JOURNAL OF CHILD AND ADOLESCENT PSYCHOPHARMACOLOGY
Volume 26, Number 7, 2016

Pp. 1–5
DOI: 10.1089/cap.2016.0070

Brief Report

Seizure Induced by Deep Transcranial Magnetic Stimulation in an Adolescent with Depression

Kathryn R. Cullen, MD,[1] Suzanne Jasberg, MD,[1] Brent Nelson, MD,[1]
Bonnie Klimes-Dougan, PhD,[1] Kelvin O. Lim, MD,[1] and Paul E. Croarkin, DO, MSCS[2]

Abstract

Objective: Deep transcranial magnetic stimulation (TMS) with an H-1 coil was recently approved by the U.S. Food and Drug Administration (U.S. FDA) for treatment-resistant depression (TRD) in adults. Studies assessing the safety and effectiveness of deep TMS in adolescent TRD are lacking. The purpose of this brief report is to provide a case history of an adolescent enrolled in an investigational deep TMS protocol.

Methods: A case history is described of the first participant of a sham-controlled clinical trial who had a seizure in the course of deep TMS with parameter settings extrapolated from the adult studies that led to US FDA approval (H-1 coil, 120% target stimulation intensity, 18 Hz, 55 trains of 2-second duration, total 1980 pulses).

Results: The participant was a 17-year-old unmedicated female, with no significant medical history and no history of seizures or of drug or alcohol use. Brain magnetic resonance imaging showed no structural abnormalities. She initially received sham, which was well tolerated. During active treatment sessions, titration began at 85% of motor threshold (MT) and increased by 5% per day. Her weekly MT measurements were stable. On her first day of 120% MT (8th active treatment), during the 48th train, the participant had a generalized, tonic–clonic seizure that lasted 90 seconds and resolved spontaneously. She had an emergency medicine evaluation and was discharged home without anticonvulsant medications. There were no further seizures reported at a 6-month follow-up.

Conclusions: We report a deep TMS-induced generalized tonic–clonic seizure in an adolescent with TRD participating in a clinical trial. Given the demonstrated benefits of deep TMS for adult TRD, research investigating its use in adolescents with TRD is an important area. However, in light of this experience, additional precautions for adolescents should be considered. We propose that further dose-finding investigations are needed to refine adolescent-specific parameters that may be safe and effective for treating adolescents with TRD with deep TMS.

Introduction

Major depressive disorder frequently emerges during adolescence and can be difficult to treat. Only 50%–60% of adolescents respond to conventional treatments (e.g., antidepressant medication and cognitive behavioral therapy) after 12 weeks (March et al. 2006; Brent et al. 2008). Expert reviews of longer term follow-up studies suggested that 40% of adolescents with depression do not achieve remission with treatment and can therefore be said to have ''treatment-resistant depression'' (TRD) (Maalouf et al. 2011). Since these adolescents with TRD are at risk for persistent depression in adulthood, morbidity, and suicide, there is an urgent need to develop novel interventions to relieve depression in adolescents with TRD (Maalouf et al. 2011).

Transcranial magnetic stimulation (TMS) is a procedure in which a magnetic coil that generates a pulsatile magnetic field from a rapidly oscillating electrical current is placed on the scalp, to induce electrical currents in the brain (Roth et al. 2007). TMS is used in neuroscientific research to investigate brain functioning, and when used repetitively over the dorsolateral prefrontal cortex (a brain region that is hypoactive in depression) (Mayberg 1997), has been shown to alleviate depression symptoms (Kedzior and Reitz 2014). In 2008, the U.S. Food and Drug Administration (US FDA) approved the use of repetitive TMS with the Neurostar TMS system, which uses a figure-8 coil, with a protocol that included specified settings regarding intensity, frequency, and number of pulses. Recent advances in custom coil technology led to the development of H coils that support stimulation of deeper, nonfocal limbic structures (Roth et al. 2007) relevant to depression and other neuropsychiatric disease. Use of the H-1 coil has been termed ''deep TMS.'' Deep TMS was approved by the US FDA in 2013 for adults with TRD based on pivotal studies (Berlim et al. 2014; Levkovitz et al. 2015).

[1]Department of Psychiatry, University of Minnesota, Minneapolis, Minnesota.
[2]Department of Psychiatry and Psychology, Mayo Clinic, Rochester, Minnesota.
Funding: This study was supported by the MnDRIVE Neuromodulation Innovation Grant. The study was also supported, in part, by Brainsway, who provided the use of the deep TMS machine at no charge.

