



Brain mapping: Faradization of the mind

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Electromagnetic induction of focal currents in the brain – ‘transcranial magnetic stimulation’ – can be used to study cortical development and plasticity, as well as the organization of sensory and cognitive functions. It may also prove to be a useful tool in the treatment of depression.

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Michael Faraday is well known as an historical figure in physics and chemistry, and the consequences of his discoveries are appreciated in many fields. It nevertheless may come as some surprise to learn that one of his best known, and on the face of it simplest, observations is responsible for a technique that has gained an important place in the array of non-invasive methods for the direct study of human brain function. The technique, called transcranial magnetic stimulation (TMS), is based on the principle of electromagnetic induction, inferred by Faraday from the observation that a moving magnetic field can induce an electrical current in a nearby conducting material [1]. TMS has great potential in that it allows activity in precisely defined regions of the brain to be non-invasively and reversibly disrupted and, as discussed below, it is being used to study a wide range of sensory and cognitive functions, including visual perception, phantom limb

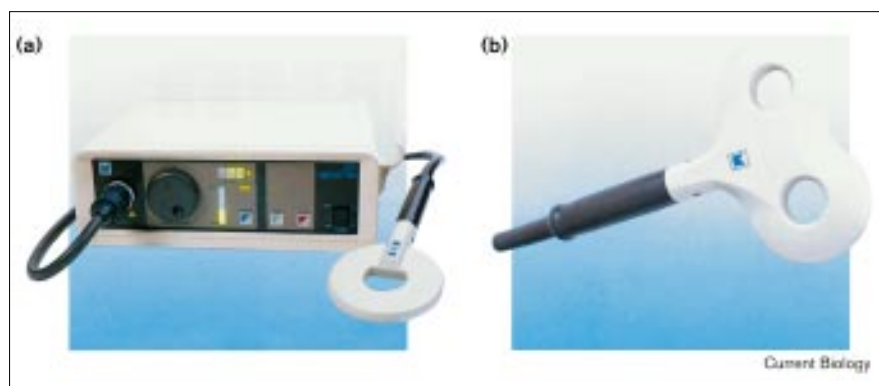
phenomena, memory, motor coordination and, recently, the reorganization of the visual cortex in the blind.

New resolutions: spatial, temporal and functional

Biologists of the late 19th and early 20th centuries attempted to exploit Faraday's discovery of electromagnetic induction to induce currents in the human brain by exposing subjects to changing magnetic fields. The most common reported effects of such treatments were of phosphenes — visual perceptions of flashes or patterns of light elicited non-visually — produced by stimulation of the retina, but there was no success in the attempts to stimulate the brain. The limiting factors were that the size of the induced electrical current depends upon the rate of change and strength of the magnetic field, and it was not until 1985 [2] that the technology existed to produce safely large, rapidly changing magnetic fields.

The physics underlying the TMS technology is apparently simple, but the achievement of making it practical for use in biological studies should not be underestimated [3]. In TMS, a magnetic coil (Figure 1) is placed against a subject's head over the area of interest. The passage of a brief current through the coil results in a focal magnetic field, which passes through the skin and skull without attenuation. The result is an induced electrical current in the subject's brain. There are two main types of stimulation: repetitive (rTMS), in which small magnetic fields may be applied over a period of several hundred milliseconds at a rate of up to 50 Hz; and single-pulse, in which a brief pulse, usually of larger amplitude

Figure 1



(a) A typical magnetic stimulation unit. The one shown discharges an 8 kA current into the stimulating coil, which is placed against the subject's head and which generates a magnetic pulse up to ~2 tesla. The rise time of this pulse is only 100 μ sec. The effect of the magnetic pulse is to induce a brief current in the underlying cortical tissue. The machine shown is designed to deliver single pulses, but stimulators are available which can deliver smaller fields at rates of up to 50 Hz. (b) A figure-eight coil. This type of coil is perhaps the most commonly used in TMS experiments. The current travels through each of the two loops in the coil, and the resulting summation of current where the two loops meet in the centre of the coil produces a focal peak in the magnetic field and thus allows reliable spatial localization of stimulation sites.

than that used in rTMS, is applied at a particular time during the performance of a task.

