Chronic Pain With Beneficial Response to Electroconvulsive Therapy and Regional Cerebral Blood Flow Changes Assessed by Single Photon Emission Computed Tomography

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Background: Recent neuroimaging studies suggested that chronic neuropathic pain may be largely sustained by a complex neuronal network involving the thalamus. Although recent studies have demonstrated the efficacy of electroconvulsive therapy (ECT) in the treatment of a variety of types of chronic neuropathic pain, the effects of ECT on regional cerebral blood flow (rCBF) have not been studied.

Objectives and Methods: We present a 50-year-old female postsurgical chronic pain patient whose pain had failed to respond to standard pain treatment, but was resolved by ECT. To investigate the potential role of rCBF in ECT's analgesic effect, we measured significant changes in the rCBF in the thalamus before and after a course of bilateral ECT using technetium-99m ethyl cysteinate dimer (99mTc-ECD) single photon emission computed tomography (SPECT).

Results: 99mTc-ECD SPECT showed a significant bilateral decrease in the thalamus on the side of the pain, and this decreased rCBF in the thalamus increased after ECT.

Conclusions: The results from the SPECT suggest that ECT increases abnormally decreased thalamus activity in chronic neuropathic pain. *Reg Anesth Pain Med 2002;27:211-213.*

Key Words: Chronic pain, Electroconvulsive therapy (ECT), Regional cerebral blood flow (rCBF), Single photon emission computed tomography (SPECT).

Recent studies have revealed that central mechanisms are involved in chronic neuropathic pain.[1-4] In particular, the thalamus has an important role in pain processing in chronic neuropathic pain patients.[2,5,6] Other studies demonstrate the efficacy of electroconvulsive therapy (ECT) in chronic neuropathic pain syndromes in which other standard therapies have failed.[7,8] In these clinical reports,[7,8] the effects of ECT on regional cerebral blood flow (rCBF) were not studied. We present a chronic postsurgical pain patient who had failed to respond to standard treatment, but responded to a course of ECT treatment. To examine one of the mechanisms of the analgesic effect of ECT, we measured significant changes in the CBF of the thalamus using technetium-99m ethyl cysteinate dimer single photon emission computed tomography (99mTc-ECD SPECT),[9] before and after ECT.

Case Report

A 50-year-old women underwent left lobe liver resection for an intrahepatic bile duct sclerosing cholangitis 5 years earlier. After surgery, she developed severe right-sided neuropathic pain at the incision. Visual analog scale (VAS) levels of pre-ECT pain severity were rated between 4 and 9 (0, no pain; 10, maximal pain). The pain had stabbing and dull qualities, and was resistant to standard analgesics, including antiepileptics, antidepressants, nerve blocks, and cognitive behavioral therapy. She was dependent upon opioids, which produced minimal

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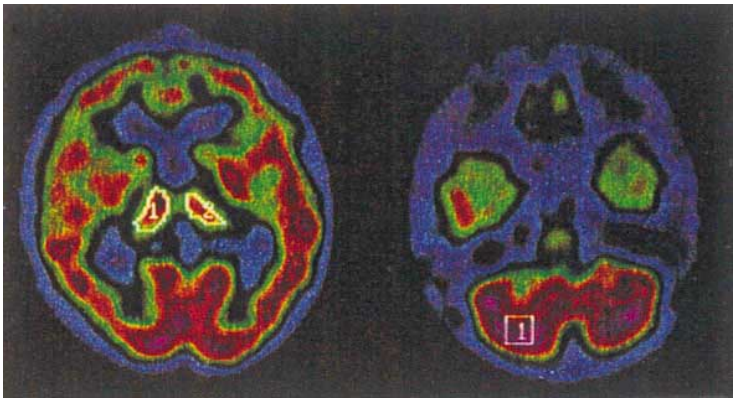

Fig 1. SPECT scan transverse section for rCBF measurement. We measured the rCBF of the thalamus before and after ECT using a 99m Tc-ECD SPECT scan at the level of the basal ganglia, which is parallel to the OM line 5 cm above OM line. ROI template placed on the thalamus and cerebellum on the selected transaxial SPECT image.

analgesia. She was referred to our pain clinic for bilateral ECT treatment for the persistent pain. The patient was informed about the treatment protocol (which was approved by the Hospital's Ethics Committee), and about the possible benefits and side effects of ECT. Informed oral and written consent was obtained before ECT.

At the time of ECT, she was receiving 16 mg of buprenorphine per day. The ECT was conducted twice a week over 4 weeks, bilaterally, using a Thymotron DGX (Somatics, Inc, Lake Bluff, IL). Seizure adequacy was assured with electroencephalogram (EEG) monitoring and by monitoring isolated limb seizures. Hypnosis was induced with a bolus injection of thiopental (2 to 3 mg/kg), and muscle relaxation was achieved by intravenous (IV) succinylcholine (1 to 1.5 mg/kg) administered before the ECT procedure. Ventilation was assisted using a face mask with 100% oxygen, and nicardipin (0.5 to 1 mg) was injected to attenuate acute cardiovascular side effects.