The two TMS systems (with their respective protocols that have some differences in settings) have been deemed by the US FDA to be equivalent with respect to efficacy and safety (www.accessdata.fda.gov/cdrh_docs/pdf12/k122288.pdf).

Although TMS is thought to be generally safe in children and adolescents (Krishnan et al. 2015), there is a dearth of research about the use of TMS as a treatment for adolescent depression. Initial small, open-labeled repetitive TMS studies have been conducted in adolescent TRD, using a standard figure-8 TMS coil. These studies suggested response rates ranging from 30% to 70% (Bloch et al. 2008; Wall et al. 2011). No results from any randomized, controlled trials testing the application of repetitive TMS (using any coil) in adolescent TRD have yet been published. Furthermore, to date, no studies have examined deep TMS (with an H-1 coil) in adolescent TRD. Prior commentaries have raised important concerns regarding the application of noninvasive brain stimulation in developing children. Dosing guidelines, relevant translational work, and the understanding of the effects in this population are limited (Davis 2014). Given the limited information on safety of applying deep TMS in adolescents with depression, we thought it was important to report on an induced seizure in an adolescent with TRD from a recent deep TMS clinical trial.

Methods

We recently initiated a single-site, sham-controlled clinical trial to test the safety and efficacy of deep TMS as an intervention for adolescents with an H-1 coil. The protocol consists of two phases. Phase 1 consists of 20 treatments over 4 weeks of active treatment or sham (1:1 randomization). All participants are unblinded at the end of Phase 1. Clinical response is defined as at least a 50% improvement in depression symptoms as measured by the Children's Depression Rating Scale, Revised (CDRS-R) (Poznanski et al. 1985). The optional Phase 2 consists of 4 weeks of active treatment (five times per week for nonresponders to active treatment or sham, twice per week for responders to active treatment; responders to sham do not go on to Phase 2).

The deep TMS protocol consists of energy intensity at 120% of motor threshold (MT), 55 trains (or bursts of stimulations) of 18 Hz, each train was 2 seconds in duration, 20-second intertrain intervals, with 1980 total pulses per session. MT is defined as the lowest stimulation intensity, delivered over the left motor cortex, which leads to either an observable muscle twitch or a motor-evoked potential in the right abductor pollicis brevis as measured by electromyography. All MT measurements in this case were evaluated by the same clinician (B.N.). The protocol involves an initial titration period in which the first treatment is given at 100% of MT (or as low as 80% as tolerated), and increasing intensity at a maximum of 10% per day to the target of 120% over a maximum titration length of 2 weeks.

Results

The first participant was a 17-year-old, unmedicated female with TRD. She had previously failed trials of multiple antidepressant medications, either due to ineffectiveness or intolerability. Medical history was notable only for a history of chronic frequent headaches beginning in childhood, which were treated with over-the-counter pain relievers about once a week. She had no history of seizures, and there was no history of or current alcohol or substance use. A brain magnetic resonance imaging at baseline revealed no structural abnormalities. She was randomized to sham in the first phase, which was well tolerated. Weekly MT measurements were stable at 65% of device intensity. The patient did not show any clinical improvement. For example, raw CDRS-R scores at baseline and after Phase 1 were both 60.

As per the approved protocol, the patient was given the option and chose to continue on in the study for Phase 2 of active treatment. On her first day, she did not tolerate 100% of MT intensity due to pain at stimulation site and so was given 85% of MT intensity, which was tolerated. She was able tolerate titration increase by 5% per day. Her MT was reassessed on her fifth day of active treatment, which was 64% of device intensity. The titration reached the target energy of 120% on the eighth day of active treatment. During the 48th train, her right zygomaticus and risorius muscles contracted and remained contracted following the train. The patient and operator were aware of this and the machine was stopped. She then exhibited bilateral convulsions. The helmet was removed from the participant, the chair was lowered, and the rapid response medical team was called. The generalized, tonic–clonic seizure lasted for $\sim$90 seconds and resolved spontaneously. She did not bite her tongue and was not incontinent of urine. She was confused and disoriented following the event. She was transferred via gurney to an ambulance and delivered to the Pediatric Emergency Room at the University of Minnesota Masonic Children's hospital, where she was evaluated and discharged. A pediatric neurologist was consulted who recommended that anticonvulsant medications were not indicated. Follow-up with neurology was not recommended. She returned for her final clinical research visit 5 days later and reported that confusion had continued intermittently for 2–3 days after the incident, and was resolved completely by the time of the visit. She also reported an improvement in mood in the 2–3 days following the episode, but a return to baseline by the time of the visit (no substantial change in depression severity scores; raw CDRS-R score of 57). She then exited the study. Chart review indicates that 6 months later, the patient had no further seizures.

