

## Magnetic Seizure Therapy of Major Depression

**E**lectroconvulsive therapy (ECT) plays an important role in the treatment of severely depressed patients, especially those who do not respond to antidepressant medications. However, its cognitive adverse effects restrict its use. The dosage of the electrical stimulus and the anatomic placement of stimulating electrodes are critical in determining the efficacy and cognitive adverse effects of ECT.<sup>1-4</sup> Nonetheless, with ECT, control over the spatial distribution and magnitude of intracerebral current density is limited by high skull impedance, which shunts most of the electrical stimulus through the scalp and cerebrospinal fluid. There are also individual differences in skull anatomy that result in uncontrolled variation in intracerebral current density.

Repetitive transcranial magnetic stimulation (rTMS) may provide a more precise method of seizure induction; rTMS induces currents in the cerebral cortex through rapidly alternating magnetic fields.<sup>5</sup> Magnetic fields penetrate the scalp and skull with no resistance, offering greater control over the site of seizure initiation and extent of cortical stimulation.<sup>6</sup> We recently reported the induction of generalized seizures in nonhuman primates under anesthesia using a custom modified magnetic stimulator that matched the peak induced voltage achieved with electroconvulsive shock.<sup>7</sup>

We report the first trial to our knowledge of magnetic seizure induction under general anesthesia in a psychiatric patient. The patient provided informed consent to undergo magnetic seizure induction for her first 4 treatments, followed by conventional ECT, under a protocol approved by the Institutional Review Board of the State of Bern, Switzerland. The patient, a 20-year-old woman, had a 3-year episode of major depression, and treatment failed in trials using a selective serotonergic reuptake inhibitor, 2 tricyclic antidepressants, 2 monoamine oxidase inhibitors, and several newer agents. She also did not respond to augmentation with lithium, triiodothyronine, and methylphenidate. Each trial achieved adequate doses for periods greater than 6 weeks, but her level of functioning remained impaired.<sup>8</sup> Physical and neurological examinations, admission laboratory analysis results, findings from electrocardiogram, and brain computed tomographic scans were unremarkable.

Magnetic seizure therapy (MST) sessions were conducted under general anesthesia 3 times per week for 4

treatments. Electroencephalogram (EEG) and electrocardiogram results, pulse oximetry, and blood pressure were monitored. Etomidate (0.3 mg/kg intravenously) was used as the anesthetic agent for the first 2 treatments, as this is the standard ECT anesthetic used at this center (University Hospital of Bern). Etomidate has been reported to have proconvulsant properties.<sup>9,10</sup> The 2 subsequent treatments were performed with thiopental anesthesia (5 mg/kg intravenously) to establish capacity for seizure induction using a standard short-acting barbiturate anesthetic. Succinylcholine (1 mg/kg) was used for muscle relaxation, and the patient was ventilated with positive pressure 100% oxygen. The EEG electrodes (frontomastoid) were slotted to prevent heating<sup>11</sup> from magnetic stimulation, and the patient wore earplugs to protect hearing.<sup>12</sup>

Treatments were delivered with a custom-modified magnetic stimulator (Magstim Super Rapid; Magstim Company Ltd, Whitland, Wales) that had a broader pulse width and more charging units than commercially available devices, permitting stimulation up to 40 Hz at peak intensity. The rTMS was administered with a precooled, double-cone coil held at the vertex or a figure 8 coil on the right prefrontal cortex (**Table**).

Each of the MST trials produced a tonicoclonic seizure (from 30-270 seconds), documented by both motor and EEG manifestations. The magnetic seizure threshold was titrated at the second session by administering trains of increasing duration until a seizure was induced. Generalized seizures characteristic of ECT were reliably obtained with stimulation at 40 Hz, 100% of maximal stimulator output, administered for 4 seconds.

Each treatment was well tolerated. After the fourth treatment, the Hamilton Rating Scale for Depression<sup>13</sup> score decreased to 13 from a baseline of 20. The Mini-Mental State<sup>14</sup> score remained unchanged at 30 throughout the treatment course. Following the MST sessions, the patient received 8 conventional ECT treatments (right unilateral, 200% above initial seizure threshold), and had a final posttreatment Hamilton Rating Scale for Depression score of 6.

This case demonstrates that magnetic seizure induction under general anesthesia is feasible in the treatment of psychiatric disorders. Recent brain imaging studies suggest that manipulations of ECT electrode placement and electrical dosage that are associated with greater efficacy produce more robust functional changes in prefrontal cortex.<sup>15,16</sup> The enhanced control over both dosage and focality of stimulation that may be achieved with MST offers the capacity to restrict seizure induction to specific cortical areas, such as prefrontal cortex regions,

## Magnetic Seizure Therapy Trials\*

Trial	Premedication	Anesthesia	Pulse Width, ms	Coil	Placement	Parameters of Stimulation			
						Frequency, Hz	Intensity	Duration, s	Intertrain Interval, s
1	Atropine, 0.5 mg	Etomidate	0.4	Double cone	Vertex	40	100% Output (240% of MT)	6.3	...
2	Atropine, 0.5 mg	Etomidate	0.4	Double cone	Vertex	40	100% Output (240% of MT)	2.0	...
3	None	Thiopental	0.4	Double cone	Vertex	40	100% Output (240% of MT)	4.0	28
			0.4	Figure 8	Right lateral prefrontal cortex	20†	100% Output (213% of MT)	6.3	...
4	None	Thiopental	0.4	Double cone	Vertex	35†	100% Output (240% of MT)	6.3	136
			0.5	Double cone	Vertex	40	70% Output‡ (292% of MT)	4.5	...

