

INFLUENCE OF SUSTAINED STRETCH ON LATE MUSCULAR RESPONSES TO MAGNETIC BRAIN STIMULATION IN PATIENTS WITH UPPER MOTOR NEURON LESIONS

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ABSTRACT. Late muscular responses to transcranial magnetic stimulation occur in healthy subjects only in tonically active muscles with a proportional relationship between the amount of the EMG-response and the voluntary innervation strength. In hemiparetic stroke patients late potentials are elicited in chronically spastic hand flexors without voluntary background muscular activity probably reflecting enhanced excitability of spinal α -motoneurons in the spastic state. When spastic muscle hypertonus has been diminished by sustained muscle stretch late EMG-potentials are reduced or have disappeared completely. The relation between spastic muscle hypertonus and the late muscular response potentials as well as the possible mechanisms of sustained muscle stretch on the response characteristics to transcranial magnetic stimulation in spastic flexor muscles of the hand are discussed.

Key words: muscular hypertonus, sustained muscle stretch, transcranial magnetic stimulation, physiotherapy.

Since the introduction of transcranial electrical (26) and transcranial magnetic (3) stimulation most studies have been focussed on the short-latency EMG-responses that are produced in the contralateral limb musculature. These early responses have been attributed to fast conducting monosynaptic or oligosynaptic pathways from the motor cortex to the α -motoneuronal pool (7, 8, 15). Delayed onset of EMG-responses was observed in patients with lesions in cortical and subcortical motor structures (4, 12), multiple sclerosis (7), motoneuron disease and other peripheral motor neuropathies (18).

Apart from the delayed onset of early responses late muscular responses have occasionally been observed in healthy subjects and patients with motor impairments (7, 8, 27). They follow the magnetic brain stimulus with a latency longer than 50 ms and have been attributed to peripheral and central neuronal

loops (27). Generally, the second response could be mediated by slow conducting and/or polysynaptic corticospinal pathways which have less secure transmission properties (19, 21). A peripheral contribution could simply be a monosynaptic stretch reflex elicited by the muscle twitch of the early response potential. Nevertheless, late potentials are rarely observed in healthy subjects without a voluntary preinnervation of the target muscle. A tonic preactivation enhances the frequency of occurrence and the amount of the late responses. Calancie et al. (8) found late compound EMG-responses exclusively in those trials involving a background muscle contraction and only when strong (electrical) stimuli were delivered.

In the course of our experiments dealing with the facilitatory and inhibitory influence of physiotherapeutic interventions (21, 22) we occasionally observed long-latency muscular responses to transcranial magnetic stimulation that were present even when no voluntary muscular preactivation was detected.

We think it worthwhile to consider the nature of these late responses and to describe how they are influenced by sustained muscle stretch which is one of the most frequently applied physiotherapeutic techniques to inhibit enhanced muscle tone. As spasticity in the upper extremity is typically most pronounced in flexor muscle groups, our interest here is focussed on the data obtained from the flexor carpi radialis muscle. A preliminary report of our findings has been presented to the Paneuropean Society of Neurology (20).

PATIENTS AND METHODS

The data presented here have been obtained from 15 stroke patients with a severe chronic spastic hemiparesis due to an ischemic infarction in the territory of the medial cerebral artery (delay between stroke event and participation in our study: 3-9 months). The 8 women and 7 men were between 47 and 72 years old (mean age = 61 years). No patient was able to perform voluntary hand or finger movements except in a coarse synergism starting in shoulder or proximal arm musculature. The amount of spasticity was individually

assessed for each patient according to the Ashworth-scale (2, 6, 30). In our patients spasticity was regularly characterized by a sustained tonic resistance against passive extension in the wrist flexors or even by a rigid fixation of hand and fingers in a flexed position as has been described by Little & Merritt (25) as a typical feature in severe chronic central paresis. In all patients sustained electromyographic activity could be recorded in the hand flexors during slow "tonic" passive extension of the hand. Consequently, spasticity of all patients was scored grade 4 or grade 5 on the Ashworth-scale. Four patients showed mild hand and finger clonus.

After assessment of the individual degree of spasticity in each patient transcranial magnetic stimulation was carried out using a circular coil (Magstim 200, Madaus Corp.; inside diameter of the coil 9 cm, outside diameter 14 cm) with the center positioned flat over the vertex at Cz (international 10–20 system of electrode placement). The position and orientation of the coil was carefully maintained throughout the experiment. The maximum magnetic field generated by the stimulator was 1.5 Tesla (according to the manufacturer's specifications). The stimulation intensities can be varied on a linear scale ranging from 10% to 100% of the maximum stimulus intensity.