The specificity of TMS is remarkable in both space and time. Figure 2 compares the spatio-temporal resolution of TMS and some of the other techniques used in studying brain function in human subjects. It is clear from this comparison that there is often a trade-off between spatial and temporal resolution. Thus, event-related potentials (ERPs) have good temporal but poor spatial resolution, but the reverse is true of positron emission tomography (PET) and functional magnetic resonance imaging (fMRI), which have good resolution in the spatial but not the temporal domain. Like magneto-encephalography (MEG) [4], TMS combines good spatial and temporal resolution: the rapid rise time and short duration of the magnetic pulses offer millisecond precision, and with modern, focal coils (Figure 1) the experimental resolution can be brought down to a square centimetre.

The good spatial and temporal resolution of TMS are impressive, but the question to be asked of any technique is “what new functional resolution does it offer?” Can TMS be used to explore functions that could not be studied by other means? And can it offer a more elegant, quicker or less invasive solution to some of the problems that can be addressed through other techniques?

What to measure?

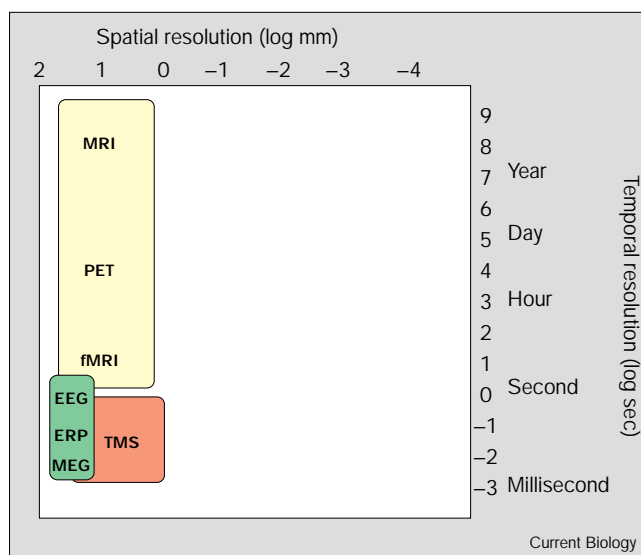
The application of TMS to the skull has the effect of stimulating neuronal activity, and thus of disorganizing the functioning of the underlying cortex. There are a number of ways the experimenter can record responses to TMS. One can record changes in muscle activity at a distal site (see below). The subject could be asked to report subjective changes in experience (as in the early phosphene experiments). Behavioural measures, such as reaction time or errors on a task (see below), could be recorded. Or changes in regional cerebral blood flow, as a function of stimulation, could be measured by PET (as recently achieved by Paus and colleagues [5]).

In common with PET, fMRI, ERPs and MEG, most of the above measures provide a correlation between the site at which brain activity is disrupted and some function. But using behavioural paradigms turns TMS into a means of mimicking the effects of a short-term, reversible ‘lesion’ in a region of cortex, and with the lesion technique one can ask not whether activity in an area is correlated with something but, more informatively, whether it is necessary for a given function.

Development and plasticity

A good illustration of the correlational power of TMS comes from a study [6] in which juvenile monkeys received TMS over the motor cortex, and electrical activity

Figure 2



Spatial and temporal resolution of TMS in comparison with other available techniques. EEG, electroencephalography (see text for other abbreviations).

was recorded distally from one finger. Over time, between birth and 4.5 months of age, the strength of the TMS pulse required to elicit electrical activity at the finger declined by approximately 60% and then remained stable. The onset of this stability coincided with the onset of fine finger movements in the monkey. The implication is that fine finger movements are dependent on corticomotor connectivity.

A related experiment extended this finding to show the relationship between corticomotor and corticospinal development in the emergence of fine finger movements. Eyre *et al.* [7] measured the threshold TMS pulse required to elicit muscle activity in human subjects between the ages of 8 months and 55 years. Activity initially decreased by four years of age — when fine independent finger movements develop — and continued to decrease until adolescence, up to which time myelination of the human pyramidal tract continues. This result stands in contrast to the results of applying TMS to the cervical spine. In this case, the TMS thresholds matured within the first two years of life, indicating the completion of development. The experiments point to two further advantages of TMS — it can be used with very young human subjects, and comparable experiments can be carried out in humans and non-human primates.

TMS has also been used successfully to investigate the long- and short-term reorganization of sensory maps in people who lack sensory input from a particular sense organ or body part. Pascual-Leone and colleagues [8] applied single-pulse TMS over the scalp of Braille readers

and sighted readers and measured the ability to detect small electrical stimuli applied to the reading or non-reading fingers. TMS disrupted tactile detection at many more cortical sites in Braille readers than with sighted subjects — a clear demonstration that use of the Braille reading finger had led to an expanded representation in the sensorimotor cortex.