Discussion

Very little information has been published regarding the treatment of adolescent depression with repetitive TMS. Bloch et al. (2008) studied 9 adolescents using the figure-8 coil, 80% of MT intensity, 20 minutes/day over 14 working days, 10 Hz for 2 seconds per train, and intertrain interval of 58 seconds. Wall et al. (2011) treated 8 adolescents, also using a figure-8 coil, 30 treatments given 5 days per week over 6–8 weeks, using intensity 120% of calculated MT, 10 Hz, with stimulus train duration of 4 seconds, and an intertrain interval of 26 seconds, for a total of 3000 stimulations per treatment session. Both studies suggested promising effects and no seizures were reported in either of these studies. A recent systematic review examined the acute safety and effects of repetitive TMS in 322 children and adolescents enrolled in published studies. Of these participants, two (<1%) had a reported seizure (Krishnan et al. 2014).

Both prior published reports of a TMS-induced seizure in adolescents with depression involved the use of a standard figure-8 coil. Hu et al. (2011) reported on a 15-year-old female with depression (concurrently taking sertraline with limited benefit) who was initiated on a repetitive TMS protocol with the figure-8 coil over the left dorsolateral prefrontal cortex at 100% of resting MT, 10 Hz, 60 trains of 5-second duration, 25-second intertrain interval, and 3000 total pulses. During the first treatment, she had a generalized, tonic–clonic seizure. The case report noted that the patient developed some hypomanic symptoms on the evening following the seizure, but these attenuated the next day. She did not receive further repetitive TMS treatments, but did continue sertraline. In 3 weeks, her depressive

symptoms improved and she was considered ''clinically stable.'' She did not have further seizures. Authors noted that the concurrent use of sertraline may have reduced the seizure threshold in this patient (Hu et al. 2011). Chiamberro et al. (2013) reported on a 16-year-old girl with depression (concurrently treated with sertraline, olanzapine, and hydroxyzine, also with limited benefit) who was initiated in a repetitive TMS treatment protocol using the figure-8 coil over the dorsolateral prefrontal cortex, at 10 Hz, with 60 trains of 5-second duration, 25-second intertrain interval, and 3000 stimuli per day, 5 days a week. A seizure occurred on her 12th day of stimulation. It was noted that she had a high level of blood alcohol concentration (0.20%) in the postseizure examination. In contrast to prior reports of adolescent TMS-induced seizures, the adolescent in this report had no risk factors, was taking no current medications, and denied any alcohol use.

It is critical to consider several other factors that may have contributed to higher risk of seizure in this case, including the type of coil and parameter settings such as intensity and frequency. First, in contrast to prior reports, this study applied deep TMS using the H-1 coil. This intervention has the potential to target deep limbic neurocircuitry with limitations in focality (Deng et al. 2013). The risk of seizure in adults with repetitive TMS using a figure-8 coil has been estimated as 3/1000 per treatment, or <1% risk per overall acute treatment course (Carpenter et al. 2012). Less information is available about seizure rates in deep TMS, since it is a newer intervention. In the pivotal sham-controlled trial, 1 out of 101 patients had a seizure (Levkovitz et al. 2015). A very recent case has been reported in the literature of a 27-year-old man with depression and anxiety who had a seizure during deep TMS treatment with an H-1 coil (Boes et al. 2016). It should be noted that the patient had several other seizure risk factors, including multiple past head injuries, intake of a large amount of alcohol the night before treatment, and poor sleep the night before treatment. In a review of studies to date using deep TMS in adults with depression, out of more than 7000 patients treated with the protocol used in the present study, only eight seizures have been reported to date; all cases so far, except for one, had risk factors such as excessive doses of medications that increase neuronal excitability or withdrawal from alcohol use (Dr. Yiftach Roth, Chief Scientist, Brainsway Ltd., pers. comm.). However, the rate of deep TMS-induced seizure in adolescents with the H-1 is unknown. The fact that a seizure emerged in our first participant in a protocol based on adult studies is concerning and suggests that additional caution may be necessary with deep TMS in adolescents.