Early and/or late compound muscular action potentials were recorded from the flexor carpi radialis muscle by means of conventional surface electrodes, 0.7 cm in diameter and separated from each other by about 3 cm. Although recordings were taken as well from the extensor carpi radialis muscle the results will not be presented in this context. Signals were rectified, filtered (30 Hz to 3 kHz, Toennies Universal Physiologie-Verstärker) and fed into a commercial data acquisition system (MacLab, World Precision Instruments Corp.) for off-line analysis. During stimulation and recording the patients were comfortably seated in a relaxed position with the arm supported on a desk. The hand lay in a middle position between pronation and supination. Patients were instructed to avoid voluntary innervation; relaxation of extensor and flexor carpi radialis muscles was continuously monitored electromyographically by means of a two-channel digital oscilloscope. Patients with cardiac pacemaker, intracranial metal implants, or a history of epilepsy were excluded. All patients gave their informed consent to participate in the study. The experimental protocol was approved by the local ethical board.

At first, transcranial magnetic stimulation (6–15 stimulations at each stimulus intensity) was performed without any physiotherapeutic intervention and without any voluntary preinnervation. As it is a common observation that the first stimulus has a more pronounced effect than following stimulations, the responses to the first two stimuli were excluded from later analysis. After the second stimulus no relevant habituation effects were seen. Nevertheless, care was taken that at least 90 seconds elapse between two successive stimulations. Stimulation threshold (in % of the maximum stimulus intensity), response latency and response duration were measured for the early and the late responses. After that, the spastic muscular hypertonus was diminished according to the Bobath concept (5) by stretching spastic muscles slowly and tonically in a proximo-distal sequence beginning with a prolonged outward scapula rotation. Then the arm was abducted and outward rotated in the shoulder and extended in the elbow, followed by an extension in the wrist and finger joints and an abduction of the thumb. In that position where most spastic flexor muscles were tonically stretched, muscle tone gradually decreased. After reduction of muscle tone had reached its maximum (normally after about 10 to 15 minutes)

and after repositioning of the arm into the previous position the degree of spasticity was scored again according to the Ashworth-scale. Then response latency, response duration and stimulation threshold for the early and the late muscular responses to transcranial magnetic stimulation were determined again.

RESULTS

A typical recording from the flexor carpi radialis muscle of a healthy subject is shown in Fig. 1. In the relaxed state (A) only early responses at 19 ms can be obtained by transcranial magnetic stimulation. When stimulation takes place during a constant voluntary preinnervation (B) a late potential at 145 ms is observed following the (larger) early potential. Amplitude and duration of both potentials increase with increasing stimulus intensity and with increasing voluntary preinnervation strength.

Transcranial magnetic stimulation in our 15 stroke patients was only applied when no voluntary muscular activity was present. In four patients late response potentials followed the early responses, in 8 patients only early or only late potentials were observed, and in 3 patients both potentials were completely lacking (Table I). The mean latency of the early potentials was 26 ms (range 19–41 ms), the mean latency of the late potentials 79 ms (range 61–151 ms). The mean duration of the late responses was 47 ms (range 28–79 ms) and significantly longer than that of the early responses with 25 ms (range 21–40 ms), their latencies showed more variation, the threshold to elicit late response potentials was higher (mean value 90%) and their reliability to occur after each stimulus was less (Table I). Fig. 2A illustrates the data obtained from a patient having no early responses, but a pronounced late response starting at a latency of 74 ms. In this patient, as an exception, another late potential followed at 180 ms. Early and late muscular responses to the magnetic brain stimulus in a further patient are illustrated in Fig. 3A.

As all patients were scored grade 4 and 5 on the Ashworth-scale, a correlation between the degree of spasticity and the characteristics of the muscular responses to transcranial brain stimulation was not possible in this context.