The same group of workers has recently investigated cross-modal plasticity in Braille readers [9]. There has long been a question about the functions of primary visual cortex in the absence of visual inputs; claims have been made to the effect that people who are blind from birth have improved tactile perception, and that the visual cortex of blind subjects can be activated by tactile stimuli. By stimulating the occipital cortex during the performance of tactile discrimination tasks, Cohen *et al.* [9] were able to distort the tactile perceptions of blind, but not normally sighted, subjects, thus demonstrating that the reorganized tactile sensitivity of ‘visual’ cortex is functionally organized, rather than random.

Cortical reorganization can occur as a consequence of losing, as well as using, a body part. Cohen *et al.* [10] used TMS to study cortical plasticity following amputation of an upper limb. The motor reorganization that occurs after amputation includes an increase in the motor excitability of muscles close to the stump. Consistent with this, Cohen *et al.* [10] found that stimulation over the motor area contralateral to the stump elicited activity in nearby muscles more easily — at lower stimulation intensities and at more sites on the scalp — than stimulation over the motor cortex ipsilateral to the stump elicited activity in the corresponding muscles of the intact arm. Learning is also a type of cortical reorganization, and the use of TMS has shown that some visual areas are important in learning complex visual detection tasks but are no longer required once the task is learned [11].

Cognition

The use of TMS as a lesion technique for studying cognitive function has been illustrated by Seyal *et al.* [12]. Following damage to the right parietal cortex, patients often ‘neglect’ the left side of space or the left side of objects. One possible explanation for this is that, because the two brain hemispheres operate in a mutually inhibitory manner [13], damage to the right cortical hemisphere not only leads to a reduced capacity to orient to information in the left-world, but also to disinhibition of the left parietal cortex and thus an exaggerated tendency to attend to the right-world [14]. Seyal *et al.* [12] have used TMS to test this idea, in particular to see whether disrupting activity in one hemisphere enhances the perception of stimuli by the opposite hemisphere. They applied single-pulse TMS to the parietal cortex 50 milliseconds before subjects were required to detect a small electrical stimulus delivered to

the fingers and were able to demonstrate that sensitivity to tactile stimuli was increased in the hand ipsilateral to stimulation. As somatosensory input from this hand goes to the opposite hemisphere to that subjected to TMS, the findings are consistent with the view that mutual inhibition of the hemispheres influences perception.

Using repetitive-pulse TMS, Pascual-Leone *et al.* [15] investigated visual extinction, another feature of parietal cortex damage. Subjects were asked to detect either one or two asterisks presented on a computer monitor and received trains of TMS pulses at 25 Hz. Stimulation to the parietal cortex reduced the ability to detect stimuli contralateral to the stimulated hemisphere only when targets were presented in both hemifields simultaneously, again supporting the view that inter-hemisphere competition influences the ability to attend to one or other halves of the world.

Clinical uses

Magnetic stimulation has a number of uses in surgery and diagnosis [16]. It has been used to measure nerve conduction times before, during and after spinal surgery, as an aid to diagnosis in spinal diseases and as a way of monitoring recovery after stroke. In addition, magnetic stimulation may also have value in the treatment of depression. For many years, the treatment of choice for intractable, drug-resistant depression has been electroconvulsive therapy (ECT), which requires anaesthesia and an induced seizure; TMS treatment requires neither.

There have been indications that repetitive-pulse TMS applied over the prefrontal cortex may have positive effects on mood — another avenue of research within the remit of TMS. And following these indications, attempts have been made to treat severely depressed patients with TMS rather than ECT. George *et al.* [17] applied TMS to the left prefrontal cortex in six patients and, over the course of several weeks, noted gradual improvements in mood. Although this aspect of the use of TMS is in its infancy, the potential benefits for both basic and clinical research should stimulate an increase in the research activity in this field in the near future.

Safety

In the course of his research on electricity, Faraday — following the physiology tradition of “do experiments unto oneself” — often used himself as a conductor to establish the existence of currents under different conditions, the presence or absence of an electric shock being his dependent measure. Every time we switch on a light we should perhaps be thankful that Faraday did not have to explain his methods to a local Health and Safety or Ethics committee. Nevertheless, a technique that induces neuronal activity, can mimic the effects of brain lesions, affect mood and elicit perceptions clearly needs to be treated with respect.

