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## Modulatory effect of repetitive peripheral magnetic stimulation on skeletal muscle tone in healthy subjects: stabilization of the elbow joint

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**Abstract** To investigate the role of repetitive peripheral magnetic stimulation (RPMS) on the postural component of motor performances, the long-lasting modulatory effect of RPMS on the stabilization of the elbow joint was examined in 13 healthy subjects. The resistance against very slow passive movements in the relaxed state was recorded simultaneously with the electromyogram (EMG) of the forearm extensor and flexor muscles. The experiments show that RPMS performed on the forearm flexor muscles increased the degree of stabilization of the elbow joint, whereas RPMS on the forearm extensor muscles caused a decrease in stabilization. This leads to the assumption that the postural component of motor tasks depends on the motor task itself: motor tasks like manipulation, pointing or grasping which are fine skilled movements require an increase in stabilization while goal-directed movements require a decrease in stabilization. Therefore RPMS is involved in sensorimotor integration and may modulate the motor program at the cortical level.

**Keywords** Sensorimotor control · Repetitive peripheral magnetic stimulation · Neuromodulation · Postural component of motor tasks · Joint stabilization · Muscle spindle

### Introduction

Recent studies in healthy subjects have demonstrated that somatosensory input in the form of peripheral nerve stimulation or muscle stretching results in functional changes in corticomotor excitability: 300 passively induced wrist extension and flexion movements elicited by a torque motor showed a higher activation (fMRI) of contralateral primary motor cortex (cM1), even though

this effect of motor performance improvement is significantly lower than the improvement caused by voluntary (active) movements (Lotze et al. 2003).

Ridding et al. (2000) showed that a prolonged period of peripheral nerve stimulation can induce a lasting increase in corticomotoneuronal excitability to stimulated body parts. The importance of the conjoint activity of somatosensory afferents and intrinsic cortical motor circuits was shown by Stefan et al. (2000) by using low frequency median nerve stimulation paired with transcranial magnetic stimulation (TMS). The motor evoked potentials (MEP) were increased if the somatosensory input of these stimulations was synchronous at the level of the motor cortex. Kaelin-Lang et al. (2002) concluded that electrical ulnar nerve stimulation elicited a focal increase in corticomotoneuronal excitability which outlasted the stimulation period and probably occurred at cortical sites.

Repetitive peripheral magnetic stimulation (RPMS) in the area of the muscle supplying terminal branches represents an alternative method to transcutaneous electrical stimulation (TES). In contrast to TES, the biologically effective electrical field is considerably lower. This avoids activation of cutaneous receptors like nociceptors as well as the activation of mechanoreceptor afferents from the skin and fiber groups III and IV. The spatial field distributions are also different in terms of spreading. The magnetic field depends upon the ion environment and penetrates deeper regions of the muscle, whereas the current caused by the electrical field will take the path of lowest resistance, thus being fairly limited spatially on the surface.

RPMS in the area of the muscle supplying terminal branches elicits a proprioceptive input to the central nervous system (CNS) in two different ways:

- Adequate activation (indirectly due to stimulation) of mechanoreceptors (fiber groups Ia, Ib, II) during the rhythmic contraction and relaxation as well as vibration of the muscles.

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- Inadequate activation (directly due to stimulation) of sensorimotor nerve fibers with orthodromic and antidromic conduction.

This afferent input leads to sensations such as movement and vibration and is conveyed simultaneously at higher CNS levels. Earlier studies have shown that RPMS elicits improving effects at various levels of the sensorimotor and the cognitive systems (Struppler et al. 2003; Struppler and Havel 2001).

RPMS caused a dramatic decrease in spasticity in a clinical experimental investigation of spastic paresis of finger and hand extensors as well as spastic paraplegia (Struppler et al. 2003). In a PET study investigating the different cerebral activation during a simple motor task, after RPMS the activation was focused on a frontoparietal circuit (Spiegel et al. 2000).

To investigate the influence of RPMS on a pure cognition ability, the effect of RPMS on local tactile extinction in patients after right-sided brain lesions was examined in a study of cognitive functions showing a significant reduction of cognition errors after RPMS (Heldmann et al. 2000). To consider the modifying effect of RPMS on spatial cognition, the position sense under static as well as the position sense during goal-directed pointing tasks with the index finger has been investigated. This also shows a remarkable improvement following RPMS.

Clinical observations show that the regularity of disturbed goal-directed motor performances such as reaching and grasping can be improved. These findings strongly indicate that not only transient spinal mechanisms are responsible for the improvement of voluntary movements but also cortical neuroplasticity.