Second, it is possible that the target intensity chosen for this study (selected based on the parameters that have been shown to be effective in adults) (Berlim et al. 2014; Levkovitz et al. 2015) may have increased risk for seizure in this adolescent. The risk of TMS-induced seizure is known to increase both with increasing intensity of the stimulation and with frequency of the stimulation (Rossi et al. 2009). In the case reported here, the adolescent participant tolerated lower intensities of TMS but had the seizure during the first treatment with the target intensity of 120%. Levkovitz et al. (2009) studied different deep TMS settings in 65 adults with MDD and found that high intensity (120% of MT) but not low-intensity (110% of MT) deep TMS for 4 weeks was an effective treatment (and no participants in the study experienced seizures) (Levkovitz et al. 2009). Although one of the initial pilot studies in adolescents with depression (using a standard, figure-8 coil) used lower intensity (Mayer et al. 2012), the other work has used 120% intensity with no reported seizures to date (Wall et al. 2011; Croarkin et al. 2016).

Third, the frequency setting of 18 Hz in our protocol, which is higher than that used in previous adolescent depression studies (Bloch et al. 2008; Wall et al. 2011), may have played a role in the induced seizure. Krishnan et al. (2015) noted that most TMS studies to date have used frequencies of 1–10 Hz, but three reports did use higher frequencies. First, Graf-Guerrero et al. (2004) reported two cases of children with epilepsy (aged 7 and 11) who were treated with a figure-8 coil over the left frontal cortex (the epileptogenic focus), using a frequency of 20 Hz, 15 trains of 2 seconds, 600 total pulses for 15 minutes, one session total. For one of the cases, authors reported using 50% of the maximum stimulator output, and the other case, 128% of resting MT was used. No adverse effects were reported in those cases. Wu et al. (2012) examined 40 children aged 8–17 with Tourette Disorder or healthy controls. They used a figure-8 coil, 50%–80% active MT intensity, 30–50 Hz, continuous intermittent theta burst, intertrain interval 8 seconds, 600 total pulses, 0.667 minutes per session, 43 sessions, targeting the motor cortex. No seizures were reported. Third, Oberman et al. (2014) reported on 19 adolescents ages 9–18 with autism. They used a figure-8 coil over the left motor cortex, intensity 80% of resting MT, 50 Hz frequency, continuous theta burst, 600 total pulses, and one 40-second session (Oberman et al. 2014). There were no induced seizures in these three reports (Graff-Guerrero et al. 2004; Wu et al. 2012; Oberman et al. 2014). Considering the outcome of the present report, caution is warranted in applying higher intensities and frequencies of stimulation for adolescents with depression.

Finally, given ongoing brain development during adolescence, there may be development-dependent effects of stimulation, both with respect to efficacy and safety. Adolescents could have a higher risk for TMS-induced seizure based on their earlier stage in brain development. The trajectory of cortical excitability in development and the impact of depression on this trajectory have only recently been examined. Croarkin et al. (2012) have reported that in adolescents with TRD, treatment with repeated TMS (using a figure-8 coil, 10 Hz, 120% MT intensity) can lead to increased cortical excitability (measured by decreased MT) after 5 weeks of treatment, which potentially could increase the seizure risk. In addition, younger patients may have higher MTs (Croarkin et al. 2014). As adolescents may have lower seizure thresholds, yet higher MTs relative to adults (Frye et al. 2008), neurodevelopment should be considered in future study designs. Specifically, the selection of developmentally sensitive, optimal treatment parameters represents an important clinical area in need of empirical investigation.

Conclusion

In conclusion, we report a generalized tonic–clonic seizure induced by deep TMS in an adolescent with TRD. Given the prior experience and success of repetitive TMS in treating adult TRD, both with a figure-8 coil and deep TMS using an H-1 coil, further research investigating the use of these devices in adolescent TRD is warranted. Furthermore, given the potential additional benefit of the H-1 coil, compared to the standard figure-8 coil, based on its capacity to stimulate deeper structures relevant to depression, future studies in adolescent depression are imperative. While the case reported here could have represented a random event, in which case modifications to the adult H-1 coil protocol may not be needed, the case highlights the lack of important information needed for selecting optimal parameters for deep TMS treatment in adolescents. Thus, in light of this case report, which represents the first reported use of deep TMS technology in adolescent TRD, we urge clinicians and researchers to appreciate the risk of seizure and take additional caution in selecting the coil and stimulation parameter settings for

treatment of adolescents with depression. When considering deep TMS, the depth of stimulation and decreased focality relative to standard repetitive TMS may necessitate special considerations for selecting frequency and intensity, given the developmental differences in excitatory/inhibitory balances (Deng et al. 2013).