Of the two types of TMS, it seems that single-pulse TMS is safe as long as the number of stimulations in a day is kept within a reasonable number, and there is no indication that single-pulse TMS can have long-term or short-term cognitive effects. Repetitive-pulse TMS needs to be treated with more caution; for example, it can cause seizures. However, the incidence of TMS-induced seizures is extremely rare, even when TMS has been used to study populations of epileptic patients. Headaches and dizziness are more frequently reported by subjects, but there is no evidence of any longer-term effects of TMS. Guidelines — constantly under review — are available in the literature [18], and some modern stimulators are designed to prevent stimulation being applied outside the guidelines. The TMS community now also has access to a well-run e-mail list (<http://pni.unibe.ch/maillist.htm>), and anyone with specific queries about protocols is advised to use this to keep up to date with protocol developments.

The future

The strength of TMS lies in the fact that it forces the user to have hypotheses about when and where in the brain a function may be performed. In future developments, it will be increasingly common to use TMS in conjunction with techniques that determine where (PET, fMRI) and when (ERP) brain activity occurs. Issues to which these techniques may contribute include an understanding of the distribution of activation following application of TMS; the question of what kind of temporal information is provided by TMS and ERPs; and how the effects of TMS in neuropsychological patients may differ — for example in terms of the underlying pattern of activation — from the effects of applying magnetic pulses to an intact brain. If alive today, Faraday would clearly have a great future as a neuroscientist.

References

1. Faraday M: *Experimental Researches in Electricity. First Series*. London: Richard & John Edward Taylor; 1832.
2. Barker AT, Jalinous R, Freeston IL: **Non-invasive magnetic stimulation of human motor cortex**. *Lancet* 1985, **i**:1106-1107.
3. Jalinous R: **Technical and practical aspects of magnetic nerve stimulation**. *J Clin Neurophys* 1991, **8**:10-25.
4. Gallen CG, Bloom FE: **Mapping the brain with MSI**. *Curr Biol* 1993, **3**:22-24.
5. Paus T, Jech R, Thompson CJ, Comceau 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**:3178-3184.
6. Flament D, Hall EJ, Lemon RJ: **The development of corticomotorneuronal projections investigated using magnetic brain stimulation in the infant macaque**. *J Physiol* 1992, **447**:755-768.
7. Eyre JA, Miller S, Ramesh V: **Constancy of central conduction delays during development in man: investigation of motor and somatosensory pathways**. *J Physiol* 1991, **434**:441-452.
8. Pascual-Leone A, Torres F: **Plasticity of the sensorimotor cortex representation of the reading finger in Braille readers**. *Brain* 1993, **116**:39-52.
9. Cohen LG, Celnik P, Pascual-Leone A, Corwell B, Faiz L, Dambrosia J, Honda M, Sadato N, Gerloff C, Dolores Catal M, Hallett M: **Functional relevance of cross-modal plasticity in blind humans**. *Nature* 1997, **389**:180-183.
10. Cohen LG, Bandinelli S, Findley TW, Hallett M: **Motor reorganization after upper limb amputation in man**. *Brain* 1991, **114**:615-627.
11. Walsh V, Ashbridge E, Cowey A: **Cortical plasticity in perceptual learning demonstrated by transcranial magnetic stimulation**. *Neuropsychologia*, in press.
12. Seyal M, Ro T, Rafal R: **Increased sensitivity to ipsilateral cutaneous stimuli following transcranial magnetic stimulation of the parietal lobe**. *Ann Neurol* 1995, **38**:264-267.
13. Kinsbourne M: **Hemi-neglect and hemisphere rivalry**. *Adv Neurol* 1977, **18**:41-49.
14. Cohen JD, Romero RD, Servansschreiber D, Farah MJ: **Mechanisms of spatial attention — the relation of macrostructure to microstructure in parietal neglect**. *J Cog Neurosci* 1994, **6**:377-387.
15. Pascual-Leone A, Gomez Tortosa E, Grafman J, Alway D, Nichelli P, Hallett M: **Induction of visual extinction by rapid rate transcranial magnetic stimulation of parietal lobe**. *Neurology* 1994, **44**:494-498.
16. Jalinous R: *Guide to Magnetic Stimulation*. The MagStim Company, 1995.
17. George MS, Wassermann EM, Williams WA, Callahan A, Ketter TA, Basse P, Hallett M, Post RM: **Daily repetitive transcranial magnetic stimulation improves mood in depression**. *Neuroreport* 1995, **6**:1853-1856.
18. Pascual-Leone A, Houser CM, Reese K, Shotland LI, Grafman J, Sato S, Valls-Sole J, Brasil-Neto JP, Wasserman EM, Cohen LG: **Safety of rapid rate transcranial magnetic stimulation in normal volunteers**. *Neurophysiology* 1993, **89**:120-130.