The aim of the experimental investigations presented in this paper was to give a greater insight into the underlying modulatory mechanisms of RPMS. We attempted to clarify whether RPMS modifies muscle intrinsic factors such as viscoelasticity or if it works at a central, i.e., cortical level.

## Materials and methods

### Subjects

The investigations were performed on 13 healthy subjects aged from 25 to 80 years with an average age of 35 years.

### Methods

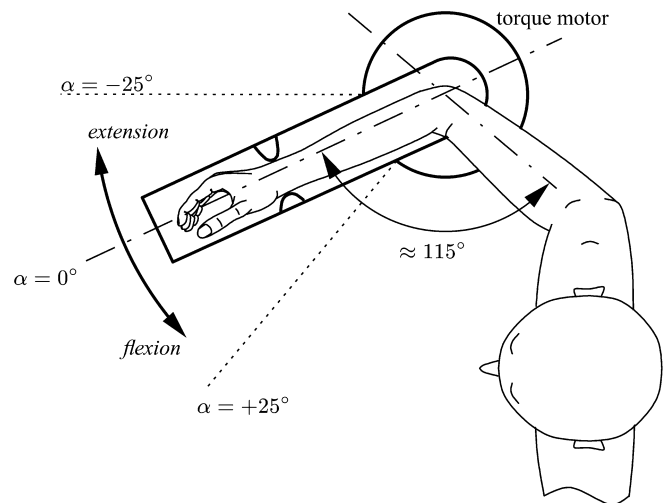
To evaluate the resistance against very slow alternating movements, a torque motor (TM) was used. This TM was controlled by a closed-loop position control to impose the movements on the subject's forearm. The schematic mechanical arrangement for this purpose is depicted in Fig. 1. The reference of the TM is equivalent to an almost relaxed sitting position, which is around  $115^\circ$  at the elbow joint.

The alternating movements applied to the subject's elbow joint can be seen in Fig. 2, where the desired angle of the TM is depicted over time. The velocity of the movements is shown to be really slow ( $2.5^\circ/\text{s}$ ); hence the inertia of the forearm and the lever of the TM can be neglected.

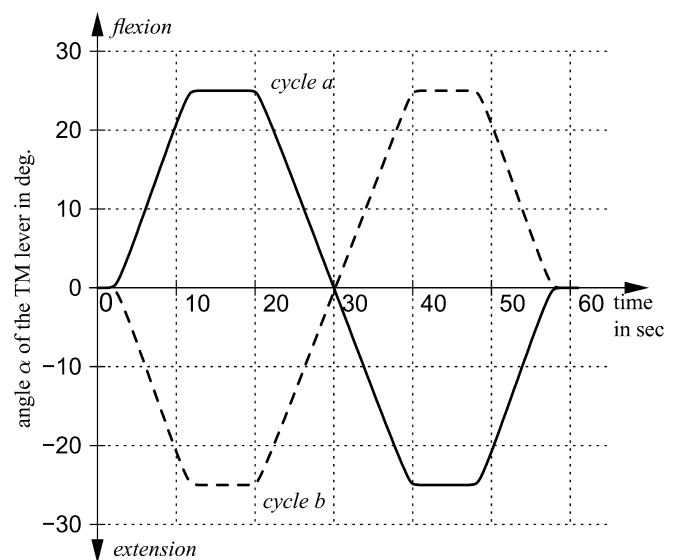
In order to exclude the role of the preceding movements, two different movement schemes were used: "cycle a" and "cycle b."

### Cycle a

From the starting position at  $0^\circ$  the lever was moved to  $25^\circ$  (flexion) at a velocity of  $2.5^\circ/\text{s}$ . After a break of 8 s in this



**Fig. 1** Mechanical arrangement and definition of the reference for the position  $\alpha$  of the TM; the figure shows the subject in a comfortable and relaxed sitting position; the forearm is fixed at the lever of the TM



**Fig. 2** Desired angle  $\alpha$  of the TM over time for the different movement schemes cycles a and b

**Table 1** Definition of the three different subject groups including the reference group

	Pre-registration sequence	Conditioning RPMS	Postregistration sequence
Group A (seven subjects)	Measurement of the mechanical and EMG parameters (pre-RPMS)	Stimulation of the m. triceps brachii	Measurement of the mechanical and EMG parameters (post-RPMS)
Group B (nine subjects)	Measurement of the mechanical and EMG parameters (pre-RPMS)	Stimulation of the m. biceps brachii	Measurement of the mechanical and EMG parameters (post-RPMS)
Group C (seven subjects)	Measurement of the mechanical and EMG parameters	No stimulation	Measurement of the mechanical and EMG parameters

position, an extension of  $50^\circ$  at the same velocity followed. After another break of 8 s, the system returned to the starting position by a flexion of  $25^\circ$ .

