgovori u aktivnom mišiću. U prosjeku je šest odgovora analizirano prije vježbe, te svaka 25. kontrakcija za vrijeme vježbe i u fazi oporavka.

Rezultati

Prosječan broj izometričkih kontrakcija prije nastupanja umora kod ispitanika bio je 175 ponavljanja. Za vrijeme vježbe, amplitude mehaničkih, kao i električnih odgovora značajno su se mijenjale ($p<.001$ i $p<.002$). Potencijal elektrofizioloških odgovora bio je istaknut samo na početku zadatka dok je sila kontrakcije još bila visoka sve do nastupanja konačnog umora. Obje su se mjere smanjile nakon završetka zadatka. Ipak, smanjenje elektromiografskih odgovora bilo je veće. U fazi oporavka sila kontrakcije se u potpunosti oporavila, dok je elektrofiziološki potencijal i dalje ostao smanjen ($p<.05$).

Rasprava i zaključak

Za vrijeme i nakon umarajućeg zadatka, modulacija mehaničkih i elektrofizioloških odgovora na transkranijalnu magnetsku stimulaciju nije tekla paralelno. Dodatna kvalitativna analiza elektrofizioloških odgovora pokazala je sistematičan prijelaz sa bi-fazičnog odgovora, zabilježenog u mjerenju prije testa, na poli-fazičan odgovor koji se javlja u fazi umaranja i oporavka. Ovaj fenomen može ukazivati na prijelaz s monosinaptičkih na oligosinaptičke kortikospinalne projekcije što, naime, može uzrokovati vremenski različitu selekciju i aktivaciju motoričkih jedinica. Amplituda vala M, dobivena stimulacijom ulnarnog živca zgloba šake nakon produžene ponavljane umarajuće voljne izometričke kontrakcije, nije se značajno razlikovala od iste dobivene stimulacijom primijenjenom prije ovog iscrpljujućeg protokola. Val F, kao mjera periferne pobuđenosti, nije pokazao značajne modifikacije za vrijeme eksperimenta. Na temelju dobivenih rezultata moguće je isključiti utjecaj perifernih faktora na ove modulacije.

Mehanički odgovori na transkranijalnu magnetsku stimulaciju nisu striktno odražavali elektrofiziološke evocirane potencijale, štoviše, ponašali su se potpuno različito u nekim točkama mjerenja. Za ukupni obrazac evociranih odgovora najvjerojatnije su odgovorni kortikalni mehanizmi. Čini se da je razina pobuđenosti evociranih odgovora snažno pod utjecajem aferentnog ulaza. Nesrazmjer između mehaničkih i elektrofizioloških odgovora mogao bi se objasniti modulacijom cervikalnog propriospinalnog sustava te mehaničkim objašnjenjem povezanim s ulogom mišićne čvrstoće u produkciji sile mišićnog trzaja.