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Coil design considerations for deep transcranial magnetic stimulation

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HIGHLIGHTS

- The focality advantage of smaller TMS coils over larger coils diminishes with increasing target depth.
- At best (for large TMS coils), the electric field attenuation in the brain relative to the head surface is directly proportional to the target depth.
- Direct rTMS of targets at depths of $\sim$ 4 cm or more is likely unsafe as it results in superficial stimulation strength that exceeds the upper limit in current rTMS safety guidelines.

ABSTRACT

Objectives: To explore the field characteristics and design tradeoffs of coils for deep transcranial magnetic stimulation (dTMS).
Methods: We simulated parametrically two dTMS coil designs on a spherical head model using the finite element method, and compare them with five commercial TMS coils, including two that are FDA approved for the treatment of depression (ferromagnetic-core figure-8 and H1 coil).
Results: Smaller coils have a focality advantage over larger coils; however, this advantage diminishes with increasing target depth. Smaller coils have the disadvantage of producing stronger field in the superficial cortex and requiring more energy. When the coil dimensions are large relative to the head size, the electric field decay in depth becomes linear, indicating that, at best, the electric field attenuation is directly proportional to the depth of the target. Ferromagnetic cores improve electrical efficiency for targeting superficial brain areas; however magnetic saturation reduces the effectiveness of the core for deeper targets, especially for highly focal coils. Distancing winding segments from the head, as in the H1 coil, increases the required stimulation energy.
Conclusions: Among standard commercial coils, the double cone coil offers high energy efficiency and balance between stimulated volume and superficial field strength. Direct TMS of targets at depths of $\sim$ 4 cm or more results in superficial stimulation strength that exceeds the upper limit in current rTMS safety guidelines. Approaching depths of $\sim$ 6 cm is almost certainly unsafe considering the excessive superficial stimulation strength and activated brain volume.
Significance: Coil design limitations and tradeoffs are important for rational and safe exploration of dTMS.

1. Introduction

Transcranial magnetic stimulation (TMS) uses brief, strong magnetic pulses to induce an electric field in the brain that modulates neural activity. Repetitive TMS (rTMS) can produce changes in neural activity that persist beyond the period of stimulation. Therefore, rTMS can be used as a probe of higher brain functions

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and an intervention for psychiatric and neurological disorders (Fitzgerald et al., 2006; Fitzgerald and Daskalakis, 2011).

Due to the rapid attenuation in depth of the electric field of conventional stimulation coils, TMS has been restricted to superficial cortical targets, typically 2–3 cm in depth. For example, the most common target in TMS depression treatments is superficial–the dorsolateral prefrontal cortex (Fitzgerald and Daskalakis, 2011). However, alternative stimulation targets for depression may include non-superficial (∼3–5 cm depth) brain areas such as frontopolar, medial frontal, and orbitofrontal cortices (Downar and Daskalakis, 2013; Seminowicz et al., 2004; Johansen-Berg et al., 2008), as well as deeper (∼6–8 cm depth) brain areas such as subcallosal cingulate cortex (Mayberg et al., 2005; Lozano et al., 2008; Kennedy et al., 2011; Holtzheimer et al., 2012), the ventral portion of the anterior limb of the internal capsule and adjacent dorsal ventral striatum (Greenberg et al., 2005; Malone et al., 2009), nucleus accumbens (Roth and Zangen, 2006; Schlaepfer et al., 2008; Bewernick et al., 2010), amygdala (Roth and Zangen, 2006), inferior thalamic peduncle (Jiménez et al., 2005), and lateral habenula (Sartorius and Henn, 2007; Sartorius et al., 2010).

While accessing such deep brain therapeutic targets directly with deep TMS (dTMS) is compelling, the induction of deeply penetrating electric field has fundamental physical limitations. It has been theoretically proven that inside a spherically symmetric volume conductor, it is impossible for any TMS coil configuration to produce three-dimensional focusing of the electric field in depth (Heller and van Hulsteyn, 1992). The induced electric field is always strongest on the surface of a uniform conductor and drops off in depth. Further, in a uniformly conducting sphere or spherical shells, the radial electric field component is always zero; hence, the electric field at the center of the sphere is zero (Roth et al., 1990; Eaton, 1992; Cohen and Cuffin, 1991; Ruohonen and Ilmoniemi, 2002). The non-spherical shape of a real head and the presence of tissue anisotropy and non-tangential boundaries can create local maxima of the electric field in depth (Thielscher et al., 2011; Davey et al., 2003; Miranda et al., 2003, 2007; Opitz et al., 2011). However, local electric field maxima created by the brain anatomy only partially compensate for the stronger driving electric field in more superficial regions. Furthermore, brain anatomy varies among individuals and hence is difficult to account for in coil design. Finally, the electric field of larger coils decays slower in depth but is intrinsically less focal, and figure-8 type coils are fundamentally more focal than circular type coils (Ruohonen and Ilmoniemi, 2002; Ueno et al., 1988; Rösler et al., 1989; Grandori and Ravazzani, 1991; Deng et al., 2013).