### Cycle b

The movement pattern described by cycle b is the inverse pattern of cycle a as depicted in Fig. 2 (dotted line). For evaluation purposes the angle  $\alpha$  of the TM as well as the torque  $T$  of the forearm against the lever were measured (Given et al. 1995; Struppler and Jakob 1995). The resistance against slow alternating movements (measured torque) is based on the simultaneous lengthening and shortening reactions of the involved synergistic and antagonistic muscle groups, respectively.

Hence the EMG of the agonistic and antagonistic muscles was recorded simultaneously with the mechanical parameters. The muscles recorded were m. biceps brachii (caput longum), m. biceps brachii (caput breve) and m. triceps brachii. To measure the EMG, skin-surface electrodes and a sample rate of 2,080 samples/s were used. The angle  $\alpha$  of the TM and the torque  $T$  were sampled with  $2080/4=520$  samples/s.

RPMS was transcutaneously performed on the area of muscle supplying the terminal branches by a conventional stimulation coil (Magstim double 70-mm coil). For every application of RPMS, 5,000 single magnetic field impulses at an average amplitude of  $1.2 \text{ T}^1$  were applied. The field impulses were generated by a self-built stimulator (Schmid 1992) and repeated at a physiologically orientated frequency of 20 Hz.

After every 30 impulses a break of 3 s was left to induce repetitive contractions and relaxations to the target muscles. This stimulation elicited mainly a proprioceptive inflow to the CNS together with the sensation of movement and vibration.

### Experimental protocol

To investigate the influence of RPMS on the stabilization of the elbow joint, the mechanical and EMG parameters from the synergistic and antagonistic muscles were measured before and after the conditioning RPMS.

<sup>1</sup>  $1.2 \text{ T}=12,000 \text{ G}$

To obtain more accurate results during one recording sequence, the movement cycles a and b were applied four times to each subject. With these  $2 \times 4$  cycles one average cycle a and one average cycle b was calculated for the evaluation process.

During the measurement session the subject was advised to relax the shoulder (clinically controlled) and the forearm (no burst activity in the raw EMG data). This sequence was followed by the RPMS conditioning either of the biceps or of the triceps. Approximately 30 min after the RPMS, the mechanical and EMG parameters were measured again. This was done although it could be shown that the maximum effects of RPMS developed after 2–4 h (Struppler et al. 1996, 2003).

### Subject group definition

To investigate whether the RPMS of forearm flexor muscles causes effects other than the RPMS of forearm extensor muscles, different subject groups were defined (see Table 1):

- A. RPMS of the forearm extensor muscles
- B. RPMS of the forearm flexor muscles

Each subject was assigned to one of these groups. However, it was possible to stimulate and examine the same person, after an adequate period of time (at least 4 weeks), under the conditions of the other group. To exclude any time-dependent factor during the experiment (e.g. fatigue-induced effects), a third group was defined. In this group the mechanical and EMG parameters were also measured twice. In contrast to groups A and B, instead of the conditioning RPMS a break of approximately 15 min was left between the two recording sequences. This led to a reference subject group:

- C. Pause of 15 min (control group)

### Results

For the evaluation of the conditioning effect of RPMS on the stabilization of the elbow joint (resistance against extension and flexion), the average results for the different subject groups had to be compared. For this purpose the measured torque  $T_C$  of group C was taken as the baseline to evaluate the changes in the measured torque  $T_A$  and  $T_B$ .

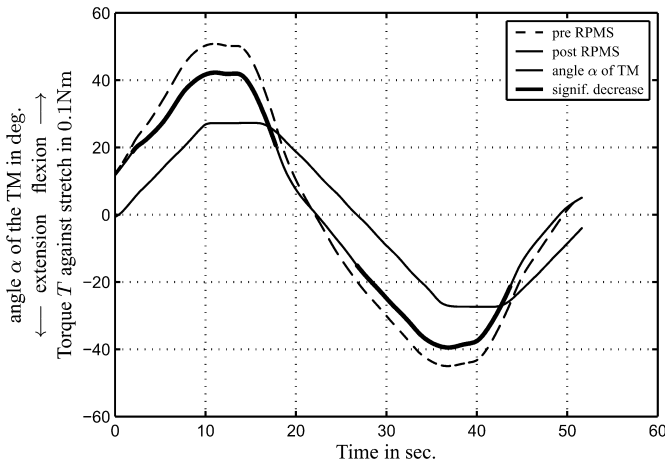
This is represented by the following equation:

$$\delta T_{A/B} = T_{A/B} - T_C \quad (1)$$

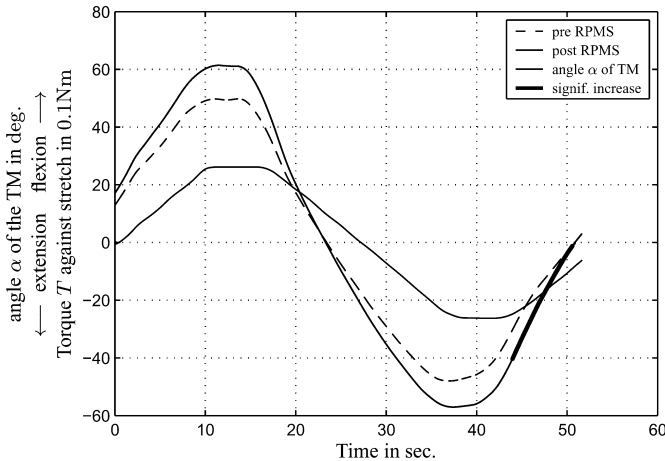
In order to analyze the change of the measured torque  $\Delta T_{A,B}$  related to the conditioning RPMS, the difference in the measured torque before and after the RPMS has to be considered. This leads to the equation:

$$\begin{aligned} \Delta t_{A/B} &= \delta T_{A/B, \text{post}} - \Delta T_{A/B, \text{pre}} = \\ &= (T_{A/B, \text{post}} - T_{C, \text{post}}) - \\ &= (T_{A/B, \text{pre}} - T_{C, \text{pre}}) = \\ &= (T_{A/B, \text{post}} - T_{A/B, \text{pre}}) - \\ &= (T_{C, \text{post}} - T_{C, \text{pre}}) \end{aligned} \quad (2)$$

This equation is used for statistical evaluation. However, Figs. 3 and 4 show the absolute values  $T_{A/B, \text{pre, post}}$ .



**Fig. 3** Decrease ( $p < 0.1$ ) in the stabilization of the elbow joint for group A vs group C (triceps RPMS vs no RPMS; left cycle a, right cycle b); the dashed line represents the torque before the RPMS application whereas the medium solid line represents the torque



**Fig. 4** Increase ( $p < 0.1$ ) in the stabilization of the elbow joint for group B vs group C (biceps RPMS vs no RPMS; left cycle a, right cycle b); the dashed line represents the torque before the RPMS application whereas the medium solid line represents the torque

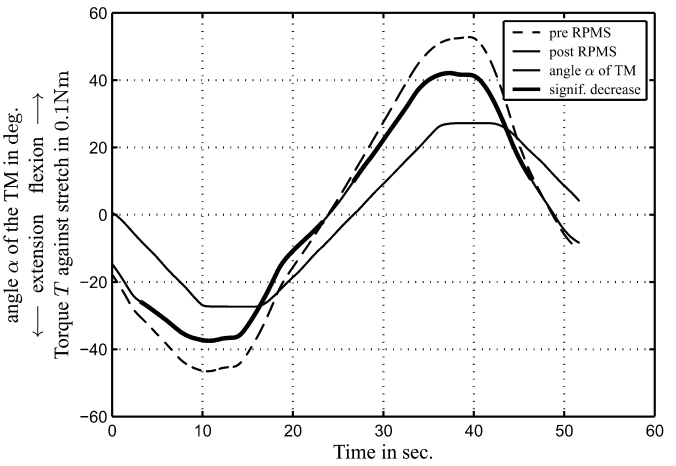
The data presented in Figs. 3 and 4 are the average of all subjects in the corresponding group. Hence significant changes can only be seen in some areas of the applied movements, which are marked by thick lines. Due to measurement noise the significant areas are additionally reduced.

#### Results for group A

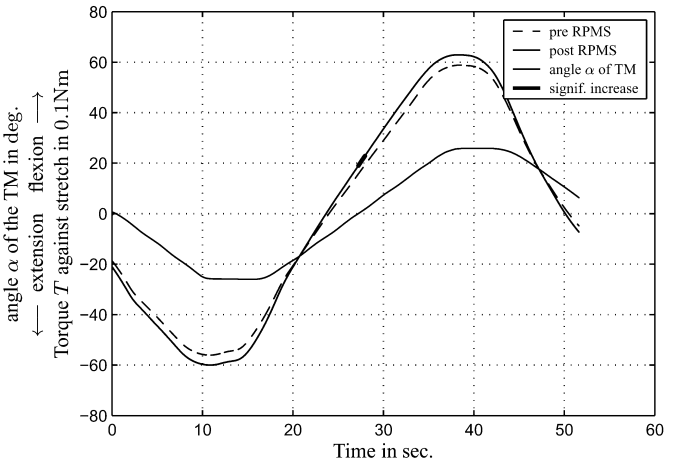
In group A RPMS applied on the triceps muscle tended to result in a decrease ( $p < 0.1$ ) of the stabilization of the elbow joint, as can be seen in Fig. 3.

