

Editorial

Transcranial magnetic stimulation

In the past year, *Brain* has published an average of one article per issue on transcranial magnetic stimulation (TMS). In this issue there are two more, and they illustrate part of the range of uses to which TMS is presently being applied. The article by Magistris *et al.* (1998) describes a modification of its traditional use as a technique for studying the integrity of the corticospinal system in conscious humans. It has always been very easy to measure the latency of muscle responses evoked by TMS over the motor cortex, but measurements of the size of the response, which would give a way of quantifying the effectiveness of the corticospinal volley, are much more difficult to interpret. In fact, EMG responses to cortical stimulation are often only 20–50% of the size of the maximum response evoked by stimulating the peripheral muscle nerve, so that it is not even obvious whether or not the corticospinal input can discharge all the motor neurons in a spinal pool. Marsden *et al.* (1983) were the first to answer this question by showing that the force of the muscle twitch produced by a single shock to the motor cortex was equal to that produced by a single supramaximal peripheral nerve stimulus. They thus argued that despite appearances, all the motor neurons in the muscle had been discharged, and the smaller EMG potential after cortical stimulation was simply due to dispersion of the volley as it was conducted through the corticomotoneuronal synapse and peripheral nerve. There was always the possibility that some motor neurons had actually fired twice in response to the cortical shock, and therefore that some had not fired at all. However, this objection was readily dealt with by showing that the twitch produced by simultaneous stimulation of cortex and peripheral nerve was no larger than that seen after peripheral stimulation alone. The antidromic peripheral nerve volley had collided completely with the orthodromic cortical volley: under the conditions of their experiment, there were no double discharges of spinal motor neurons.

Although theoretically elegant, the technique has two practical limitations. First, it is difficult to measure accurately the force of a maximal muscle twitch because of possible contributions from other neighbouring muscle groups. Second, in most circumstances, TMS tends to make some motor neurons fire twice in response to a single shock (Day *et al.*, 1987, 1989). The technique of Magistris *et al.* (1998) circumvents both by applying a double collision method that allows EMG response amplitudes to be compared directly.

The second paper, by Ohtsuka and Enoki (1998), illustrates how TMS, after spending years in the hands of motor physiologists, is coming of age as a general non-invasive

technique for exploring all aspects of brain function. One of the original disappointments of TMS was that single stimuli only seemed to have any effect when given over the motor cortex, when a twitch could be seen in contralateral muscles. Stimulation over sensory cortex produced no paraesthesias, nor did temporal stimulation evoke memories. The reason is probably that complex sensations and memories are evoked only by trains of several stimuli. However, while single stimuli are ineffective in producing positive phenomena, they are quite capable of interfering with the normal patterned activity that occurs during task performance. Thus, applied at the correct time and place, single stimuli can, for example, produce transient foveal blindness (Amassian *et al.*, 1989), suppress perception of visual motion (Beckers and Zeki, 1995) or delay the onset of a voluntary movement (Day *et al.*, 1989). It is this aspect of TMS, particularly because of its high temporal resolution, which is achieving wider recognition. When combined with PET or fMRI, we can build up a picture of not only which areas of brain are active in a task, but also the time at which each one contributes substantially to task performance. Indeed, workers in the Human Motor Control Section at the National Institute of Health, Bethesda, Md, USA recently gave this approach an elegant new twist. Sadato *et al.* (1996) used PET imaging to show that blood flow increased in the occipital cortex of congenitally blind subjects when they read Braille. To demonstrate that this activation contributed to task performance, they went on to show that TMS over the occiput interfered with Braille reading in blind subjects, but not in normal subjects (Cohen *et al.*, 1997).

