Abstract We investigated the time course of changes in motor cortex excitability after median nerve and digit stimulation. Although previous studies showed periods of increased and decreased corticospinal excitability following nerve stimulation, changes in cortical excitability beyond 200 ms after peripheral nerve stimulation have not been reported. Magnetoencephalographic studies have shown an increase in the 20-Hz rolandic rhythm from 200 to 1000 ms after median nerve stimulation. We tested the hypothesis that this increase is associated with reduced motor cortex excitability. The right or left median nerve was stimulated and transcranial magnetic stimulation (TMS) was applied to left motor cortex at different conditioning-test (C-T) intervals. Motor-evoked potentials (MEPs) were recorded from the right abductor pollicis brevis (APB), first dorsal interosseous (FDI), and extensor carpi radialis (ECR) muscles. Right median nerve stimulation reduced test MEP amplitude at C-T intervals from 400 to 1000 ms for APB, at C-T intervals from 200 to 1000 ms for FDI, and at C-T intervals of 200 and 600 ms for ECR, but had no effect on FDI F-wave amplitude at a C-T interval of 200 ms. Left median nerve (ipsilateral to TMS) stimulation resulted in less inhibition than right median nerve stimulation, but test MEP amplitude was significantly reduced at a C-T interval of 200 ms for all three muscles. Digit stimulation also reduced test MEP amplitude at C-T intervals of 200–600 ms. The time course for decreased motor cortex excitability following median nerve stimulation corresponds well to rebound of the 20-Hz cortical rhythm and supports the hypothesis that this increased power represents cortical deactivation.

Key words Motor cortex · Magnetic stimulation · Excitability · Nerve stimulation · Cortical rhythm

Introduction

Activity of pyramidal tract neurons in the primate motor cortex changes in response to peripheral stimulation (Evarts 1973; Wiesendanger 1973; Porter and Rack 1976). In humans, there are periods of increased (Deuschl et al. 1991; Rossini et al. 1991; Deletis et al. 1992; Komori et al. 1992; Maertens de Noordhout et al. 1992; Hirashima and Yokota 1997) and decreased (Mariorenzi et al. 1991; Rossini et al. 1991; Maertens de Noordhout et al. 1992; Clouston et al. 1995; Inghilleri et al. 1995; Hirashima and Yokota 1997; Manganotti et al. 1997) corticospinal excitability in the first 100–200 ms following median nerve or digit stimulation. Changes in motor cortex excitability beyond 200 ms after peripheral nerve stimulation have not been reported.

Electrocorticographic (Jasper and Penfield 1949; Gastaut et al. 1952), magnetoencephalographic (MEG) (Salmelin and Hari 1994; Salmelin et al. 1995; Salenius et al. 1997a) and electroencephalographic (EEG) (Pfurtscheller et al. 1996) studies have suggested that the rolandic rhythm consists of 10-Hz and 20-Hz components, and the 10-Hz rhythm is mainly generated in the somatosensory cortex while the 20-Hz rhythm predominantly arises from the motor cortex. Median nerve stimulation leads to an immediate decrease in the 20-Hz rolandic MEG rhythm (event-related desynchronization, ERD), followed by increased activity above the baseline level (event-related synchronization, ERS) at 200–1000 ms after the stimulus (Salmelin and Hari 1994; Salenius et al. 1997b; Schnitzler et al. 1997). The rebound in 20-Hz activity following median nerve stimulation is decreased by activation of the motor cortex with voluntary movement, motor imagery or
Tactile stimulation of the hand (Salenius et al. 1997b; Schnitzler et al. 1997).

It has been hypothesized that while decreased cortical rhythm (ERD) represents cortical activation, increased cortical rhythm (ERS) represents an inactive, idling state of the cortex (Pfurtscheller 1992; Pfurtscheller et al. 1996). If this is so, the time of increased 20-Hz rolandic rhythm corresponds well with reduced motor cortex excitability.

**Materials and methods**

We studied ten healthy volunteers (eight men, two women, mean age 28.4 years, range 19–47 years). All subjects gave their written informed consent and the protocol was approved by the institutional review board.

Transcranial magnetic stimulation

TMS was performed with a figure-of-eight coil (external diameter 5.5 cm for each wing), powered by a Cadwell high-speed magnetic stimulator (Cadwell Laboratories Inc., Kennewick, WA). The coil was placed over the optimal position of the head for evoking motor-evoked potentials (MEPs) from the right abductor pollicis brevis (APB) muscle, with the handle of the coil pointing backwards. The optimal position was marked on the scalp to ensure identical placement of the coil throughout the experiment. Stimulus intensities were adjusted to produce MEPs of about 1 mV in the relaxed APB muscle. The subjects relaxed throughout the study and EMG silence was monitored. Trials contaminated with voluntary muscle activities were rejected.