Sustained muscle stretch led to a significant reduction in the spastic hypertonus in elbow, hand and finger flexors in all patients. Hand and fingers could now passively be extended with only minimal resistance in the complete range of motion. No patient had a rigid muscular fixation of hand or fingers in the

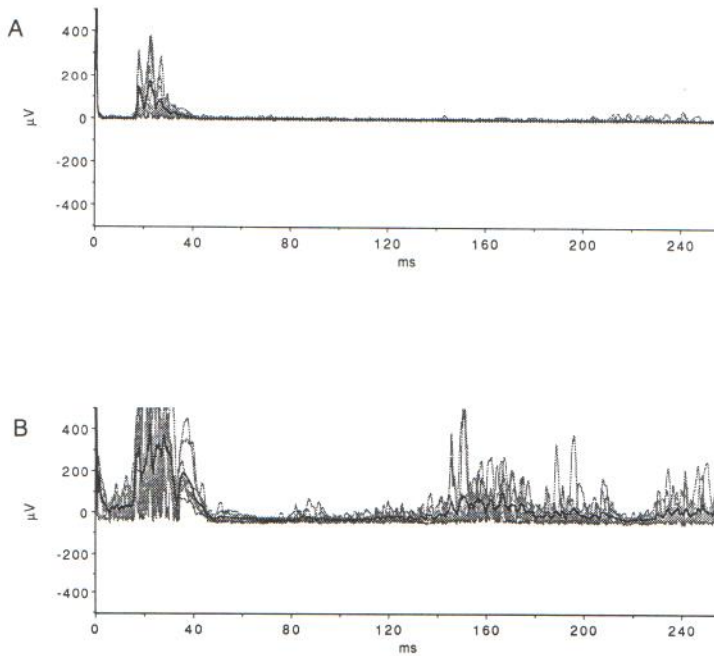


Fig. 1. EMG-recording from the flexor carpi radialis muscle of a healthy subject (100% stimulus intensity; 8 responses superimposed). (A) Stimulation without voluntary innervation; (B) Stimulation during constant voluntary preinnervation. (Thick black line: average.)

flexed position. All patients were now scored grade 3 or 4 on the Ashworth-scale. No patient showed hand or finger clonus after the period of sustained stretch.

After the described physiotherapeutic reduction of the spastic flexor hypertonus those features of the muscular responses reflecting α -motoneuronal excitability were reduced. Eight patients had no muscular responses (Fig. 2B), 4 patients had only early responses (Fig. 3B), 1 patient had only late responses and 2 patients had early and late responses. No patient showed enhanced muscular responses, no patient without late responses before sustained stretch had late muscular responses after stretching. The stimulation threshold for the early and the late responses were markedly increased (93% for the early, 100% for the late responses), the mean latency for the early responses showed only a minor increase of 2 ms, whereas the mean latency for the late responses increased from 79 ms to 110 ms. The late response only occurred in 25% of all stimulations (Table II). In all patients—including those without late potentials before the sustained muscle stretch—the magnitude of the early response was reduced.

DISCUSSION

As it could be shown in healthy subjects (8, 16) a complex sequence of excitability changes in the motoneuronal pool follows the transcranial brain stimulus. Excitability can be enhanced by central facilitation, i.e. voluntary preinnervation of the target muscle (14), and—as our results demonstrate—diminished by physiotherapeutic techniques applying sustained muscle stretch.

It is unlikely that the reduced response characteristics after sustained muscle stretch are due to the patients' habituation to repeated magnetic brain stimulation because the delay between each stimulation was at least 90 seconds, the response magnitudes did not gradually decrease and because muscle stretch by the physiotherapist lasted between 10 and 15 minutes. During this time, habituation effects should at least have disappeared in part.

In general, the chronic spastic condition of our stroke patients and the state of voluntary preinnervation in the target muscle seem to be comparable situations for the occurrence of late muscular response

Table I. Latency, duration, threshold and frequency of occurrence of early and late responses to transcranial magnetic stimulation (100% stimulus intensity) before sustained stretch

(no response in 3 patients; early response in 4 patients; late response in 4 patients; early and late responses in 4 patients).

	Early response	Late response
Threshold (mean values) (%)	78	90
Latency (mean value) (range) (ms)	26 (19-41)	79 (61-151)
Duration (mean value) (range) (ms)	25 (21-40)	47 (28-79)
Frequency (%)	72*	62*

* In 8 patients.

potentials. Up to now numerous hypotheses about the origin of the late response potentials are discussed:

- (i) The magnetic field generated by the stimulation coil covers a large cortical and probably subcortical area including premotor, supplementary motor and sensory areas giving rise to slow-conducting descending pathways parallel to the classical pyramidal tract. The signals travelling in these pathways are transmitted via several subcortical and interneuronal relay stations with several intercalated synapses (13, 19). Therefore, the latency of the second potential could be explained by synaptic delays and by the slower conduction velocity of the involved descending pathways.
- (ii) The majority (about 92% in monkeys (29)) of the fibers running down from the motor cortex to the spinal motoneurons is slow conducting and its excitatory effect on spinal cells may be inhibited by the signals travelling in the fast conducting part of the corticospinal tract and therefore arriving first at the spinal level. In the spastic condition, when motoneuronal excitability is enhanced (1, 11), this inhibition may be insufficient and the late potentials be unmasked. There-