#### Results for group B

In group B RPMS applied on the biceps muscle tended to result in an increase ( $p < 0.1$ ) of the stabilization of the elbow joint, as can be seen in Fig. 4. Concerning the only



30 min after RPMS; the thick line depicts the area of statistically relevant decrease in comparison to the reference group; the fine solid line describes the position of the forearm



30 min after RPMS; the thick line depicts the area of statistically relevant increase in comparison to the reference group; the fine solid line describes the position of the forearm

obvious small difference between the control group and the conditioned group, the different muscle masses and the completely different representation in motor tasks between biceps and triceps have to be considered.

Comparison of groups A and B

However, if the conditioned groups are directly compared, the difference between biceps and triceps results in a broad area of a significant ( $p < 0.05$ ) decrease of resistance against slow movements, which is depicted in Fig. 5. This means that the stabilization of the elbow joint is significantly

lower after the conditioning RPMS is applied to the triceps than to the biceps. All statistical proofs were done by the Institute of Statistics in Medicine and Epidemiology (TUM). The analysis was performed using a general linear model with repeated measurements and a between-subjects factor. An interaction term was included.

Electromyogram

In Fig. 6 the ratio of the mean EMG before and after the conditioning stimulation can be seen together with the standard deviation. For an assessment of this figure it

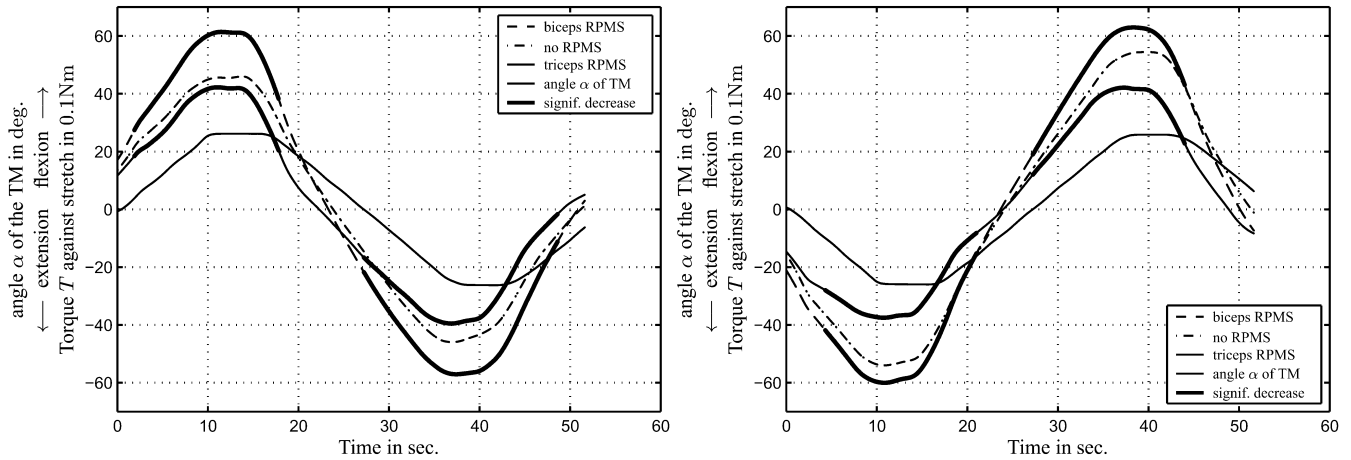


Fig. 5 Significant decrease ( $p < 0.05$ ) in the stabilization of the elbow joint after RPMS performed on the triceps in comparison to the stabilization of the elbow joint after RPMS performed to the biceps; left cycle a, right cycle b; the dashed line represents the torque 30 min after RPMS on the biceps whereas the medium solid

line represents the torque 30 min after RPMS on the triceps; the thick line depicts the area of significant decrease; the fine solid line describes the position of the forearm; the dashed-dotted line corresponds to the reference group with no RPMS intervention

