Research Submission

Development and Positioning Reliability of a TMS Coil Holder for Headache Research
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Objective.—Accurate and reproducible coil positioning is important for headache research using transcranial magnetic stimulation protocols. We aimed to design a transcranial magnetic stimulation coil holder and demonstrate reliability of test–retest coil positioning.

Methods.—A coil holder was developed and manufactured according to three principles of stability, durability, and three-dimensional positional accuracy. Reliability of coil positioning was assessed by stimulating over the motor cortex of four neurologically normal subjects and recording finger muscle responses, both at a test phase and a retest phase several hours later.

Results.—In all four subjects, repositioning of the transcranial magnetic stimulation coil solely on the basis of coil holder coordinates was accurate to within 2 mm.

Conclusions.—The coil holder demonstrated good test–retest reliability of coil positioning, and is thus a promising tool for transcranial magnetic stimulation-based headache research, particularly studies of prophylactic drug effect where several laboratory visits with identical coil positioning are necessary.

Key words: coil positioning, prophylaxis research, research methods, transcranial magnetic stimulation

(Headache 2005;45:37-41)

Transcranial magnetic stimulation (TMS) is a non-invasive method of investigating cerebral function. The technique is based on the principles of electromagnetic induction discovered by Faraday in 1831. TMS works by using a pulse of magnetic field to create a flow of current in cortical tissue. Barker and coworkers1 carried out the first stimulation of the human motor cortex using TMS, placing a 100 mm coil over the vertex of a human participant and eliciting a hand movement. Since then, TMS has undergone rapid development. Commercial TMS machines are now widely available and are used extensively in both clinical and research settings.

TMS, unlike other techniques for evaluating the relations between brain activity and human behavioral or physiological function, is noninvasive, easy to learn and relatively cheap. The rapid onset and short duration of the magnetic pulse offers excellent temporal resolution. Spatial resolution depends on a number of factors, including coil design, but is generally regarded as being at least as good as PET.2 These characteristics have made TMS an increasingly popular and productive tool in headache research, particularly among groups of researchers looking at visual cortex excitability.3,4 In such research, coil placement and positioning is a particularly crucial issue as slight variations in placement over the skull can alter the cortical area being stimulated.5,6

At the same time, interest in migraine prophylaxis is growing, and several researchers have become interested in using TMS as an objective index of drug activity before, during, and after treatment.7,8 Typically, such research involves the patient in several laboratory visits, during each of which the aim is to run a standardized TMS testing protocol. It is evidently a sine qua non
of such research that the coil be positioned accurately and consistently at each laboratory visit that the patient makes. In other words, the test–retest placement reliability of the coil holder should be high. A gold standard way of achieving this would be to use MRI-guided coil positioning, which allows online referencing of the TMS coil to a three-dimensional rendering of the individual patient’s brain, derived from structural MRI images. This is both costly and logistically difficult, however, particularly if large numbers of patients are to be tested (as is necessary in many drug trials).

We, therefore, aimed to develop and test a robust, inexpensive TMS coil holder with good test–retest placement reliability. We assessed placement reliability in an objective fashion by stimulating over the motor cortex and recording the anatomical location and extent of muscular activity in the contralateral hand.

METHODS

Design of the Coil Holder.—The main requirements for the design of a coil holder for use in headache research are threefold: first, to ensure stability of the TMS coil during testing; second, to be durable so as to allow frequent use; and third, to include some form of three-dimensional coordinate system to enable repositioning of the coil in the same position and thus permit reproducibility of results.

Several technical considerations also influenced the choice of design. First was the weight of the stimulation coils. Two coils, a circular and a figure-of-eight coil, are commonly used with the Magstim SuperRapid™ (MagStim Company, U.K.), the machine available in our laboratory. Both coils are relatively heavy, weighing between 2 and 2.5 kg. The material for the construction needed to be strong enough to support this weight. Second, the clamping system to hold coils in a fixed position needed to be robust and free of any drift in coil positioning. Third, none of the final design should be adversely affected by the proximity of magnetic fields of up to 2.5 T from the stimulating coil. In particular, the coil holder should not warm up over a period of magnetic stimulation. In light of these technical requirements, it was decided to use aluminum as a construction material, for its strength, ease of machining, and rapid heat dissipation.

The coil holder was designed using a construction of aluminum beams, lockable screw knobs, and plastic protractors (Figure, panel A). The design provided movement in three dimensions via four joints.

(A) A lateral view of the coil holder supporting a figure-of-eight coil. (B) The wall joint of the coil holder, with calibrating protractor visible. The black knob manually locks and unlocks this joint. (C) The chin rest mounted in its calibrated runners.
Protractors were positioned at these joints with angle markers to permit repositioning (Figure, panel B). In addition, the coil could be rotated about the long axis of its handle to ensure tangential coil placement relative to skull curvature. The coil holder was then fixed to the laboratory wall and was found to be very satisfactory in terms of coil stability and lack of positional drift. It was next necessary to ensure subjects were sitting in a constant position; to this end, a chin rest was designed, bolted to a table, and wooden runners were secured to either side of it, with a centimeter rule being used for one of these runners to record the position of the rest on the table (Figure, panel C).

