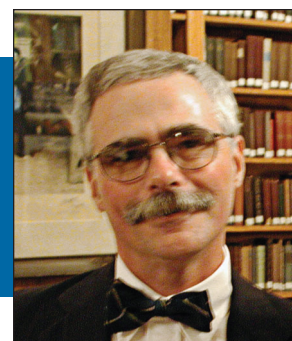


# Right Unilateral Electroconvulsive Therapy Treatment for CRPS

Results and implications of this increasingly utilized option for the treatment of refractory CRPS.



*“In the inaugural article of the CRPS Department, Mr. Michaels reports on his investigation of Electroconvulsive Therapy (ECT) as a possible treatment option for refractory Complex Regional Pain Syndrome (CRPS). Currently, ECT is not even mentioned in the published consensus-derived CRPS Treatment Guidelines. His conclusion may surprise you.”*

— James W. Broatch, MSW



By Franklin Michaels, Jr.

The use of electric fish/eels in pain treatment has been documented to Roman times,<sup>1</sup> and electroconvulsive therapy (ECT) has been known to relieve chronic pain since the 1940's—including the complete remission of chronic cases of what has become known as CRPS-1 since at least 1957.<sup>2</sup> Yet even with many modifications in the therapy that have ensued, physicians have remained reluctant to utilize ECT, primarily because of the concern of injury and the negative image associated with ECT.<sup>1</sup> The side-effect of greatest concern is retrograde amnesia, which has been significantly associated with Bilateral ECT (BL), the dominant form of the treatment. Nevertheless, a series of case reports going back to 1975<sup>3</sup> give strong support that, contrary to accepted wisdom, an alternative form of treatment—often referred to as Right-Unilateral (RUL) ECT, but more properly characterized as “non-dominant unilateral”—has equivalent effectiveness in the treatment of certain forms of chronic pain—including CRPS—without persistent cognitive side effects. Such treatment should therefore be considered for refractory cases of CRPS-1.

Among various forms of chronic pain, CRPS has stood out as a condition that tends to respond well to a series of typically between six and twelve ECT treatments, resulting in significant and long lasting improvement in approximately two out of three cases.<sup>1,2,4-6</sup> Of six case studies, the most recent report is perhaps the most dramatic: over a period of time following one automobile accident in which she suffered a flexion-extension injury to her neck, and a second accident three years later in which she fractured her left wrist, a woman who had been working as a judge, developed severe CRPS in all of her extremities, back and face—along with internal complications—to the point that she became too ill to work. Notwithstanding extensive treatments, including a four-day course of inpatient IV lidocaine, the patient had no relief from pain four years from the time of her initial accident. Finally, two years later and after developing severe, medically refractory depression, the patient received a series of 12 BL ECT treatments under standard anesthesia. Within a month she reported an

almost complete remission of her CRPS symptoms. Four years later, in 2007, the patient was seen again, at which time she had no criterion factors for CRPS or depression, and had returned to a normal life working full-time as an attorney.<sup>6</sup>

Notwithstanding the fact that most, if not all, of the patients referred to in the case studies above had co-morbid depression, it has been established in an inpatient study at the Chronic Pain Treatment Service of the Johns Hopkins Department of Psychiatry and Behavioral Medicine that ECT has a demonstrable effect on chronic pain independent of the patient's level of depression or degree of recovery. The study used a matching system where each ECT patient was matched to another patient—based as much as possible on race, pain syndrome diagnosis, and number of previous psychiatric hospitalizations—who would be receiving medication only. Of the 36 patients beginning the ECT treatment, 28 completed charts remained at the end of the study. Of those, 25 could be matched—with 3 members of the control group being used twice for matching purposes. The major findings of the study are as follows:

“The data presented here indicate that ECT has analgesic properties independent of its effect on depression in patients with both chronic pain and major depression. Improvements in depression scores were statistically similar between groups, while improvements in pain were greater in the ECT group. Of great interest is that, despite starting at a higher pain level (8.1 vs 6.9), the ECT group had a lower level of pain at the end of treatment (3.4) than the control group (5.5), who were treated with medications alone. The difference in baseline pain scores between groups may be a confounder, but the more profound drop in pain score to below a 4.0 in the ECT group speaks against this. The ECT group improved to a pain level lower than 4.0, which is a level consistent with significant gains in functionality, while the control group remained above 4.0. Their lower post-treatment pain scores suggest a specific analgesic effect of ECT. The significant partial correlation coefficient controls for the effect of the improvements in depression between groups and affirms the analgesic properties of ECT. The longer length of

stay in the ECT group (40 vs 20 days) may have contributed to their improvements in pain, since they received more multidisciplinary treatment. But, patients in the ECT group had an average of 10 treatments, and they were unable to fully participate in multidisciplinary treatment on those days. This mitigates the confounding effects of longer length of stay on analgesic response. The number of patients in each specific pain diagnosis group was too small to determine if a particular pain syndrome responded preferentially to ECT. But, these data indicate that ECT has analgesic effects across a wide variety of pain syndromes.

“While the ECT group had a more robust improvement in major depression, this improvement was not significantly different between the groups. This finding is consistent with previous studies showing a depression treatment response rate of up to 90% with ECT, while, on average, antidepressant treatment has an 80% response rate.”<sup>7</sup>

### ECT Therapies

As alternative forms of ECT were developed to minimize cognitive side effects (persistent retrograde amnesia), at least one early report had shown that RUL was effective for chronic pain—providing persistent relief for four of six patients.<sup>3</sup> Unfortunately, those findings, along with a study showing no improvement in post-stroke thalamic pain,<sup>8</sup> were subsequently characterized as supporting the proposition that “while the use of unilateral electrode placement over the non-dominant frontal lobe reduced confusion, it may have resulted in lower response rates of intractable pain to ECT and subsequent abandonment of the procedure for pain syndromes.”<sup>9</sup> This conclusion has since been repeatedly cited in the literature for the proposition that only Bilateral ECT was effective for the treatment of chronic pain.<sup>5,6</sup> It was, however, specifically challenged in one 2003 report of a CRPS-1 patient having had eight treatments of RUL, sustaining complete remission of both depression and CRPS.<sup>5</sup>

We are left with the fact that, to date, there have been no double-blind controlled studies of the respective efficacies of BL and RUL for chronic pain—an issue addressed in a somewhat more general context by Rasmussen and Rummans in their comprehensive 2002 review:

“Ideally, the literature to establish that

ECT may benefit at least some patients with pain syndromes would include randomized, double-blind trials with well defined, clinically homogeneous samples, but such trials are lacking. The next best line of evidence would be extensive case series that include descriptions of the onset and course of the pain syndrome, concomitant depression if present, the time course of change in pain and depressive symptoms during the course of ECT—preferably using quantitative scales—and long-term follow-up data on both pain and depression to insure that any analgesic benefits are not merely transient effects. In this manner, it would be possible to conclude whether or not ECT has a primary benefit in a given pain syndrome or whether the analgesic effect is simply secondary to an antidepressant benefit.”<sup>2</sup>

Two years later, Wasan et al. established

*“Among various forms of chronic pain, CRPS has stood out as a condition that tends to respond well to a series of typically between six and twelve ECT treatments, with significant and long lasting improvement in approximately two out of three cases.”<sup>1,2,4-6</sup>*

that ECT, in fact, relieved pain independently of its effect on depression<sup>7</sup> and meeting in part the test set down by Rasmussen and Rummans. With respect to the choice of technique, substantial evidence supports the claim that even at “moderately super-high” strengths, RUL does not pose a significant risk of long-term cognitive impairments<sup>10</sup> in contrast to BL, which produces more profound retrograde amnesic effects—particularly for memory of impersonal events.<sup>11</sup>

During the course of ECT, stimulus dosage is systematically increased until a seizure is induced, thereby quantifying a seizure threshold (ST) which, in turn, has an inverse relationship to seizure duration.<sup>12</sup> In general, the closer an electrical charge is to mimicking endogenous neuroelectrical signals in the brain, the less energy is required to induce ST,<sup>13</sup> and the less likely the signal is to create cognitive side effects.<sup>14</sup> ST is markedly higher with BL as compared to RUL. Accordingly, in the treatment of major depressive episodes (MDE), high dosage RUL and BL have equivalent therapeutic effects, but BL ECT produced significantly more cognitive effects.<sup>15,11,16</sup> It has also been hypothesized that a right-left

asymmetry commonly observed with RUL believed to be derived from a focal onset early in the seizure within the non-dominant cerebral hemisphere—followed by less than complete seizure generalization in the dominant hemisphere—may explain the relative sparing of verbal memory function.<sup>16</sup> In this regard, the mechanism of action triggering amnesia may be the reduced cerebral metabolic rates for glucose in left temporal regions following the application of BL.<sup>17</sup>