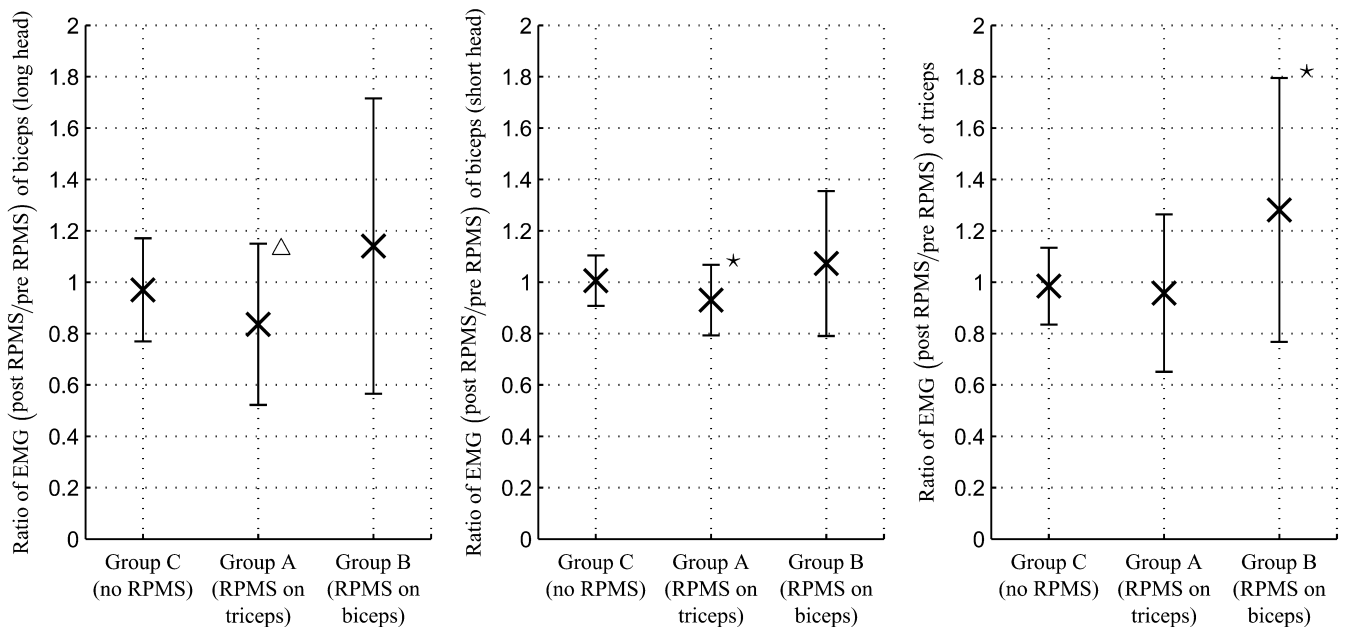


Fig. 6 Ratio of the EMG between pre-RPMS and post-RPMS ( $1$  no change,  $>1$  increase,  $<1$  decrease); together with the standard deviation; the significant ( $p < 0.05$ ) changes between groups A and B in comparison to the reference group are marked with an asterisk,

whereas tendencies ( $p < 0.1$ ) are marked with a triangle; the comparison between groups A and B always shows a significant ( $p < 0.05$ ) decrease in the EMG after RPMS applied to the triceps in contrast to RPMS applied to the biceps

needs to be considered that the EMG under relaxation is really low, since only a few small motor units are activated and only the superficial ones are recorded. To obtain more accurate results, the movement schemes cycle a and b are put together and the EMG activity is averaged over the complete movement cycle. Hence the results of the EMG are only complementary to the torque and should satisfy that the changes in the torque are based on neuronal activity.

The results of the EMG correspond with the measured torque since an increase in the stiffness after RPMS performed on the biceps (group B) shows a higher activity in the biceps and triceps muscles in comparison to the control group (group C). This means that the balance in the elbow joint is raised to a higher level on stiffness, which increases the torque against extension and flexion but leaves the relaxed position unchanged. On the other hand, RPMS performed on the triceps (group A) shows a lower activity in the biceps and triceps together with a decrease in stiffness around the elbow joint.

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## Discussion

The role of RPMS on skeletal muscle tone regarding stiffness and tonic activity around the elbow joint has been investigated during slow alternating passive movements under relaxed state conditions in 13 healthy subjects. RPMS performed on the biceps (flexor muscles) increased the stiffness and EMG in comparison to the control group, whereas RPMS applied to the triceps (extensor muscles) caused a decrease in comparison to the control group. Depending on the location of the conditioning RPMS, the muscle tone changed in the same way in the agonists and the antagonists. This influence of the conditioning RPMS outlasted the displacement at least 8 s. These 8 s correspond to the break during the movement cycles as can be seen in Fig. 2. This means that there is no reciprocal effect as under dynamic passive or active movements.