There was a progressive lessening of pain over the course of ECT treatment. A course of 8 bilateral ECT treatments resulted in a dramatic reduction in pain. VAS levels of post-ECT pain severity were rated 1-2. She was able to stop her opioid and other medication for pain treatment, except flunitrazepam (2 mg), which was used to help her sleep. ECT improved her mental state and daily activities. She was able to enjoy life in general, and hobbies, such as swimming and traveling abroad. Temporary retrograde and anterograde memory impairments were observed transiently, but recovered within a month. The patient reported complete pain relief 6 months after the treatment.

To investigate one of the possible mechanisms of ECT in relieving chronic pain, we assessed changes in rCBF of the thalamus using 99mTc-ECD SPECT before and 7 days after ECT (Fig 1).

Image acquisition started 20 to 60 minutes after 600 MBq (20 mCi) ^{99}mTc ECD injection. Then, 30-minute cerebral SPECT scanning was performed with a triple-detector device (Toshiba GCA9300A/HG, Tokyo, Japan) equipped with ultra-high-resolution fan beam collimators. SPECT images (128 × 128 matrices: 5-mm slice thickness) were reconstructed from projection data by a filtered back projection technique.[9] SPECT measurements were estimated by a computer (GMS5500/UI UNIX system, Tokyo, Japan) connected to the SPECT device. Transaxial SPECT slice images were taken from the orbito-medial (OM) plane. For visual analysis, perfusion abnormalities revealed by SPECT were independently analyzed by a physician experienced in nuclear medicine. For quantitative SPECT analysis, one transaxial brain slice was selected for the analysis of the thalamus at the level of the basal ganglia, which is parallel and approximately 5 cm above the OM line. Regions of interest (ROI) were marked over the thalamus and cerebellum on the selected transaxial SPECT images (Fig 1). ROI were marked over both thalami. The rCBF values for each ROI were then calculated using the average number of counts. To quantify regional ECD uptake, the mean counts in each selected region were normalized with respect to the mean counts in the cerebellum (region-to-cerebellum ratio [R/CE]). Thus, scintigraphic abnormalities in the thalamus were evaluated both visually, by radiologists, and by the R/CE. For quantitative SPECT analysis, we measured the thalamus-to-cerebellum ratio as the ratio of cerebellum to thalamus uptake.[9]

Visual examination of the brain SPECT scans by the radiologists showed a significant bilateral decrease in the thalamus and decreased rCBF in the thalamus normalized after ECT. Before ECT, the left and right thalamus-to-cerebellum ratios were 73.0% and 75.2%, respectively. After ECT, SPECT revealed that the left and right thalamus-to-cerebellum ratios elevated to 80.5% and 80.5% when the pain subsided. The left and right thalamus-to-

cerebellum ratios after ECT increased 11.3% and 11.0% compared with the ratios from before ECT.

Discussion

Our case again suggests that chronic pain patients who are resistant to multiple analgesics may respond to ECT. Although the mechanism of the analgesic action of ECT is unclear, recent reports suggested the following potential mechanisms for ECT's analgesic action: (1) ECT improves the emotional component in chronic pain patients and the mental state could affect the pain threshold[10]; (2) ECT may block a pathologic localized corticothalamic reverberatory loop involved in maintaining chronic neuropathic pain[11]; (3) ECT may activate inhibitory pathways via activation of serotonergic, noradrenergic, and dopamine neurotransmission systems in the brain[12]; (4) ECT may inhibit long-term potentiation (LTP), which is involved in a form of synaptic plasticity and pain memory[13]; and similar to *N*-methyl-D-aspartic acid receptor antagonists, ECT may inhibit this "wind-up"; (5) from our brain-SPECT data, it is speculated that ECT increases abnormally decreased thalamus activity in chronic pain patients.

We observed decreased rCBF in the thalamus before ECT, which is in agreement with previous reports on chronic neuropathic pain.[2,3] However, the reduction in the rCBF in the thalamus was seen bilaterally, contrary to previous reports, which suggested that there was decreased thalamic activity only contralateral to the symptomatic side.[2,5] The presence of the bilateral spinothalamic and spinoreticular tract fibers[14] and differential pain pathways (varying amounts of ipsilateral corticospinal projections) may be due to a reduction in the rCBF in the thalamus bilateral on the affected side.

In our case, ECT alleviated postsurgical chronic neuropathic pain, which had been resistant to multiple pharmacologic trials and anesthetic interventional procedures. Although studies have demonstrated the efficacy of ECT in a variety of types of chronic neuropathic pain,[7,8] the effects of ECT on rCBF have not been studied. In our patient, rCBF in the thalamus was increased after ECT. This rCBF change may be related to the analgesic efficacy of ECT.

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