After years of debate, the study findings of objective cognitive outcomes of some 341 patients treated at six New York City hospitals with ECT<sup>18</sup> concluded:

“BL ECT results in broader and more severe short-term cognitive effects than RUL ECT, particularly with respect to retrograde amnesia. With respect to the

AMI-SF scores, BL ECT resulted in greater retrograde amnesia than the other electrode placements and, even at the six-month time point, this effect was linearly related to the number of BL treatments administered during the acute ECT course. The average decrement in AMI-SF scores in patients treated exclusively with BL ECT was 3.4 and 2.8 times the amount of forgetting seen in the healthy comparison groups at the post-ECT and six-month time points, respectively, suggesting that the deficits were substantial. Furthermore, of a variety of treatment technique and patient characteristic variables, only receipt of BL treatment distinguished the group with marked and persistent retrograde amnesia. For decades, BL ECT represented the gold standard with respect to ECT efficacy, and the equivalence of RUL ECT was uncertain. Based on accumulating evidence that the efficacy of RUL ECT is strongly influenced by dosage relative to seizure threshold, highly effective forms of RUL ECT are available. Indeed, recent work suggests that high dosage RUL ECT delivered with an ultra-brief stimulus maintains efficacy and results in minimal retrograde amnesia even in the period

immediately following the ECT course. Consequently, there appears to be little justification for the continued first-line use of BL ECT in the treatment of major depression [Citations omitted].”<sup>18</sup>

Subsequent to its publication, this study was responsible for the production of a special issue of the *Journal of ECT*<sup>19</sup> dedicated to articles attacking and rebutting the conclusions set forth therein. Nevertheless, in a commentary, the editor of the journal concluded that although the methodological arguments that had been advanced against the paper “score[d] some hits . . . neither ‘sinks the ship.’”<sup>20</sup> He then went on to note in a separate editorial that:

“This issue of *J ECT* includes five commentaries on a recent article published by Sackeim et al. That article concludes that different forms of ECT are associated with differing and sometimes persistent cognitive deficits over the six months after ECT. The study was conducted with a prospective cohort design. The ensuing commentaries here in *J ECT* question the validity of the prospective cohort design for data ascertainment and challenge the ability to draw scientific conclusions from designs other than randomized controlled trials (RCTs). Although RCT is the “currency of the realm,” other designs such as case reports, case series, and cohort studies have their place and make their own important contribution—indeed, *J ECT* includes many of these contributions and continues to welcome investigations using designs other than RCT. *Outside of the ECT field, I am reminded that a causal link between cigarette smoking and lung cancer has never been established in humans with an RCT, yet this is now accepted by the medical community as a fact [Emphasis added].*”<sup>21</sup>

As such, on the basis of ethical considerations, the time for performing a double-blind study of the effects of BL and RUL on a chronic pain population may have come and gone.

Supplementing RUL, McDaniel et al.<sup>22</sup> found that the use of ketamine, an N-methyl-D-aspartate (NMDA) antagonist dissociative anesthetic—administered as an anesthetic immediately before seizures—appears to offer significant protection against short-term memory loss as measured two to three days after treatment, following the clearance of the anesthesia from the patient’s system:

“Alterations in hippocampal morphology were noted in the brains of animals

that had undergone electrically-induced seizures. After such treatment, mammalian brains consistently show thickening of the mossy-cell layer, with both hyperplasia and increased dendrification. The same thing is found in mammalian brains after seizures induced by injection of kainic acid, probably an adequate proof that this reaction is not specific to electrical stimulation. This mossy-cell layer thickening has been shown to be dependent on the release of brain-derived neurotrophic factor and to be blocked by the NMDA receptor antagonist, ketamine. Other NMDA antagonists have not been examined regarding this activity. Given the importance of the hippocampus in memory acquisition, it is likely that hippocampal mossy-cell layer thickening is a marker for the process responsible for memory loss during ECT.”<sup>22</sup>