The target for stimulation in the paper by Ohtsuka and Enoki (1998) is a little lower on the scalp, just over the posterior vermis in the cerebellum. In the past there had been some debate as to whether it was even possible to use TMS to activate the cerebellum, since the thickness of the skull at the inion means that the cerebellar surface is several centimetres from the magnetic stimulating coil. However, this now seems to have been positively resolved (Werhahn *et al.*, 1996), with recent work by Ohtsuka and colleagues (Hashimoto and Ohtsuka, 1995) suggesting that it may even be possible to study different subareas. Again, to observe any effect, the stimulus has to be given during task performance, since stimulation alone has no obvious effect. However, when applied during either saccades or smooth pursuit eye movements, stimulation has a direction-selective effect on the size of saccades and the velocity of smooth pursuit.

It is clear that TMS is an excellent addition to the many

new tools that we have for non-invasive imaging of the function of the human brain. Recent advances in which combined approaches have been used, such as TMS and PET (Paus *et al.*, 1997) or TMS and EEG (Ilmoniemi *et al.*, 1997), suggest that the applications of TMS will continue to grow rapidly.

John Rothwell

References

- Amassian VE, Cracco RQ, Maccabee PJ, Cracco JB, Rudell A, Eberle L. Suppression of visual perception by magnetic coil stimulation of human occipital cortex. *Electroencephalogr Clin Neurophysiol* 1989; 74: 458–62.
- Beckers G, Zeki S. The consequences of inactivating areas V1 and V5 on visual motion perception. *Brain* 1995; 118: 49–60.
- Cohen LG, Celnik P, Pascual-Leone A, Corwell B, Faiz L, Dambrosia J, et al. Functional relevance of cross-modal plasticity in blind humans [letter]. *Nature* 1997; 389: 180–3.
- Day BL, Rothwell JC, Thompson PD, et al. Motor cortex stimulation in intact man. 2. Multiple descending volleys. *Brain* 1987; 110: 1191–209.
- Day BL, Rothwell JC, Thompson PD, Maertens de Noordhout A, Nakashima K, Shannon K, et al. Delay in the execution of voluntary movement by electrical or magnetic brain stimulation in intact man. Evidence for the storage of motor programs in the brain. *Brain* 1989; 112: 649–63.
- Day BL, Dressler D, Maertens de Noordhout A, Marsden CD, Nakashima K, Rothwell JC, et al. Electric and magnetic stimulation of human motor cortex: surface EMG and single motor unit responses [published erratum appears in *J Physiol (Lond)* 1990; 430: 617]. *J Physiol (Lond)* 1989; 412: 449–73.
- Hashimoto M, Ohtsuka K. Transcranial magnetic stimulation over the posterior cerebellum during visually guided saccades in man. *Brain* 1995; 118: 1185–93.
- Ilmoniemi RJ, Virtanen J, Ruohonen J, et al. Neuronal responses to magnetic stimulation reveal cortical reactivity and connectivity. *Neuroreport* 1997; 8: 3537–40.
- Magistris MR, Rosler KM, Truffert A, Myers JP. Transcranial stimulation excites (or almost all) motor neurones supplying the target muscle. *Brain* 1998; 121: 437–50.
- Marsden CD, Merton PA, Morton HB. Direct electrical stimulation of corticospinal pathways through the intact scalp in human subjects. *Adv Neurol* 1983; 39: 387–91.
- Ohtsuka K, Enoki T. Transcranial magnetic stimulation over the posterior cerebellum during smooth pursuit eye movements in man. *Brain* 1998; 121: 429–35.
- Paus T, Jech R, Thompson CJ, Comeau R, Peters T, Evans AC. Transcranial magnetic stimulation during positron emission tomography: a new method for studying connectivity of the human cerebral cortex. *J Neurosci* 1997; 17: 3178–84.
- Sadato N, Pascual-Leone A, Grafman J, Ibanez V, Deiber MP, Dold G, et al. Activation of the primary visual cortex by Braille reading in blind subjects [see comments]. *Nature* 1996; 380: 526–8. Comment in: *Nature* 1996; 380: 479–80.
- Werhahn KJ, Taylor J, Ridding M, Meyer BU, Rothwell JC. Effect of transcranial magnetic stimulation over the cerebellum on the excitability of human motor cortex. *Electroencephalogr Clin Neurophysiol* 1996; 101: 58–66.