**Test–Retest Reliability of Coil Positioning.**—The accuracy and reproducibility of the positioning of the coil was next tested, using four volunteer subjects. All four subjects were right handed, aged between 18 and 40 years, were free of any neurological disorder, and were not taking any daily medication. Approval for the use of human subjects was granted by the Ethics Committee of the Department of Psychology, Lancaster University. Written informed consent was obtained. In the test phase, subjects were first seated and positioned with their chin resting on the chin rest, and left hand placed on the table in a natural resting position. The TMS coil was positioned near the vertex of the skull and several single TMS pulses were delivered to the motor cortex. A stimulation intensity of between 45% and 55% of the maximal stimulation intensity of approximately 2 T was used. The intensity was increased in 1% units over a series of trials and the position of the coil gradually varied until stimulation was just sufficient to produce a visualizable finger movement in the left hand. The coil was then locked into position and coordinates recorded using the protractor readings attached to the arm joints and the metric rule measuring the position of the chin rest on the table. Additional stimulations were then performed to ensure consistency of motor response to stimulation with this coil position.

Subjects were then disengaged from the apparatus, and asked to return to the laboratory later in the same day for the retest phase. On their return, subjects were again seated in the chair with their chin resting on the chin rest, positioned as recorded in the test phase. The TMS coil was placed against the skull with the coil holder repositioned according to the test phase coordinates. The motor cortex was then stimulated using single pulse TMS, with a stimulation intensity identical to that used in the test phase. Finger movements were visualized and recorded.

**RESULTS**

Visualized finger movements from each subject, in the test and retest phases, are shown in the Table. For subjects 1 and 3, the test stimulation produced extension of the fourth finger and the retest stimulation produced extension of the third and fourth fingers. For subject 2, the test stimulation produced extension of the fifth finger and the retest stimulation produced extension of the fourth and fifth fingers. In subject 4, test stimulation produced abduction of the thumb, and retest stimulation produced extension of the second finger and some abduction of the thumb. Coil position differences between test and retest stimulations were estimated on the basis of a recent high-resolution fMRI study examining finger somatotopy in the human motor cortex, in which the mean distance between centers of mass of BOLD activations for the second and fifth fingers was 4–5 mm. We, therefore, estimated the difference in distance between individual fingers at 2 mm, and test–retest coil position differences calculated on this basis are also shown in the Table. In no subject was the test–retest coil position difference greater than 2 mm.

**COMMENTS**

The design and construction of this coil holder provided a stable and safe method of holding the TMS coil securely in place against subjects’ heads. Informal feedback from subjects indicated that the apparatus was comfortable and unthreatening. The use of protractors on the angle joints of the coil holder, and the calibration of chin rest position allowed for recording of the position of the TMS coil, in three dimensions. In turn, this permitted accurate repositioning of the coil at retest. In all four subjects, the test–retest variation in coil position was estimated at 2 mm of cortical surface or less.

Coil positioning for TMS-based research is an important methodological issue, as has been pointed out by several authors. Although the coil holder we
have developed does not solve the problem of how consistent the relationship is between external skull landmarks and underlying cortical anatomy, it does provide investigators with a tool to ensure reliable and consistent coil positioning across laboratory visits that may be widely separated in time. In the context of clinical research into the efficacy of candidate migraine prophylactics, such test–retest reliability is particularly crucial. From a practical point of view, the coil holder uses inexpensive and readily available components, and can be constructed at very modest cost (approximately $300) in any well-equipped machine shop. Further details of the components and construction methods may be obtained from the corresponding author.

In conclusion, test–retest reliability for coil positioning appears to be good for the motor cortex, and this device shows promise for use in TMS studies of migraine prophylaxis. Two next steps in the development of the coil holder are now desirable. First, a better estimate of test–retest variation in coil position over the motor cortex might be obtainable through the use of motor-evoked potentials, rather than the simple observation of finger movements. This was not undertaken in the present study as the appropriate equipment was unavailable. Second, it is evident that good coil-positioning reliability over the motor cortex does not necessarily guarantee equally good reliability in studies of the visual cortex. An important goal, therefore, is to calibrate the test–retest placement reliability for the visual cortex against a gold standard of MRI-guided placement. Our laboratory is in the process of initiating such research.

Acknowledgments: We thank Phil Smith and Gordon Johnston (Lancaster University) for their outstanding help and technical expertise in constructing the coil holder and chin rest. Tom Ormerod (Lancaster University) provided invaluable comments during the preparation of the manuscript. This research was partially supported by the Dr. Hadwen Trust for Humane Research, and a NIH Fogarty Fellowship to Cheryl Matthews.

REFERENCES