“The mechanism by which memory performance is decreased by seizures and by ECT is still poorly understood. What is known, however, revolves around glutamatergic systems. It was noted that, after seizures provoked by N-methyl-D-aspartate injection, there is cell death and that this can be attributed to excitotoxicity mediated by NMDA receptor activity. Subsequently, kainic acid, hypoxia, and electrically-stimulated seizures were shown to cause a similar reaction. NMDA receptor antagonists, including ketamine, amantadine, and memantine, have been thought to diminish excitotoxic effects, although only ketamine has been clearly shown to have this effect. It may be that glutamate-mediated excitotoxicity is responsible for the decrement in memory after ECT. The effect we have shown of ketamine diminishing memory loss during ECT suggests that either excitotoxicity or another glutamatergic effect at NMDA receptors mediates the effect of ECT on patients’ memory function.”<sup>22</sup>

There have also been studies providing an indication that another form of ECT—in which the electrodes are placed on the forehead and referred to as “bi-(frontal) temporal” (BIF)—has no greater cognitive impairment than RUL. However, two recent studies to have made that determination also found that RUL was as effective in the treatment of depression and, as significantly, made the determination of equivalent level of cognitive impairments based primarily upon the Mini-Mental State Examination (MMSE).<sup>23,24</sup> Indeed, one of the studies explicitly

acknowledged that the “MMSE grossly accesses global cognitive status, and not the central cognitive effects of ECT, particularly retrograde amnesia,”<sup>24</sup> while the other one included an additional test for anterograde memory of verbal material, but no specific instrument for retrograde amnesia.<sup>25</sup> As such, the cognitive effects of BIF have not been as extensively explored as that of RUL.

### Mechanism of Action

The possible neurobiologic mechanisms of action include modulation of endogenous opiate systems and inhibition of frontal lobe function. Rasmussen et al. write: “As Abrams elegantly discusses, there is a virtually dizzying array of neuroreceptors, neurotransmitters, neuromodulators, and neurohormones that change in one way or another during [ECT].”<sup>7</sup> That said, while it is now known that ECT relieves pain independently of its effect on depression,<sup>7</sup> the mechanism(s) whereby ECT affects MDE is separate and distinct—even if some of the patterns of cortical reorganization in chronic pain patients mimic those of depression.

Despite a long history of use, the mechanism of action of ECT and, in particular, with regard to the treatment of CRPS-1, remains subject to conjecture. What is known are many of the physical effects of electrical stimulation ranging from changes in cerebral blood flow to, more recently, the suggestion from a primate study that it increases cellular neurogenesis in the hippocampus.<sup>25</sup> Perhaps the best single summary of the possible explanation for the effect of ECT on pain processes appears in Wolanin et al.:

“The mechanism of action of ECT is still unknown, although several observations have been made regarding the effect of ECT on pain processes. King et al. and McDaniel both postulated that massive quantities of neurotransmitters are released during ECT that induce changes in CNS post-synaptic receptors throughout the nervous system. The neurotransmitters affected include serotonin, dopamine, norepinephrine, substance P, neuropeptide Y, somatostatin, TSH, and CRH. Other neuromodulators—including enkephalin, immune-reactive dynorphin, and beta-endorphins—have also been implicated in the effects of ECT on pain. King et al. and Abdi et al. have postulated that the electrical current transmission through the thalamus and hypothalamus, which occurs

during bilateral ECT, alters pathways for pain sensation and perception. Wasan et al. suggested that disrupted affective processing of pain in CRPS leads to enhanced receptive fields, intensified pain perception, and increased pain sensory input. ECT may interrupt this inappropriate processing of pain by disrupting the memory for pain. In addition, Wasan et al. have postulated that ECT may stimulate the lateral thalamic structures involved in descending pain inhibition. Fukui et al. have studied the effect of ECT on regional cerebral blood flow. They found that patients with chronic neuropathic pain have decreased blood flow to the thalamus. After treatment with ECT, one of their patients had increased regional cerebral blood flow to the thalamus and a dramatic reduction in pain.<sup>76</sup>