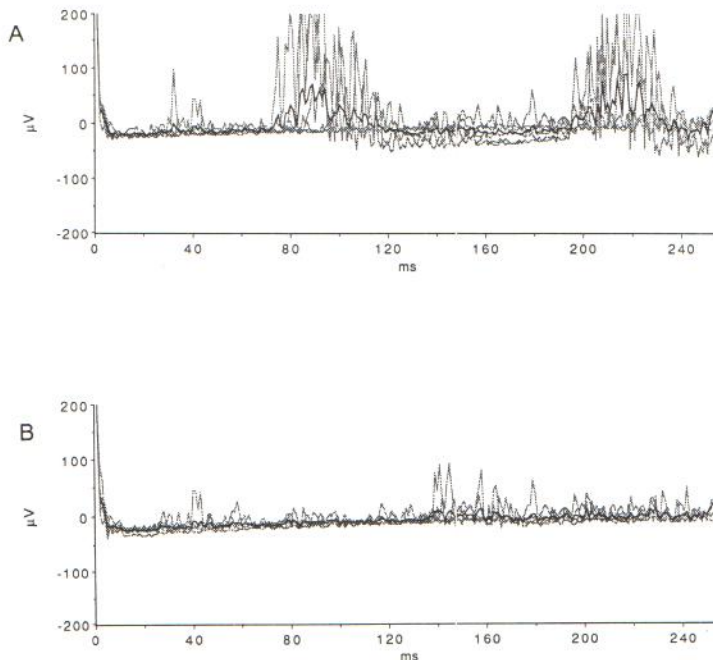


Fig. 2. EMG-recording from the flexor carpi radialis muscle on the affected side of a patient with a left-sided central hemiparesis (100% stimulus intensity; 8 responses superimposed). (A) Stimulation before sustained muscle stretch. Strong late responses at 74 ms and 180 ms; (B) Stimulation after sustained muscle stretch. No late responses. (Thick black line: average.)

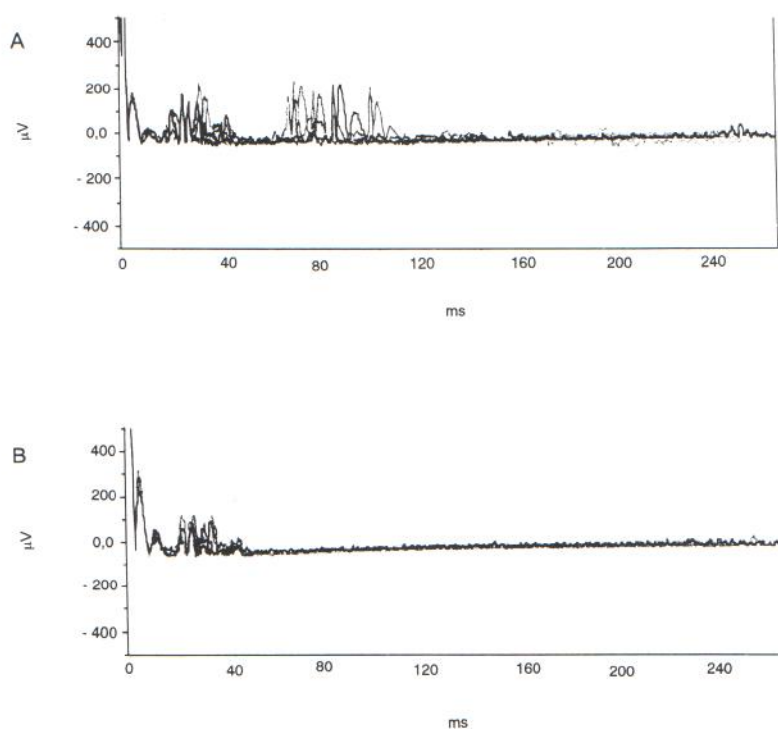


Fig. 3. EMG-recording from the flexor carpi radialis muscle on the affected side of a patient with a right-sided central hemiparesis (100% stimulus intensity; 6 responses superimposed). (A) Stimulation before sustained muscle stretch. Late response at 57 ms; (B) Stimulation after sustained muscle stretch. No late response. (Thick black line: average.)

fore, whether late potentials are observed or not may depend on the degree of intactness of the fast conducting fiber systems.

