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Transcranial magnetic stimulation reduces masseter motoneuron pool excitability throughout the cortical silent period

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Abstract

Objective: To evaluate the time-course of changes in masseter motoneuron pool excitability following transcranial magnetic stimulation of motor cortex, and relate this to the duration of the masseter cortical silent period (CSP).
Methods: Surface EMG was recorded bilaterally from masseter and digastric muscles in 13 subjects. Focal TMS was applied at 1.3× active motor threshold (AMT) to motor cortex of one hemisphere to elicit a muscle evoked potential (MEP) and silent period bilaterally in masseter as subjects maintained an isometric bite at ~10% maximum. With jaw muscles relaxed, a servo-controlled stretcher evoked a stretch reflex in masseter which was conditioned by TMS (1.3× AMT) at 14 different conditioning–testing intervals. There were 20 trials at each interval, in random order. TMS evoked no MEP in resting masseter, but often produced a small MEP in digastric.
Results: Mean (±SE) masseter CSP was 67 ± 3 ms. The masseter stretch reflex was facilitated when stretch preceded TMS by 8 and 10 ms, which we attribute to spatial summation of corticobulbar and Ia-afferent excitatory inputs to masseter. Masseter stretch reflex amplitude was reduced when TMS was given up to 75 ms before stretch, and for up to 2 ms afterwards.
Conclusions: We conclude that descending corticobulbar activity evoked by TMS acts bilaterally on brainstem interneurons that either inhibit masseter motoneurons or increase pre-synaptic inhibition of Ia-afferent terminals for up to 75 ms after TMS. The reduction of masseter motoneuron pool excitability following TMS has a similar time-course to the CSP.
Significance: In contrast to the situation for spinal and facial (CN VII) muscles, the masseter CSP appears to have no component that can be attributed exclusively to cortical mechanisms. Abnormalities in the masseter cortical silent period observed in neurological conditions may be due to pathophysiological changes at cortical and/or sub-cortical levels.

Keywords: Silent period; GABA; Mastication; Trigeminal; Corticobulbar; Stretch reflex

1. Introduction

The cortical silent period (CSP) is a period of reduced electromyographic (EMG) activity induced in a voluntarily active muscle by transcranial magnetic stimulation (TMS) of the motor cortex. The suppression of ongoing activity can last up to 300 ms in limb muscles (Inghilleri et al., 1993) and is due to a combination of factors operating at the level of the spinal cord (and brainstem for cranial muscles) that affect motoneuron excitability, as well as cortical inhibitory processes affecting the corticofugal descending drive. The contribution of changes in motoneuron pool excitability to the CSP is assessed by testing reflex responses at intervals during the cortical silent period after TMS. Responses differ between muscles. In upper limb muscles, H-reflexes are markedly suppressed early in the silent period following TMS and return to control levels before the end of the CSP (Fuhr et al., 1991; Cantello

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et al., 1992; Uncini et al., 1993). In resting soleus, H-reflexes are unchanged or facilitated throughout the CSP (Roick et al., 1993; Ziemann et al., 1993). Cortical inhibitory mechanisms contribute to the CSP and predominate in the later component when segmental reflex excitability is normal in spinal muscles (Inghilleri et al., 1993; Roick et al., 1993; von Giesen et al., 1994; Chen et al., 1999). In facial muscles (CN VII), the R1 component of blink-like reflexes induced by cutaneous trigeminal stimulation is not reduced during the CSP, which suggests a largely cortical origin for the CSP in these muscles (Leis et al., 1993; Cruccu et al., 1997). $GABA_B$ receptors are thought to be involved in the cortical inhibition of the CSP (Werhahn et al., 1999). The cortical silent period is abnormal in a number of neurological conditions (reviewed by Abbruzzese and Trompetto, 2002; Cantello, 2002; Currà et al., 2002), which is believed to reflect pathophysiological changes in cortical inhibition based on the evidence cited above.