This report also underscores broad considerations for child and adolescent psychiatry research. For example, the importance of developmentally appropriate outcome and measures of illness severity are often underappreciated. As with psychopharmacologic research, there are key but frequently understated differences in outcome and severity measures. Pharmacokinetic, pharmacodynamic, and neurodevelopmental considerations are frequently overlooked in study design. The practice of extrapolating findings and dosing patterns from adults to youth has been problematic for pharmacologic research (Emslie 2012), and this lesson may be even more important in application to brain stimulation research. Moving forward, we suggest that dose-finding, modeling, and patient registry studies are needed to advance the safe and ethical development of these potentially life-changing treatments for children and adolescents.

Clinical Significance

This is the first case report of a deep TMS-induced seizure in an adolescent with TRD. The characterization of this event will inform future protocol development and off-label practice.

Acknowledgments

The authors thank the adolescent and family who volunteered to participate in this research study. Dr. Croarkin has received grant support from Pfizer, Inc., the National Institute of Mental Health (NIMH) (K23 MH100266), the Brain and Behavior Research Foundation, and the Mayo Clinic Foundation. He has received in-kind support for equipment and support for a multicenter trial from Neuronetics, Inc. The content of this report is solely the responsibility of the authors and does not necessarily represent the official views of the US Department of Health and Human Services, the National Institutes of Health, or the NIMH. **Trial Registration:** clinical trials.gov identifier: NCT02611206; https://clinicaltrials.gov/ct2/show/NCT02611206?term = Adolescent±TMS&rank = 7

Disclosures

No competing financial interests exist.

References

Berlim MT, Van den Eynde F, Tovar-Perdomo S, Chachamovich E, Zangen A, Turecki G: Augmenting antidepressants with deep transcranial magnetic stimulation (DTMS) in treatment-resistant major depression. World J Biol Psychiatry 15:570–578, 2014.

Bloch Y, Grisaru N, Harel EV, Beitler G, Faivel N, Ratzoni G, Stein D, Levkovitz Y: Repetitive transcranial magnetic stimulation in the treatment of depression in adolescents: An open-label study. J ECT 24:156–159, 2008.

Boes AD, Stern AP, Bernstein M, Hooker JE, Connor A, Press DZ, Pascual-Leone A: H-coil repetitive transcranial magnetic stimulation induced seizure in an adult with major depression: A case report. Brain Stimul 2016 [Epub ahead of print]; DOI: 10.1016/j.brs.2016.04.013.

Brent D, Emslie G, Clarke G, Wagner KD, Asarnow JR, Keller M, Vitiello B, et al.: Switching to another SSRI or to venlafaxine with or without cognitive behavioral therapy for adolescents with SSRI-resistant depression: The TORDIA randomized controlled trial. JAMA 299:901–913, 2008.

Carpenter LL, Janicak PG, Aaronson ST, Boyadjis T, Brock DG, Cook IA, Dunner DL, Lanocha K, Solvason HB, Demitrack MA: Transcranial magnetic stimulation (TMS) for major depression: A multisite, naturalistic, observational study of acute treatment outcomes in clinical practice. Depress Anxiety 29:587–596, 2012.

Chiramberro M, Lindberg N, Isometsä E, Kähkönen S, Appelberg B: Repetitive transcranial magnetic stimulation induced seizures in an adolescent patient with major depression: A case report. Brain Stimul 6:830–831, 2013.

Croarkin PE, Nakonezny PA, Lewis CP, Zaccariello MJ, Huxsahl JE, Husain MM, Kennard BD, Emslie GJ, Daskalakis ZJ: Developmental aspects of cortical excitability and inhibition in depressed and healthy youth: An exploratory study. Front Hum Neurosci 8:669, 2014.

Croarkin PE, Nakonezny PA, Wall CA, Murphy LL, Sampson SM, Frye MA, Port JD: Transcranial magnetic stimulation potentiates glutamatergic neurotransmission in depressed adolescents. Psychiatry Res 247:25–33, 2016.

Croarkin PE, Wall CA, Nakonezny PA, Buyukdura JS, Husain MM, Sampson SM, Emslie GJ, Kozel FA: Increased cortical excitability with prefrontal high-frequency repetitive transcranial magnetic stimulation in adolescents with treatment-resistant major depressive disorder. J Child Adolesc Psychopharmacol 22:56–64, 2012.

Davis NJ: Transcranial stimulation of the developing brain: A plea for extreme caution. Front Hum Neurosci 8:600, 2014.