Indeed, the role of amnesia in breaking up the apparent continuity of the pain experience may actually be palliative. In addition to improving the affective processing of pain, ECT may extinguish a “kindling” process at the level of disrupting the memory for pain.<sup>7,12,26</sup> In this regard, mechanism of action would parallel that hypothesized for certain calcium channel blocking drugs.<sup>27</sup> However, the specific causality that any combination of those effects may have in the alleviation of pain is subject to interpretation. That said, ECT continues to play a role in understanding aspects of CRPS and other forms of central pain and their relief in general. Indeed, this relationship may have begun with a seminal paper in 1994 on thalamocortical connectivity and dynamic reverberation which noted that ECT for chronic pain “seems well suited to stop a reverberation loop.”<sup>28</sup> Furthermore, chronic pain was soon to be described as a thalamocortical dysrhythmia, where a slow rhythm is produced by a disruption of thalamocortical feedback.<sup>29</sup>

In this sense, ECT may be considered as potentially complementing the effect of general anesthesia, which ultimately blocks the synaptic transmission of sensory information through the thalamus by diminishing the high frequency rhythms that characterize the spontaneous activity associated with consciousness.<sup>30</sup> In the case of conventional general anesthesia, it has been proposed that reduced thalamic metabolism during anesthesia could primarily reflect a drug-induced decrease in primary corticothalamic reverberant activity.<sup>30</sup> ECT, on the

other hand, presents a radically different regional cerebral blood flow (rCBF) “signature” when it is applied to both CRPS and fibromyalgia patients. In the latter population, increased thalamic blood flow is the predominantly observed change.<sup>34</sup> The closest analog is the use of the dissociative anesthetic ketamine which produces remarkably similar patterns of rCBF during the actual moment of implementation of treatment.<sup>31,32</sup>

### Relationship Between Chronic Pain and Cortical Reorganization

The relationship between chronic pain and cortical reorganization was first identified by Birbaumer et al. in the context of phantom limb pain.<sup>33</sup> After amputation, it was found that the representation of the amputation-side lip had shifted medially into the cortical region that had previously represented the now-amputated hand in persons experiencing phantom limb pain. Maihofner et al. subsequently not only found the same pattern of cortical reorganization in CRPS patients,<sup>35</sup> but also showed that it was reversible following treatment for CRPS.<sup>36</sup>

Along with reorganization of the primary somatosensory cortex (S1), contralateral to the CRPS affected side, long-lasting changes of rCBF in the contralateral thalamus of the CRPS patient have been observed with modern imaging techniques.<sup>4,36</sup> This stands in contrast, for instance, to the response of neuropathic pain patients to motor cortex stimulation where, although sustained cortical changes have been observed, thalamic activation has been described as “phasic and short lasting.”<sup>37</sup>

As set forth in the conclusion to a murine study showing a decrease in the basal activity of the thalamus following the ligation of the sciatic nerve:

“The decrease in basal activity in the thalamus is not unexpected, as thalamic dysfunction has long been thought to play a role in chronic pain. Clinical studies have reported spontaneous pain and disturbed sensations produced by thalamic lesions and several recent PET studies have demonstrated that there is reduced thalamic rCBF and/or regional glucose metabolism in patients with chronic pain... Because of the strong reciprocal thalamocortical connections, it is possible that the increased somatosensory cortical activity is directly related to the reduced thalamic activity we observed, and that these

changes represent long-term adaptive responses to the ongoing nociceptive activity associated with tissue damage. This would in general accord with the proposal of Canavero (1994) and Canavero and Bonicalzi (1998) that sensory thalamocortical axis is functionally deranged in certain chronic pain states.”<sup>38</sup>

In this regard, there is an interesting footnote from work using mirror visual feedback as an intervention for dependent cortical feedback states that were maintaining CRPS-1.<sup>39</sup> There, the authors noted that the mirror feedback technique produced dramatic relief for patients who had suffered the onset of pain within eight weeks of treatment, mixed results for those patients who had the disease for between five and twelve months, and no relief for those more chronically afflicted. This suggested, among other things, that neural pathways may become more established over time and specifically referenced Fukumoto’s finding of long-term hypoperfusion in the thalamus.