TMS evokes a CSP in the trigeminally innervated masseter muscle (Cruccu et al., 1989, 1997; Desiato et al., 2002; Pearce et al., 2003; Jaberzadeh et al., 2008). The corticobulbar projection to the trigeminal motor pools is bilateral, with stronger excitatory effects evoked contralaterally following focal TMS (reviewed by Nordstrom, 2007), but with symmetrical CSPs in masseter muscles on both sides (Jaberzadeh et al., 2008). The masseter CSP is shorter than those in hand and some other cranial muscles at comparable intensities of focal TMS (Jaberzadeh et al., 2008). This may reflect a relatively weaker influence of cortical inhibitory systems on corticobulbar neurons of the trigeminal motor system than corticospinal neurons. This interpretation is not clear at present, however, because the relative importance of cortical and sub-cortical factors in the trigeminal CSP has not been directly tested. The muscle-specific differences in the effects of TMS on segmental reflexes (*vide supra*), and differences in reflex and descending control of trigeminal motoneurons compared with spinal and other cranial systems (Luschei and Goldberg, 1981), mean that the results from other systems cannot be simply extrapolated to the trigeminal system.

The aim of the present study was to assess masseter motoneuron pool excitability during the CSP following TMS. Because H-reflexes are technically difficult to elicit in the mandibular nerve, we used a servo-controlled muscle stretcher to evoke a stretch reflex in resting masseter muscles at intervals before and after focal TMS. The time-course of stretch reflex inhibition and recovery after TMS provides an indication of the component of the masseter CSP that can be attributed to cortical inhibitory mechanisms (Fuhr et al., 1991; Cantello et al., 1992; Uncini et al., 1993). This information is important for interpreting the site of pathophysiologic changes in the trigeminal motor system associated with changes in masseter cortical silent periods, such as its shortening in amyotrophic lateral sclerosis (Desiato et al., 2002). The masseter CSP also has potential application in assessment of pathophysiological changes in other disorders involving the masticatory muscles, such as cranial dystonias (Currà et al., 2000), bruxism (Lobbezoo and Naeije, 2001; Lavigne et al., 2003) and temporomandibular dysfunction (Raudino, 1994).

2. Methods

A total of 38 volunteers (22 females and 16 males) aged 25.6 ± 1.6 (SD) years was recruited to the study with their informed, written consent. The study was approved by the Human Research Ethics Committee at The University of Adelaide, and procedures were in accordance with the Declaration of Helsinki. All subjects completed a modified version of the TMS Adult Safety Screen Questionnaire (Keel et al., 2001) to ensure that there was no contraindication for TMS. After preliminary testing, 25 subjects were excluded due to either (a) small or absent stretch reflex in one or both resting masseter muscles; or (b) our inability to elicit muscle evoked potentials (MEPs) in active masseter muscles on both sides with focal TMS without direct ipsilateral activation of the trigeminal nerve in the cranial fossa (root MEP; Cruccu et al., 1989). Most subjects were excluded due to the first criterion, which reflects a limitation of the servo-controlled muscle stretcher (*vide infra*). Data from 13 subjects are reported herein (9 females and 4 males; age 23.0 ± 2.3 years).

2.1. Apparatus and recording

Subjects sat upright in a chair with their upper and lower incisor teeth resting comfortably on metal bite plates connected to a servo-controlled electromagnetic device that imposed a controlled displacement of the lower jaw (Miles et al., 1993). We have used this system previously to investigate stretch reflexes in the active masseter muscles (Poliakov and Miles, 1994; Miles et al., 1995). The metal bite plates were coated with a semi-rigid dental impression material (3M Express™, Michigan) individually moulded to each subject's teeth. This ensured that only the incisor teeth were in contact with the bars during the experiment, and that the position of the upper and lower jaws on the bars remained constant throughout. Force and acceleration were measured from sensors mounted on the lower bite plate, digitized at a sampling rate of 5 kHz and stored on a computer using a CED 1401 laboratory interface (Cambridge Electronic Design, Cambridge, UK). In two subjects a piezoelectric accelerometer was attached to the mental protuberance of the mandible for direct measurement of jaw movements.

Adhesive EMG electrodes (Duotrode®, Myo-Tronics Inc, Western Australia, 2 cm inter-electrode distance) were affixed to the skin over right and left masseter muscles in a superior–inferior configuration along the longitudinal axis of the muscle fibres, 0.5 cm posterior to the anterior border of the muscle. Electrodes were also affixed to the skin over both anterior digastric muscles. The inter-electrode impedance was less than 5 kΩ in all experiments. EMG signals