To interpret these results it has to be considered that the imposed passive alternating movements around the elbow joint were performed very slowly ( $2.5^\circ/\text{s}$ ) and in an almost relaxed state. To gain a more detailed insight into the modulatory mechanism of RPMS, different effects dependent on RPMS need to be distinguished: *Skeletal muscle intrinsic factors* (like viscosity and elasticity) can be modified directly via induced repetitive contraction and relaxation of the underlying skeletal muscle fibers. Due to the opposite conditioning effect, muscle intrinsic factors are not capable of explaining such behavior since muscle intrinsic factors for the biceps and the triceps are influenced in the same way by RPMS. Therefore the stiffness can be excluded from the stabilization of the elbow joint (resistance against very slow movements) while the effects which depend on neuronal activity (skeletal muscle tone) must be taken into account. This is also shown by the EMG since the changes in activity of the biceps and triceps muscles are in the same direction.

It is assumed that under optimal voluntary relaxation there is just a small tonic activity of S-units (Petit et al. 1990). However, the EMG recordings cannot be distinguished between the three basic types of muscle units in mammalian limb muscles. The basic types are fast twitch fatigable (FF) units, fast twitch fatigue resistant (FR) units and slow (S) units which are resistant to fatigue (Burke 1999).

On a receptor level the repetitive induced movements might modify the thixotropic behavior of receptor-bearing intrafusal muscle fibers due to aftereffects of repetitive stretch and/or contractions (Hagbarth et al. 1995; Jahnke et al. 1989). Since the conditioning effect is long lasting and independent of intermediate movements, it seems that neuromodulation on a CNS (intra-neuronal) level must be involved.

Since direct effects on the underlying muscle seem to be excluded by the data, effects on neural commands should be considered: The proprioceptive inflow has modifying effects on spinal, supraspinal and cortical level as described in the "Introduction." Due to the mechanism of action of the RPMS, it is assumed that the proprioceptive inflow originates in the fiber groups Ia, Ib and II and not in the receptors lying in the skin.

The group Ia fibers with their dynamic and static components take the well-known reciprocal facilitatory and inhibitory effect in antagonistic muscles on a spinal level. Hence the Ia fibers are not capable of explaining the non-reciprocal modulatory effect in the antagonistic muscles.

It seems unlikely that the Ib afferents play a role with their negative feedback (control of muscle tension via the homonymous and synergistic motoneurons due to inhibitory Ib interneurons). Their activation via descending tracts follows a greater development of muscle tension. Furthermore, the inhibitory effect of group Ib afferents will be activated by a descending drive when the muscle tension increases (Ib: Interneuronal System; Jankowska and Lundberg 1981). In addition, the antidrome activation of the Renshaw feedback under relaxation is not likely, because this negative feedback is only effective under the activation via descending tracts, as in group Ib.

Recently there has been increasing attention on the function of the group II afferents in sensorimotor integration. Prochazka has shown that group II afferents follow muscle length changes even more clearly than Ia afferents especially during imposed movements (Prochazka and Gorassini 1998; Prochazka et al. 2002).

Furthermore muscle spindle secondaries provide strong input to  $\gamma$ -motoneurons ( $\gamma$ -MN) in the lower extremity. Gladden and Jankowska (1998) show that group II afferents of one muscle can excite  $\gamma$ -MN of the same muscle, which means a positive feedback loop. Experiments using natural stimuli (muscle stretch and vibration) to excite  $\gamma$ -MN indicate that secondary afferents are the main source of input for these neurons. The positive feedback between muscle spindle secondaries and  $\gamma$ -MN can be modulated directly and indirectly via intermediate zone interneurons (Jankowska and Gladden 1999).

Supposing that these findings in the lower extremity are also valid for the upper extremity, it can be assumed that the positive feedback between group II muscle spindle afferents and  $\gamma$ -MN could act as an enhancement of effects of the RPMS at the spinal level.

The positive feedback between secondary endings and homonymous  $\gamma$ -MN would increase muscle tone by increasing the feedback from primary and secondary endings directly to  $\alpha$ -motoneurons, and indirectly through group II interneurons.

However, the modulatory effect need not be confined to the spinal pathways—the conditioning RPMS may have changed the descending control of the interneurons from supraspinal and/or cortical level. The presented data suggest that agonistic and antagonistic muscular afferent inputs may evoke facilitation of both muscles or inhibition of both muscles at the cortical level.