While studies on patients with MDE have focused upon a significant increase in global cerebral blood flow during ECT and a significant reduction thereafter in the frontal regions,<sup>17,31</sup> equivalent changes have been demonstrated in CRPS patients.<sup>4</sup> The apparently uniform findings concerning increases in thalamic blood flow may be a salient finding of particular significance for CRPS patients since it was established—using SPECT scans in 1999—that patients with RSD (CRPS-1) showed substantial variation in thalamic blood perfusion of the side contralateral to the painful limb. Further, this was related in time from the onset of symptoms, suggesting that the thalamus undergoes adaptive changes in the course of the disorder.<sup>40</sup> The other principally observed change to the brain was the (reversible) reorganization of the primary somatosensory cortex (S1) contralateral to the CRPS affected side.<sup>35,36</sup>

### Direction of Causality

It had been suggested that the recovery of both the thalamus and the reorganization of S1 were due to the cessation of pain, as identified in the context of the recovery of cortical reorganization following regional anesthesia by Birbaumer et al.<sup>33</sup> Fukui et al. thereafter suggested that the increase of thalamic blood flow may be the cause of relief from CRPS,<sup>4</sup> while Wu argued in 2006 that it was as a result

of the lack of pain.<sup>41</sup> However, recent work may cast some of this in doubt. Mid-ictal PET scans on patients with MDE—whose disease was characterized by, among other things, diencephalic disturbances—showed significant and immediate increases in relative rCBF in the thalamus, as well as the inferior frontal, parietal and temporal cortices, and other areas of the brain. This was followed by continued elevations of rCBF in the thalamus and decreases in other areas of the brain.<sup>31</sup> It would appear unlikely that the restoration of rCBF in the thalamus could be an adaptive response to the relief of pain, especially since general anesthetic in general is now known to suppress rCBF in the thalamus.<sup>30</sup> By definition, patients under general anesthetic are not experiencing pain. Indeed, this could instead appear to support the hypothesis of Fukui et al., namely that ECT's increase in thalamic blood flow may play a unknown causal role in the relief from CRPS.<sup>4</sup>

While it remains possible that the restoration of blood flow to the thalamus was epiphenomenal in the breaking of the thalamocortical loop, it is well established that thalamocortical oscillatory rhythms depend in part upon activity in the thalamus<sup>42,43</sup> and that virtually all areas of the cortex participate in these oscillatory rhythms, reflecting a feedback loop between neurons in the thalamus and the cortex.<sup>43,44</sup> Accordingly, it may be somewhat counterintuitive to assume that the reduction in rCBF in the cortex following the blocking of thalamic projection by ECT—a physiological change occurring over a matter of seconds in essentially one-half of a relatively large physical system—would play the sole causal role in significantly modifying patterns of thalamocortical oscillation.

Perhaps not coincidentally, ketamine has been found to cause regional metabolic increases in the human brain when given at subanesthetic doses and has one of its larger regional effects localized in the thalamus.<sup>30,45</sup> In fact, ketamine is emerging as a pharmacological therapy of choice (albeit experimental) in the treatment of CRPS.<sup>46,47</sup> More fascinating still, a very recent functional imaging study of ketamine demonstrated that it “induced a rapid, focal, and unexpected decrease in ventromedial frontal cortex, including orbitofrontal cortex and subgenual cingulate, which strongly predicted its dissociative effects and increased activity

in mid-posterior cingulate, thalamus, and temporal cortical regions.”<sup>32</sup> This result appears to be remarkably similar to the profile Takano found in his mid-ictal scans:

“Cerebral blood flow during ECT increased particularly in the basal ganglia, brain-stem, diencephalon, amygdala, vermis and the frontal, temporal and parietal cortices compared with that before ECT. The flow increased in the thalamus and decreased in the anterior cingulate and medial frontal cortex soon after ECT compared with that before ECT.”<sup>31</sup>

### Specific Considerations for CRPS Patients in ECT

In the treatment of CRPS patients, issues may arise regarding the need to either clear or reverse the effects of anti-convulsant and/or sympathetic blocking agents

immediately prior to treatment. Deep muscle pain due to intense “facilitations” (involuntary twitching of muscle fibers) is routinely prevented by administration of a muscle relaxing agent (succinylcholine) and with the administration of nonparalytic dosages of curare or atracurium. Note that the typical use of a cuff to monitor motor convulsions is not recommended for CRPS patients as they cannot tolerate even momentary compression on their affected extremities. As with any patient having severe vascular insufficiency, other techniques should be used.

