Smaller magnets for smarter minds?

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Human brain stimulation for therapeutic purposes has many short- and long-term limitations. The possibility of implanting magnetic, rather than electrical, stimulation devices would present a possible solution to some of the problems. The development of a new microscopic magnetic stimulation device provides a glimpse of the realisation.

Stimulation of the human brain is at once one of the more impressive feats of modern medical neuroscience and also a surprisingly primitive affair. Deep Brain Stimulation (DBS), for example, is of proven worth in Parkinson’s Disease, dystonia, tremor [1], and tinnitus [2,3], and is under investigation for its use in various other psychiatric and neurological conditions. However, DBS is fraught with ethical issues, problems of specificity, limited longevity and, more even than all of these, it is only as good as our conceptualisation and understanding of the mechanisms of disease and cognition.

There are still many fundamentals to be understood. Does brain stimulation need to be anatomically focal? Drugs are not, and only the most naïve understanding of brain systems supports simple localisation of function in disease. One’s instinct may be towards focality, but the success of electroconvulsive therapy (ECT) [4] and transcranial magnetic stimulation (TMS) [5–7] in depression show that focality is not always the main issue.

An issue that bedevils the use of external brain stimulation in therapeutic settings is that of delivery. TMS is a good example. The efficacy of TMS for depression is comparable to that of any individual drug. Left prefrontal TMS has been repeatedly shown to be a viable treatment option for acute depression, yet its use outside the USA is neither routine nor widespread, and not even burgeoning. One of the reasons for this is that TMS requires people to deliver it and for clinician and patient to be in the same place at the same time. As such, it represents a missed opportunity. TMS is also only useful for target sites that are superficial. One cannot apply TMS to the thalamus, for example.

An effective way of improving access to TMS may be to make the delivery easier and, rather than have the magnetic coil outside the head, to implant it inside. The utility would not be limited to depression.

A challenge for the medical engineering community, then, is to develop electromagnetic stimulators that can be safely implanted into subjects and that will have long life spans after implantation. Bonmassar and colleagues [8] have recently taken the first step on this journey, by developing sub-millimetre electromagnetic coils that may provide the basis for viable implants.

The technical issues are not trivial. The first is to produce a coil that is small enough to be implanted, but still able to induce an electrical field of sufficient strength to stimulate neural tissue. The principle is simple: magnetic field pulses induce electrical fields that encircle the source. The strength of the induced field depends on the magnetic field strength and its rate of change. The induced electrical field in turn generates a current and this change in current, if sufficient, can excite neural tissue. Bonmassar et al. showed that a small coil with a 500 µm radius can generate sufficient current to stimulate retinal ganglion cells. Their next challenge was to show that their device could do this in real neural tissue.

To investigate this they stimulated rabbit retinal ganglion cells using a micromagnetic stimulation (µMS) device. We should be excited but, before we get too carried away, it is important to note that their experiment was carried out in vitro. Retinæ were isolated and patch clamp recording established the responsivity of the ganglion cells to light. Only these light responsive cells were used for the subsequent tests of the µMS. The microscopic coils were placed 300 µm above the retinal surface. The first success to report is that the ganglion cells did respond to µMS and the latency and duration of the responses were consistent with direct electrical means of eliciting action potentials. And it gets better. One of the things the TMS community like to believe is that the orientation of the coil and the induced field is a key factor in generating neural activity. Bonmassar et al. manipulated the orientation of the coil and were able to show that when the coil was oriented parallel to the ganglion cells, bursts of activity were elicited, and that when the coil was oriented perpendicular to the cells, responses did not come in bursts. At the µMS level, this may be a way of controlling the spread of activity and thus of diminishing side effects. The intensity of the stimulation also changed neuronal responses as one would predict: more is more.

The question for us is how excited should we be about this? It is true that there are limits on the use of current brain stimulation methods, but in any cost-benefit analysis, implanting a device in the brain has to be weighed heavily on the cost side. For some illnesses, and depression must top this list, less invasive methods such as TMS and tDCS need to be given more opportunity and made available to a wider base of patients. We must also be cautious about the models of magnetic stimulation that we import into the clinical sphere. Korngreen and colleagues [9], for example, have shown that current thinking about magnetic stimulation of neural tissue may be somewhat simplistic and that there are many factors to be considered (neuronal...
size and firing threshold are just two examples), in addition to orientation and intensity. Changes in neuronal state may also prove to be important [10].

So, we have a microscopic magnetic stimulator, small enough for deep brain implantation, proven to work in vitro, that can stimulate cells directly and indirectly. There is a long way to go, but Bonmassar et al. already have a list of important questions to pursue: Where effects will changing the shape of the coil have? How will multiple coils operate? What will the long-term effects of implantation be?

More pressingly from the perspective of cognitive neuroscientists, we would ask the question, once these technical advances are made and we have a new method of brain stimulation, will we have similarly impressive advances in our conceptualisation of the organisation of cognitive systems in the brain? If the answer is no, then we may do no more than prosecute our ignorance more effectively. We can only hope that improvements in understanding brain organisation will keep pace with the impressive advances in medical engineering.

References