To investigate whether the long-latency component of the human stretch reflex (LLSR) corresponds to the increase in motor cortical activity, the time course of the cortical excitability state following muscle stretch during isometric activity (deep finger flexor muscles) was tested using TMS. When the magnetic cortical stimulus was timed to produce an EMG response in the period of the later part of the long-latency stretch reflex, the response was larger than if it was timed to produce a response in the period of the short-latency spinal reflex or when superimposed on the tonic muscle activity used to resist the standing torque of the motor. When the intensity of magnetic cortical stimulation was reduced so that it was just below threshold to produce an EMG response in the short-latency reflex period or in the background tonic EMG activity, it was still capable of producing a response when superimposed on the long-latency stretch reflex. This suggests that inputs from muscle receptors of the stretched muscle contribute to the effect since neuronal afferents from skin, joint and muscle receptors of the hand could be excluded by nerve block (Day et al. 1988). However, if transcortical electrical stimulation (TES) is used, no significant facilitatory effect on the long-latency stretch reflex can be found (Day et al. 1991).

Cheney and Fetz (1984) observe in the monkey that corticospinal cell couples are activated by stretching of the wrist muscles in both the extension and flexion direction and that (transcortical) reflex bursts were seen in both agonistic and antagonistic muscles. They suggested that this could be of importance for the regulation of the stiffness across the ankle joint by eliciting co-contraction of the antagonistic muscles.

To clarify whether muscle afferents influence the excitability of corticospinal projections to antagonist muscles, the excitability of the right forearm muscles at rest was tested by TMS and electrical brain stimulation by Bertolasi et al. (1998). After nerve stimulation (median and radial nerve) the corticomotoneuronal connections to the right forearm at rest were tested. These authors propose that activation of median nerve muscle afferents can suppress the excitability of cortical areas controlling the antagonist forearm extensor muscles acting on the

hand (Bertolasi et al. 1998). The inhibitory effect occurs at short latency and might assist spinal pathways mediating reciprocal inhibition by contrasting the coactivation of antagonistic pools of corticospinal cells.

The aim of the study by Lewis and Byblow (2001) was to investigate modulations in corticomotor excitability during passive rhythmic movement, in order to elaborate the level of the neuroaxis at which such changes are mediated. TMS is delivered to cortical areas representing the flexor carpi radialis muscle during different phases of passive rhythmic flexion/extension movements of the contralateral wrist joint. The results of the static trials provide evidence that corticomotoneuronal excitability of the flexor carpi radialis muscle is altered by changes in the wrist joint angle. When the wrist is in a flexioned posture, the response amplitude is higher than if the wrist joint is in extended postures. This may reflect a reduction in static spindle receptor output at the shortened muscle lengths (Carson et al. 2000).

The aim of the experiments presented by Stinear and Byblow (2002) was to examine the regulation of inhibitory mechanism in human primary motor cortex during different patterns of rhythmical bimanual movements. Flexor carpi radialis and extensor carpi radialis corticomotor pathway as well as spinal pathway excitability were examined during synchronous and asynchronous bimanual wrist flexion/extension under active and passive conditions. The results of these experiments indicate that modulation of inhibitory activity takes place at the cortical level.

Aimonetti and Nielsen (2001) investigated how the transcortical reflexes are integrated into the central motor commands at a cortical level during contraction of either the wrist extensor or flexor muscles. The effects of homonymous and antagonist nerve stimulation on the intracortical inhibition and facilitation in the cortical areas that control the wrist extensor and flexor radialis muscles were tested by double pulse TMS.

It is suggested that the observed effects do not reflect activation of a simple reflex system, where the sensory input is relatively closely linked to the output. In both flexor and extensor muscles, antagonist nerve stimulation 40 ms before the test double pulse TMS decreased intracortical inhibition and increased intracortical facilitation. In contrast, homonymous nerve stimulation has no effect on intracortical inhibition and increased intracortical facilitation.

## Conclusion

Concerning the functional relevance of the elbow joint stabilization, it has to be considered that forearm flexor and extensor muscles are facilitated or inhibited concomitantly depending on the location of the conditioning RPMS. This means that RPMS modulates the stabilization of the elbow joint most likely at a cortical level, corresponding adequately to the planned motor tasks:

- Preceding motor tasks such as manipulation, pointing, grasping (postural component in forearm and shoulder), a stabilization of the elbow joint is necessary.
- Preceding goal-directed movements (kinetic component), the stabilization of the joint has to be decreased in order to facilitate the movements.

Increased stabilization may also ameliorate the spatial cognition of the limb due to increased proprioceptive afferent inflow especially from the group II afferents, which are responsible for the tonic component.

### Future work

To investigate whether the modulatory effect (facilitation or inhibition respectively) takes place at a cortical level, the conditioning influence of RPMS on the MEP elicited by double pulse TMS needs to be examined.

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