\*MT indicates motor threshold; ellipses, not available.

†Lower frequencies delivered due to device malfunction.

‡The 70% Output at 0.5-millisecond pulse width delivers same energy as 100% at 0.4 millisecond.

and perhaps improve the efficacy and/or reduce the adverse effects of traditional convulsive treatment.<sup>6</sup>

Considerable evidence indicates that depending on the frequency of the magnetic pulses, rTMS may enhance inhibition or excitation in targeted brain regions.<sup>17-19</sup> This leads to the possibility of selecting specific sites for seizure initiation and other sites as targets of inhibition. This approach offers the possibility of maximizing efficacy while halting seizure spread to further limit adverse effects.

This case demonstrates that magnetic induction of generalized seizures under general anesthesia in the human is feasible. The refinement of MST may ultimately offer a more precise and safer physical treatment of the brain in psychiatry.

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Seizure Duration, s	Peak Heart Rate, Beats per Minute	Peak Blood Pressure, mm Hg	Postmedications	Time to Orientation, min
112	156	145/84	Diazepam, 10 mg intravenously	22.9
0	...	...	...	...
80	...	...	Diazepam, 10 mg intravenously	30.0
0	...	...	...	...
44	136	152/87	None	8.0
30	141	147/103	None	6.9

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### Causes of Posttraumatic Stress Disorder in Psychotic Patients

The recognition of posttraumatic stress disorder (PTSD) within psychosis has been suggested to be important; it may avoid inappropriate use of antipsychotic medication, clarify professional understanding, and stimulate the design, implementation, and evaluation of more effective interventions for psychosis<sup>1,2</sup>; it may also have a beneficial effect on a wide range of problems, including depression, anxiety, substance abuse, and suicide among people with psychosis.<sup>3</sup> Despite these important clinical implications, there is little research into the occurrence of PTSD within psychosis. To date, there are only 2 empirical investigations of PTSD within acute psychosis.<sup>2,3</sup> One of these found that 52% of their sample (n=45) qualified for the *DSM-III-R* diagnosis of PTSD while in the hospital.<sup>2</sup> Of the sample (n=36) in the other study, 46% and 35% qualified for a *DSM-III* diagnosis of PTSD at 4 and 11 months, respectively, after discharge from the hospital.<sup>3</sup> These studies implicated the experience of psychosis and psychiatric hospitalization as precipitating PTSD within psychosis, but did not establish the differential contribution of such stressors. In addition, there is a growing body of literature that is consistent with the view that psychosis may actually be a response to trauma; one recent study found that 98% of a large sample (n=275) reported exposure to at least 1 traumatic event.<sup>4</sup> Therefore, it is likely that there will be various different causes of PTSD within psychosis that fall across the 3 categories of trauma considered above (psychotic symptoms, hospitalization, and other traumas).

We hypothesized that there would be a high rate of PTSD among those hospitalized after a psychotic epi-

sode, that the experience of hospitalization and psychotic symptoms would both make significant contributions to the prediction of PTSD symptoms after hospitalization for acute psychosis, and that there would be a high incidence of other traumas in these patients. Sixty adults (37 men and 23 women; all had schizophrenia spectrum disorders) admitted to a psychiatric ward after an acute psychotic episode gave written informed consent and were interviewed and completed questionnaires, including standardized measures of trauma (general and in relation to specific events, including psychosis and hospitalization) and psychotic symptoms. Their responses on a self-report measure<sup>5</sup> based on *DSM-IV* criteria suggested that the rate of likely PTSD was 67% at hospital discharge and 50% at 4- to 6-month follow-up. Hierarchical regression analyses revealed that the experience of psychotic symptoms in particular (as well as hospitalization) made a substantial contribution to the traumatization of the sample. Together, they accounted for 60% of the variance in PTSD scores, and 49% of the variance when psychotic symptoms were statistically controlled for (the experience of psychosis and hospitalization accounting for 24% and 7% unique variance, respectively). Interestingly, compulsory admission under the Mental Health Act had no effect on reported PTSD symptoms; 32% of the sample reported other traumas. These results clearly have implications for the assessment and treatment of acute psychosis; in particular, it is possible that interventions developed for PTSD may be applicable to the reduction of distress in patients with a psychotic disorder.

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This work was undertaken by staff from the Mental Health Services of Salford, who received a percentage of