Letter to the Editor

Single-pulse TMS related syncopal spell in a healthy subject

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To the Editor:

We report the following TMS-related seizure or spell. The subject was a 22-year-old healthy woman who had no risk factors and was not taking any medications. She was screened using a self-report questionnaire for contraindications for TMS, including past or present neurologic, cardiac, and psychiatric conditions, family history of epilepsy, sleep deprivation, medicinal or recreational drug use, and recent use of alcohol or high doses of caffeine. Written informed consent was then obtained.

Pulses were applied using a 70-mm figure-of-eight coil connected to a Magstim Rapid biphasic stimulator (The Magstim Co. Ltd., Whitland, Carmarthenshire, U.K.). At the time of the incident, the coil was held tangentially to the skull, over the optimal spot at the left M1 to elicit MEPs in both the ADM and FDI of the right hand, with the handle pointing backward/laterally approximately midway between the sagittal and coronal planes. We had been delivering pulses at around 0.2 Hz over left anterior parietal/posterior frontal cortex to establish the participant's motor hot spot and threshold (based on event-triggered EMG). She had a medium threshold, approximately 60% of stimulator output, and we had given pulses from around 30-75% output while probing for the hot spot, culminating at approximately 110% passive motor threshold (66% machine output).

The event occurred approximately 15 minutes into the subject's first session as a TMS participant, following approximately 30 pulses of TMS. The setting was a research laboratory with two TMS operators, one holding the coil and the other adjusting stimulator parameters. Both operators had training in first aid but neither were medical professionals. The subject was seated in a chair with her head resting on a chin rest. She had requested a fairly high position for the chin rest to keep her back straight. Immediately after a pulse, the TMS operators noted the subject's head slumping backward as she lost tone in her neck. Her eyes rolled back and then closed. Stimulation was ceased immediately. There were two to three subtle myoclonic jerks: One operator (standing to the subject's left) noticed approximately two at the left hand, and the second operator (kneeling to provide gentle support from the subject's right) noticed approximately one at the right arm/trunk. The participant remained unconscious for 5-10 seconds, then recovered spontaneously. She apologized for having fallen asleep, expressed embarrassment, and was immediately coherent and lucid. The subject seemed fully recovered, for example, being easily able to engage in conversation and report the date, and showed no signs of distress. When the incident was explained, she reported feeling a little hot during the procedure, and also noted that relaxing in the chair for stimulation had reminded her of previous experiences when she was sedated before operations. The participant was released after approximately 45 minutes of observation in the laboratory, and then contacted several times over the next few hours/days.

The subject was examined by her primary healthcare doctor (GP) at her local medical practice approximately 36 hours after the incident and findings were all normal. She was not referred for additional procedures. This episode was also reported to the City University Senate Research Ethics Committee. We suggest that the most likely diagnosis is TMS-related (convulsive) syncopy. (See the syncope video on the Brain Stimulation website http://www.brainstimjrnl.com/content/mmc_library). This was also the reported opinion from the participant’s general practitioner. We believe that this was probably not a case of neurogenic seizure given the extremely low probability of such an incident.
resulting from single-pulse TMS in healthy subjects with no neurologic disorder or use of psychotropic substances. Myoclonus was barely detectable and was not noted to progress systematically from the stimulated muscles. Furthermore, the rapid recovery of consciousness without apparent postictal confusion better suits a diagnosis of syncope rather than seizure. However, it is impossible to completely rule out an induced seizure. In this study, as in the one other seizure incident reported in a healthy subject undergoing single-pulse TMS, precise clinical diagnosis is confounded by the strong overlap between the symptoms of the main possible causes, and the absence of EEG recording during the episode.

Seizure is the most serious adverse reaction to TMS, and is very rare, but other milder side effects of the procedure may occur more frequently. These include syncope, nausea, headaches, and muscular discomfort resulting from twitches. It seems sensible to also catalogue such side effects for the benefit of participants, ethics boards, and the wider TMS community. Table 1 summarizes the frequency of milder side effects in a sample of 96 sessions occurring in our laboratory from mid-2009 to mid-2011. These data come from self-report forms administered after testing, with specific questions about pain, headache, and anxiety, and space provided for additional comments. In addition to the data shown in Table 1, and the adverse incident reported here, we also stopped testing in one further participant when she reported feeling nauseous, with a sensation “like her ears had popped.” In these studies, pulses were applied at a typical rate of 0.2 Hz or less with intensity below 120% of resting motor threshold (with occasional higher intensities during initial thresholding). TMS was administered to M1 (71 sessions), vertex and dorsal premotor cortex (17 sessions), or dorsal and ventral premotor cortex (eight sessions). Subsets of these data are likely to appear in the relevant experimental reports, where any crossover with this letter will be noted. We encourage other researchers, even those outside medical research settings, to measure and document side effects whenever feasible.

Table 1. Self-reported side effects from 96 sessions of single-pulse TMS

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<th></th>
<th>None</th>
<th>Mild</th>
<th>Severe</th>
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<tr>
<td>Muscular pain</td>
<td>76</td>
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<td>Headache</td>
<td>83</td>
<td>13</td>
<td>0</td>
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<tr>
<td>Anxiety</td>
<td>94</td>
<td>2</td>
<td>0</td>
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</tbody>
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References


3 Makris S, Hadar AA, Yarrow K. Viewing objects and planning actions: On the potentiation of grasping behaviours by visual objects. Brain Cogn, in press..