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Blunt or precise? A note about the relative precision of figure-of-eight rTMS coils

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Dear Editors,

I have recently been engaged in several conversations with individuals outside of the brain stimulation field who have been inquiring about the relative precision of TMS as a brain stimulation tool. As we in the Brain Stimulation field know, TMS is not a single monolith. When answering the question "Is TMS a blunt or precise tool?" the answer depends upon several things including 1) the type of coil being used, and 2) the individual's definition of "precise." With a growing number of TMS coil designs, and noninvasive brain stimulation techniques available to clinical researchers, I suspect that it is difficult for many individuals outside of our field to appreciate the relative spatial precision of brain stimulation approaches that are available. The intention of this Letter to the Editor is not to 'preach to the choir' but rather to provide the readers of this journal with a concise answer they could provide to their colleagues and trainees when asked about the relative spatial precision of TMS.

From the perspective of the coil being used, the focality of TMS is, of course, related to the shape of the coil. This journal has, in fact, devoted a substantial amount of effort to promoting computational modeling of electric field distributions associated with different coil shapes. Perhaps one of the most influential papers was by Deng and colleagues (2013) [1]. In that paper, they estimated the focality and penetration depth of 50 existing TMS coils of various geometric configurations. They demonstrated that the surface spread of typical figure-of-8 coil designs was as low as 5 cm^2 whereas circular coils were as low at 34 cm^2. The penetration depth of figure-of-8 coils and circular coils was similar, ranging from 1 to 3.4 cm^2.

To put this in perspective I was recently asked by a reporter **"If your brain was a map of the United States, about how much area would you be stimulating– a city, a state, a region?"** I approached this question using the following assumptions and steps: 1) The cortical surface is 1570 cm^2. 2) A single TMS pulse from a standard figure-of-8 coil stimulates a 12.5 cm^2.area. Therefore a single TMS pulse is directly effecting about 1/125 (0.8%) of the cortical surface area. The land area of the United States is 3,537,438 mi^2. A rank order of the land area occupied by each of the 50 United States, revealed that the closest state by proportion (0.8% of geographic area) was South Carolina (@32,020 mi^2). If we limit the calculation to the 48 contiguous states, a single TMS pulse from a figure-of-8 coil is about 2 times the size of Maryland. From a global perspective 0.8% of the world's surface is about 1.575 million square miles. **This is comparable to the size of India (1.269**

million square miles), half of Australia, or about 13.5 times the size of Italy. Consequently my answer to the reporter was, “We are stimulating about 0.8% of the cortical surface, which, of the 50 states is closest in size to South Carolina, and about the size of India.” While, as scientists, this is clearly not a precise answer, it is a useful estimate which provides more information than letting our trainees, collaborators, and patients believe that all forms of TMS are “blunt” or spatially imprecise tools.

Of course, limiting the effects of TMS to a single cortical regions directly affected by the magnetic field is an oversimplification as we know that there are at least monosynaptic and potentially polysynaptic effects that are directly related to single pulses of TMS in a dose-dependent manner. This can be easily displayed behaviorally through estimates of the recruitment curve, wherein an increase in TMS output leads to a predictable increase in the amplitude of the motor evoked potential (requiring at least monosynaptic propagation). Most neuroimaging studies using interleaved TMS/BOLD imaging demonstrate that there are significant increases in BOLD signal in the “vicinity” of the location that is predicted to be the direct target ot the TMS pulse. This elevated activity in the vicinity of the coil is also accompanied by elevated activity in neural regions that are monosynaptically connected to the region being stimulated – including but not limited to the contralateral homologue of the stimulated cortical region. The polysynaptic nature of TMS effects is certainly a very important aspect of many brain stimulation treatment designs and one which may contribute to the clinical utility of TMS.

The other thing to consider when answering this question of TMS as a blunt or precise tool is the spectrum of tools that are used in clinical and preclinical neurosciences. As a translational researcher is it common that we take information from optogenetic studies and evaluate if TMS can have similar effects. Of clinically available brain stimulation tools, deep brain stimulation is at least an order of magnitude more precise than the most focal TMS coils available with stimulation volumes that range from at least 10–200mm depending on the electrode configuration and design [2]. When compared to other noninvasive approaches to modulating the brain however (pharmaceutical agents, transcranial direct current stimulation, etc) TMS is fairly precise. Electroconvulsive therapy appears to effect 94% of the brain and magnetic seizure therapy effects 21% of the brain [3]. Additionally, using interleaved TMS/MRI we have shown, for example, that it is possible to differentially activate medial and lateral frontal-striatal circuits by placing a figure-of-8 TMS coil over the FP1 location and the F3 location of the EEG 10–20 system [4].

With an increasing use of less focal H-coil designs, it is easy for individuals new to the field to discount the value of cortical mapping studies and neural circuit dissociation studies which have been done using more spatially precise figure-of-8 coil designs. Although electric field modeling studies are also limited, I would like to urge the readers of Brain Stimulation to actively educate their colleagues that TMS can be a fairly precise brain stimulation tool – one that is capable of activating specific neural circuits and can even differentially activate various fingers on the hand.

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