EMG recordings

Surface EMG was recorded from the right APB, first dorsal interosseous (FDI) and extensor carpi radialis (ECR) muscles with surface electrodes (Ag-AgCl) with tendon-belly arrangement. The signal was filtered (bandpass 50 Hz to 2 kHz), amplified, displayed (Dantec Counterpoint Electromyograph, Slovunde, Denmark) and stored in a laboratory computer for offline analysis.

Experiment 1: time course of corticospinal excitability following median nerve stimulation

This experiment examined the effects of right (contralateral to TMS) and left (ipsilateral to TMS) median nerve stimulation on MEP amplitudes. Eight subjects (six men and two women, aged 19–47 years) participated. The median nerve was stimulated at the wrist with standard bar electrodes (0.2-ms square wave constant current pulses), with the cathode positioned proximally. Stimulus intensity was adjusted to produce a slight thumb twitch, similar to previous MEG studies (Salenius et al. 1997b; Schnitzler et al. 1997).

Thirteen conditioning-test (C-T) intervals were tested: 200 (TMS before median nerve stimulation), 2, 200, 400, 600, 800, 1000, 1500, 2000, 2500, 3000, 3500 and 4000 ms. The effects of median nerve stimulation on each side were studied in four blocks, and the order of median nerve (right or left) stimulation was counterbalanced across subjects. Each block consisted of five trials of each C-T interval and 36 trials with TMS alone delivered in a pseudorandom order controlled by a laboratory computer. Therefore, each median nerve stimulation study consisted of 144 trials of TMS alone and 20 trials for each C-T interval. Trials were repeated every 6 s.

Experiment 2: time course of corticospinal excitability following digit stimulation

Seven subjects (six men and one woman, aged 22–47 years) participated in the study, six of whom also participated in experiment 1. The right middle finger was stimulated with ring electrodes, with the cathode placed just distal to the metacarpal-phalangeal joint and the anode just distal to the proximal interphalangeal joint. The stimuli were 0.2-ms square-wave constant current pulses set at 3 times the sensory threshold. Sensory threshold was defined as the lowest stimulus intensity at which the subject reported sensation of finger stimulation with stimuli delivered at 0.5 Hz. The procedures for EMG recordings, TMS, the C-T intervals tested and the experimental block design were identical to that for experiment 1.

Experiment 3: effects of different stimulus intensities for digit stimulation

Four subjects (men, aged 22–47 years), who were also involved in experiments 1 and 2, participated in the study. The experimental setup was identical to that for experiment 2, except that a single C-T interval of 200 ms (the C-T interval with maximum inhibition in experiment 2) was tested and the intensity of the right middle finger stimulation varied from 1–4 times (one subject), to 6 times (two subjects) or to 8 times (one subject) sensory threshold. The order of different stimulus intensities was randomized. For each stimulus intensity, 50 trials of TMS alone and 50 trials at C-T interval of 200 ms were delivered in random order 6 s apart. After each stimulus intensity was studied, the subjects rated the sensory stimulus as mild, moderate, strong or painful.

Experiment 4: effects of median nerve stimulation on F-wave amplitude

The effects of median nerve stimulation on spinal excitability were tested by F-waves in four subjects (men, aged 23–47 years), three of whom also participated in experiments 1, 2 and 3. Surface EMG was recorded from the right FDI muscle. Median nerve stimulation at the wrist was adjusted to produce a slight thumb twitch, as in experiment 1. F-waves were elicited by supramaximal stimulation of the ulnar nerve at the wrist (0.2-ms constant current pulses). TMS intensity was adjusted to produce MEPs of about 1 mV in the FDI muscle. Four conditions were tested: TMS alone; median nerve stimulation followed by TMS at a C-T interval of 200 ms; ulnar nerve stimulation alone; and median nerve stimulation followed by ulnar nerve stimulation at a C-T interval of 200 ms. The trials were presented in random order 6 s apart, with 25 trials for each condition.

Data analysis

The peak-to-peak MEP or F-wave amplitudes were measured offline. The baseline MEP amplitude was the mean MEP amplitude from trials with TMS alone. Similarly, in experiment 4, the baseline F-wave amplitude was the mean F-wave amplitude from trials with ulnar nerve stimulation alone. The MEP or F-wave amplitude of each C-T interval was expressed as a percentage of the baseline for each subject. The results are reported as means ± standard error.