- (iii) The initial muscle twitch elicited by the magnetic brain stimulus may give rise to a secondary reflex response. This explanation, however, can probably be ruled out because late potentials are also observed in patients in whom the first potential is lacking. As transcranial magnetic stimulation is only performed when no voluntary preinnervation

can be detected the late potential cannot be interpreted as the resumption of muscular activity at the end of a silent period.

Voluntary preinnervation of the target muscle enhances the excitability of its α -motoneurons (14). If transcranial magnetic stimulation is applied in this condition enhanced early muscular responses can be observed and the frequency of occurrence of the late potentials will grow. In spastic patients, amplitude, duration and frequency of occurrence of the early and

Table II. Latency, duration, threshold and frequency of occurrence of early and late responses to transcranial magnetic stimulation (100% stimulus intensity) after sustained stretch

(No response in 8 patients; early responses in 4 patients; late response in 1 patient; early and late responses in 2 patients).

	Early response	Late response
Threshold (mean values) (%)	93	100
Latency (mean value) (range) (ms)	28 (19–44)	110 (81–159)
Duration (mean value) (range) (ms)	22 (16–31)	37 (35–40)
Frequency (%)	60*	25†

* In 6 patients.

† In 3 patients.

the late potentials are significantly higher without any physiotherapeutic intervention which aims at reducing enhanced muscle tone. After sustained muscle stretch the muscular response pattern has clearly changed: Amplitude, duration and frequency of occurrence of the early and the late potentials are reduced. That means that the quality of modification of the muscular responses is comparable between healthy subjects switching from preinnervation to the relaxed state and spastic patients before and after reduction of the enhanced muscle tone (as documented on the Ashworth-scale) by sustained stretch.

Our conclusion from these observations is that sustained muscle stretch as it was proposed by Bobath (5) is able to reduce enhanced motoneuronal excitability.

It can be hypothesized that the beneficial effect resulting from sustained muscle stretch is due to stretch receptor fatigue or adaptation to the new extended position (24, 28) with a relatively reduced excitatory drive exerted by muscle spindle afferents onto spinal α -motoneurons, particularly when hand and fingers are slightly flexed again.

Apart from the adaptation of stretch receptors under manual stretch and the resulting reduction of facilitatory input to flexor α -motoneurons the inhibitory effect on flexor spasticity could theoretically be mediated by inhibitory Ib-afferents from Golgi tendon organs. Golgi tendon organs, however, respond selectively to active tension produced by contraction of the 10 to 20 extrafusal muscle fibers inserting upon the tendons that bear the receptor (17). Therefore Golgi tendon organs can hardly be excited by passive extension of a muscle as they respond selectively to actively generated tension (17). Instead, the muscle will manifest lower tone and reduced response potentials to transcranial brain stimulation as compared to its status before because the normal "background" level of Ia-excitation on α -motoneurons is lowered by the adaptation of stretch receptors to the tonic stretch condition. Nevertheless, it cannot be ruled out that the inhibitory effect of sustained stretch on muscular response potentials in centrally paretic flexor muscles is mediated by supraspinal structures influencing directly and/or indirectly the motoneuronal responsiveness.

Quick sudden muscle stretch as well as tapping over the muscle belly and vibration are adequate facilitatory stimuli to evoke voluntary muscle activation (23). On the contrary, as our data suggest, stretch receptor

sensitivity and their mono- or polysynaptic excitatory influence on spinal α -motoneurons gradually decreases under sustained muscle stretch. All parameters reflecting α -motoneuron excitability, i.e. stimulation threshold, latency, duration and frequency of response of both the early and the late potentials are reduced.

The chronic spastic condition is supposed to be caused by an enhanced excitability of spinal α -motoneurons and spinal interneurons (1, 9, 11) as well as by a reduced reciprocal inhibition between agonist and antagonist (1) and probably by a structural muscle transformation as Dietz et al. (10) described for the lower limb musculature. Our results show that the reduced muscle tone after sustained stretch of spastic hand flexors is mediated by neuronal mechanisms and cannot be induced completely by simple mechanical effects on the muscle itself. The late EMG-response potentials to transcranial magnetic stimulation indeed reflect the enhanced motoneuronal excitability in the spastic state as they appear—contrary to healthy subjects (27)—without voluntary background EMG-activity and are reduced parallel to spasticity reduction by means of sustained muscle stretch.

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