Health and Medicine | Dr Giorgio Bonmassar

Focusing attention on transcranial magnetic stimulation

Dr Giorgio Bonmassar, Associate Professor of Radiology at Harvard Medical School, has developed a method of magnetically stimulating excitable tissues, such as those in the heart and brain, which overcomes many of the limitations of both direct electrical stimulation and transcranial magnetic stimulation.

The therapeutic and research benefits of electrically stimulating tissues are long established, from pacemakers and treatments for movement disorders such as Parkinson’s disease to the identification of causal relationships between brain regions and functional responses. Initially, these were limited to direct electrical stimulation, by inserting fine electrodes into heart or brain tissue and delivering an appropriate current.

This approach is clearly not without its problems. Electrode implantation itself poses risks to the individual, and with the advent of magnetic resonance imaging (MRI), further complications were created. During MRI scanning, the ‘antenna effect’ indicates an electrical current in the tip of the electrode which dissipates as heat, potentially causing irreversible damage to the tissue surrounding it.

DONE WITH MAGNETS

Transcranial magnetic stimulation (TMS) offered the potential to overcome these issues by firstly not requiring invasive surgical procedures. Stimulation is effected by placing a magnetic coil in close proximity to the target area of the brain; varying the magnetic field causes an electric current to flow in a small area of the brain through electromagnetic induction. It has been useful diagnostically in a range of diseases which relate to the motor cortex, such as stroke, multiple sclerosis, and motor neuron diseases, it has also been used to treat neuropathic pain (pain caused by damage or disease affecting the region of the brain which deals with bodily sensations).

One other advantage of TMS is that it can be used in conjunction with functional MRI to improve our understanding on how TMS stimulates the brain, and its probes can be built into special MRI-safe headsets and stimulation delivered during scanning. The major disadvantage is its spatial resolution; fine targeting of the stimulation is difficult due to the properties of magnetic fields and the engineering limits of electromagnetic coil design.

AN IMPRESSIVE SCIENCE

‘Bleed over’ into nearby areas of the brain means that its use as a research tool is limited. However, it has been successfully deployed to interrogate motor pathways, language organisation and for presurgical evaluation of patients. Its use as a mapping tool to assess how neural pathways are disrupted in brain tumour development, cerebral palsy and epilepsy are perhaps the most clinically relevant uses of this technology, providing vital information to physicians on the progress of these diseases.

The therapeutic uses of both TMS and direct electrical stimulation are now beginning to overlap, the networked nature of the brain means that there are nodes in the network which have the capacity to impact multiple disease expressions. These can be stimulated either directly, as is more usual for deep tissue stimulation, or by TMS which is able to operate only at relatively shallow regions due to the method of delivery.

FINER FOCUS

Dr Bonmassar’s response to this situation was to develop what might be considered a hybrid of the two methods, implantable micro magnetic stimulators (μMS) which are able to deliver focused stimulation to specific areas of the brain. As these stimulators are electrically isolated from the tissue, instead of delivering their stimulation via magnetic fields, they can be made MRI-safe and prevent the heat damage associated with traditional implantable electrodes. This one step removed property of magnetic stimulation also has the advantage of allowing the coils to be encased in bio-compatible materials, reducing inflammation at the site of implantation.

In order to assess if this concept would be viable as a means of neuronal stimulation, Dr Bonmassar and his team tested the prototypes on isolated neuronal cells. Using explanted retinal tissue from rabbits, they first measured its response to flashes of light to ensure the ganglia (a cluster of nerve cells) were active. They then lined up their μMS coils and proceeded to stimulate the same nerves by generating a time-varying magnetic field.

SEEING THE LIGHT

All the cells which responded to light stimulation also responded to μMS. Dr Bonmassar described the results in the journal Nature as, “This amplitude and kinetics of individual biphasic waveforms (where the response cycles above and below the baseline value) were nearly identical to that of action potentials elicited in response to light stimulus, strongly suggesting that the biphasic waveforms were in fact action potentials (the wave of electrical energy that underlies a nerve impulse).” These exciting results laid the foundations for further refinement of the process in vitro and demonstrated the real potential of the product he had designed.

The team continued to investigate the mechanism and salient features of the stimulation effects, showing that the orientation of the coil and the magnitude of the initiating current, amongst other parameters, were fundamental to the response obtained. This result demonstrated a level of specificity and tuning which could prove vital for both the clinical and research applications of the technology.

Dr Bonmassar designed the experiments carefully. “Potential contributions from
Micro-magnetic stimulation is an emerging technology with great promise to revolutionise therapeutic stimulation of the human nervous system.

**FOCUS ON THE FUTURE**

The team already have extensive rolling results to direct coil design, indicating that the μTMS coils produce a substantially more focused stimulation than traditional TMS probes whilst using a much smaller current. Dr Bonmassar believes this is due to micro coils being capable of eliciting action potentials at lower field thresholds due to the higher spatial gradient (their small size means a sharper decline in signal with distance).

"Micro-magnetic stimulation is an emerging technology with great promise to revolutionise therapeutic stimulation of the human nervous system," says Dr Bonmassar, "Our project is adapting this novel technology to develop the first generation of miniaturised transcranial magnetic stimulation (μTMS) probes. It will enable for the first time, ultra-high resolution non-invasive stimulation of the human brain with applications in therapeutic and exploratory neuroscience.

**References**


**How will this technology impact clinical neurobiology therapy and research?**

In clinical practice, cortical mapping of language, as well as the systematic exploration of the motor cortical outputs can be beneficial for the pre-surgical evaluation of patients in order to characterise eloquent cortex whilst reducing the need for intraoperative evaluation. In addition to the highly improved focality, which allows for precise selection of a stimulation site, the focal stimulation also decreases extraneous activation of non-targeted brain areas. Furthermore, the significantly reduced size of μTMS elements allows integrating them into multi-channel conformal head arrays for simultaneous multi-focal stimulation (i.e., a TMS helmet will be finally feasible). In the realm of network stimulation, the ability to apply TMS simultaneously in multiple sites to inhibit certain nodes while facilitating others will introduce a significant leap in the study of altered brain networks in psychiatric and neurological disorders.