Finally, benzodiazepines may raise seizure threshold and decrease seizure efficiency, while at the same time there is a risk of prolonged seizures associated with benzodiazepine withdrawal.<sup>48,49</sup> Because the time required to safely taper a patient completely off of benzodiazepines may be clinically prohibitive, some practitioners have made use of the benzodiazepine antagonist flumazenil (Romazicon®), which can be administered intravenously a minute before the induction of anesthesia, followed by a post-ictal intravenous administration of additional benzodiazepine.<sup>50,51,52</sup>

### Non-Memory Related Safety Considerations for ECT

Having performed a comprehensive review of the literature, Nuttall et al. of the Mayo Clinic recently concluded as follows:

“The rate of complications due to ECT depends on a variety of factors, such as the adequacy of the pre-ECT medical work up, the medical acuity of the population treated, intraprocedural anesthetic management during the treatments, the availability of back-up medical services in case of emergent problems and, perhaps most importantly, the definition of a “complication.” Thus, the idea of “true” morbidity and mortality rates in ECT is probably an elusive concept. Nonetheless, our large series confirms the general findings of several others that ECT is an extremely safe procedure. We found no peri-procedural mortality in 2,279 patients

*“The importance of an adequate pre-ECT work up so that potential complications can be anticipated is well known,<sup>51</sup> but what is remarkable are the low ECT mortality rates compared to anesthesia in the general population outside the tertiary medical center.”*

given 17,394 ECT treatments. The complication rate as defined was 0.9% per series (0.1% per treatment), a large portion of which was the relatively benign occurrence of prolonged seizures (all terminated promptly with diazepam). Not counting prolonged seizures, the complication rates fall to 0.6% per series and 0.08% per treatment.”<sup>53</sup>

The importance of an adequate pre-ECT work up so that potential complications can be anticipated is well known,<sup>51</sup> but what is remarkable are the low ECT mortality rates compared to anesthesia in the general population outside the tertiary medical center. By reference, the general anesthesia-related mortality rate in the United States has been stable at one death per roughly 13,000 anesthetics, or 7.7 per 100,000.<sup>54</sup> This is in marked contrast to a study in Texas—required by law since 1993 to record the deaths of all persons expiring from any cause within 14 days of an ECT treatment—which found that the statewide mortality rate associated with ECT was less than 2 per 100,000 treatments.<sup>55</sup> In addition to general mortality rates, a number of medical conditions that were hypothesized to present complications in ECT have been shown not to do so. These conditions

include severe aortic stenosis,<sup>56</sup> asthma<sup>57</sup> and long term warfarin therapy.<sup>58</sup> Indeed, it has been shown that with proper pre-ECT cardiac and pacemaker/defibrillator assessment, ECT can be safely and effectively administered to patients with an implanted cardiac device.<sup>59</sup> Finally, it should be noted that a number of large scale epidemiologic surveys have shown no evidence that ECT causes epilepsy.<sup>60,61</sup> And, perhaps not surprisingly, there is evidence indicating that ECT actually has anticonvulsant properties.<sup>62</sup>

### Alternative Technologies

In addition to ECT, two other methods of external electrical brain stimulation have been suggested for the treatment of CRPS. One that has attracted a great deal of interest is repetitive transcranial magnetic stimulation (rTMS) of the motor cortex. Unfortunately, its effects in CRPS patients appear to last only 15 minutes following the application of the stimulation,<sup>63</sup> in contrast to a study of its application in neuropathic pain, which showed a significant analgesic effect for about a week.<sup>64</sup>

Another area currently subject to research is transcranial direct current stimulation (tDCS), which is a method for selectively modulating cortical excitability, and has recently received increased interest regarding possible clinical applications. tDCS involves the application of low currents to the scalp via cathodal and anodal electrodes and has been shown to affect a range of motor, somatosensory, visual, affective, and cognitive functions. Therapeutic effects have been demonstrated in clinical trials of tDCS for a variety of conditions including tinnitus, post-stroke motor deficits, fibromyalgia, depression, epilepsy, Parkinson's disease and chronic neuropathic central pain due to traumatic spinal cord injury.<sup>65,66</sup> However, the author is not currently aware of any results published concerning its possible use in CRPS.

### Conclusion

In the light of evolving neuroscience, RUL ECT appears to be an increasingly attractive and relatively safe option for the treatment of refractory CRPS—and one that may present a relatively low risk of short term memory loss as soon as anesthetic clearance has been achieved. The study of ECT in its therapeutic role for CRPS is also yielding dividends in our understanding of brain physiology, rCBF, and CRPS pathology. ■

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*Franklin Michaels, Jr. holds a J.D. and is an inactive member of the State Bar of California, and has had bilateral lower extremity CRPS since 2001.*

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