Within these fundamental limitations, a number of dTMS coil designs have been investigated or proposed. The double cone coil–formed by two adjacent, 110 mm diameter, circular windings fixed at a 100° angle–induces a more deeply penetrating and less focal electric field compared to a planar, 70 mm winding diameter figure-8 coil (Deng et al., 2013; Lontis et al., 2006). The double cone coil has been used for direct activation of the pelvic floor and lower limb motor representation at the interhemispheric fissure (Terao et al., 1994) as well as for transsynaptic activation of the anterior cingulate cortex via stimulation of the medial frontal cortex (Hayward et al., 2007). Double cone type coils are also highly efficient for seizure induction (Lisanby et al., 2001, 2003; Deng et al., 2011; Kayser et al., 2011). This is an advantage in the context of magnetic seizure therapy, but in subconvulsive applications, this is a significant source of risk.

A family of dTMS coil designs called Hesed (H) coils has been developed with the goal of effective stimulation of deep brain structures (Roth et al., 2002; Zangen et al., 2005; Roth et al., 2007a,b). More than twenty different types of H coils have been designed and manufactured for various applications (Roth et al., 2013). H coils typically have complex winding patterns and larger dimensions compared to conventional coils and consequently have slower electric field attenuation with depth, at the expense of reduced focality (Deng et al., 2013). It has been proposed that the electric efficiency, field depth, and focality of H coils can be improved by the use of high-permeability ferromagnetic cores, but the reported improvements were minor (Salvador et al., 2009; Deng et al., 2013). H coils have been evaluated for the treatment of a variety of psychiatric and neurological disorders (Bersani et al., 2013b), including major depression (Levkovitz et al., 2007, 2009, 2011b; Rosenberg et al., 2010a,b; Harel et al., 2011; Rosenberg et al., 2011a; Isserles et al., 2011; Harel et al., 2012; Bersani et al., 2013a), schizophrenia (Levkovitz et al., 2011a; Rosenberg et al., 2011b), dystonia (Kranz et al., 2010), autism (Enticott et al., 2011; Krause et al., 2012), pain (Tartaglia et al., 2011), chronic migraine (Dalla Libera et al., 2011), post-traumatic stress disorder (Isserles et al., 2013), and logopenic primary progressive aphasia (Trebbastoni et al., 2012). An rTMS system using the H1 coil received clearance by the U. S. Food and Drug Administration (FDA) for the treatment of depression.

Other dTMS strategies have been proposed as well. Based on analysis and simulations, it was suggested that a C-shaped ferromagnetic core coil with a wide opening angle (Fig. 1(b)) can suppress the surface field and, consequently, could reduce scalp stimulation (Davey et al., 2008; Davey and Riehl, 2006; Al-Mutawaly et al., 2001). It is unclear whether the addition of ferromagnetic cores is practical as they might enter magnetic saturation in the field range needed for dTMS. In addition to the C-core coil, large circular type dTMS coils have been proposed, including the crown coil (Fig. 1(a)) (Deng et al., 2008) and the halo coil (Ishii et al., 2008; Crowther et al., 2011). The effects of low-field magnetic stimulation with large MRI gradient coils have also been investigated (Rohan et al., 2004; Carlezon et al., 2005; Volkow et al., 2010; Deng et al., 2013).

Temporal summation at the neural membrane has also been proposed for enabling focused stimulation of deep brain regions via sequential firing of TMS pulses from a set of coil windings positioned around the head, with no activation of cortical brain regions (Roth et al., 2007b). Preliminary theoretical analysis, however, indicates that sequential firing of coil windings produces less neural membrane depolarization than conventional synchronous firing of all windings, suggesting that this strategy for enhancing stimulation in depth may be ineffective (Deng et al., 2008).

All of these dTMS approaches use coils that have larger dimensions than conventional superficial TMS coils, and consequently provide slower decay rate of the electric field with distance, at the expense of reduced intrinsic focality (Deng et al., 2013). Compared to large coils, smaller coils induce an electric field that is intrinsically more focal; however, the improvement in focality is accompanied by faster field attenuation in depth (Deng et al., 2013). Therefore, in order to achieve the same electric field strength at a target depth, smaller coils would require higher coil current to compensate for the faster field drop-off. Higher coil current, in turn, could lead to larger activated brain volume, which counteracts the gain in intrinsic focality of smaller coils. Therefore, it is important to characterize how the field attenuation in depth affects the activated brain volume for different coil sizes. These results can inform dTMS coil selection for various stimulation target depths. Finally, dTMS requires higher energy than superficial TMS, but the energy requirements of various dTMS coil designs have not been systematically compared.

The present study extends our previous work (Deng et al., 2013) to systematically explore the effect of coil configuration and size on the stimulation strength, focality, and energy for deep brain tar-