Deng Z-D, Lisanby SH, Peterchev AV: Electric field depth-focality tradeoff in transcranial magnetic stimulation: Simulation comparison of 50 coil designs. Brain Stimul 6:1–13, 2013.

Emslie GJ: Are adults just big children? Am J Psychiatry 169:248–250, 2012.

Frye RE, Rotenberg A, Ousley M, Pascual-Leone A: Transcranial magnetic stimulation in child neurology: Current and future directions. J Child Neurol 23:79–96, 2008.

Graff-Guerrero A, Gonzáles-Olvera J, Ruiz-García M, Avila-Ordoñez U, Vaugier V, García-Reyna JC: rTMS reduces focal brain hyperperfusion in two patients with EPC. Acta Neurol Scand 109:290–296, 2004.

Hu S-H, Wang S-S, Zhang M-M, Wang J-W, Hu J-B, Huang M-L, Wei N, et al.: Repetitive transcranial magnetic stimulation-induced seizure of a patient with adolescent-onset depression: A case report and literature review. J Int Med Res 39:2039–2044, 2011.

Kedzior KK, Reitz SK: Short-term efficacy of repetitive transcranial magnetic stimulation (rTMS) in depression—reanalysis of data from meta-analyses up to 2010. BMC Psychol 2:39, 2014.

Krishnan C, Santos L, Peterson MD, Ehinger M: Safety of noninvasive brain stimulation in children and adolescents. Brain Stimul 8:76–87, 2015.

Levkovitz Y, Harel EV, Roth Y, Braw Y, Most D, Katz LN, Sheer A, Gersner R, Zangen A: Deep transcranial magnetic stimulation over the prefrontal cortex: Evaluation of antidepressant and cognitive effects in depressive patients. Brain Stimul 2:188–200, 2009.

Levkovitz Y, Isserles M, Padberg F, Lisanby SH, Bystritsky A, Xia G, Tendler A, et al.: Efficacy and safety of deep transcranial magnetic stimulation for major depression: A prospective multicenter randomized controlled trial. World Psychiatry 14:64–73, 2015.

Maalouf FT, Atwi M, Brent DA: Treatment-resistant depression in adolescents: Review and updates on clinical management. Depress Anxiety 28:946–954, 2011.

March J, Silva S, Vitiello B: The treatment for adolescents with depression study (TADS): Methods and message at 12 weeks. J Am Acad Child Adolesc Psychiatry 45:1393–1403, 2006.

Mayberg HS: Limbic-cortical dysregulation: Depression. J Neuropsychiatry Clin Neurosci 9:471–481, 1997.

Mayer G, Faivel N, Aviram S, Walter G, Bloch Y: Repetitive transcranial magnetic stimulation in depressed adolescents: Experience, knowledge, and attitudes of recipients and their parents. J ECT 28:104–107, 2012.

Oberman LM, Enticott PG, Casanova MF, Rotenberg A, Pascual-Leone A, McCracken JT: Transcranial magnetic stimulation (TMS) therapy for autism: An international consensus conference held in conjunction with the International Meeting for Autism Research on May 13th and 14th, 2014. Front Hum Neurosci 8:1034, 2014.

Poznanski EO, Freman LN, Mokros HB: Children's Depression Rating Scale-Revised. Psychopharmacol Bull 21:979–989, 1985.

Rossi S, Hallett M, Rossini PM, Pascual-Leone A; Safety of TMS Consensus Group: Safety, ethical considerations, and application guidelines for the use of transcranial magnetic stimulation in clinical practice and research. Clin Neurophysiol 120:2008–2039, 2009.

Roth Y, Amir A, Levkovitz Y, Zangen A: Three-dimensional distribution of the electric field induced in the brain by transcranial magnetic stimulation using figure-8 and deep H-coils. J Clin Neurophysiol 24:31–38, 2007.

Wall CA, Croarkin PE, Sim LA, Husain MM, Janicak PG, Kozel FA, Emslie GJ, Dowd SM, Sampson SM: Adjunctive use of repetitive transcranial magnetic stimulation in depressed adolescents: A prospective, open pilot study. J Clin Psychiatry 72:1263–1269, 2011.

Wu SW, Shahana N, Huddleston DA, Lewis AN, Gilbert DL: Safety and tolerability of theta-burst transcranial magnetic stimulation in children. Dev Med Child Neurol 54:636–639, 2012.

Address correspondence to:
Kathryn R. Cullen, MD
Department of Psychiatry
University of Minnesota
F256/2B West Building
2450 Riverside Avenue
Minneapolis, MN 55454

E-mail: rega0026@umn.edu