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Beneficial effects of electroconvulsive therapy on clinical features and thalamic blood flows in a CRPS type 1 patient

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Introduction

Previous neuroimaging studies have suggested that in some patients with chronic complex regional pain syndrome (CRPS) type 1, pain is largely sustained by a complex network involving the brain [1,2]. Recent reports have shown that the thalamus has an important role in pain processing of chronic CRPS [2,3].

A recent study using electroconvulsive therapy (ECT), which is usually given to patients with major depression, has shown its efficacy in CRPS patients [4]. In a previous clinical report of successful results [4], the effects of ECT on regional cerebral blood flow (rCBF) were not studied.

We present a case of CRPS type 1 whose symptoms did not respond to standard therapies, but almost completely disappeared after ECT. ECT dramatically relieved this patient's severe chronic pain and vascular abnormalities. In order to examine the analgesic effect of ECT, we measured significant changes in the rCBF of the thalamus using stable xenon-enhanced computed tomography (xenon-CT) [5] before and after ECT.

Case report

A 47-year-old man developed CRPS symptoms (ongoing pain, allodynia, vascular abnormalities, movement disorder, and trophic changes in skin and nails) after fracture of the left tibia sustained in a labor accident. He had been suffering from severe pain in the left leg for 3 years, which consisted of throbbing, aching, and a burning pain throughout. Sensory examination revealed allodynia to a light touch, and hypesthesia in the lateral aspect of the lower extremity and the instep of the foot of the left leg. There was marked atrophy of the muscle and skin of the lower extremity and nails of the foot. An X-ray showed bone atrophy of the lower extremity. Before ECT, the skin temperature on his left leg, measured using thermography, was more than 1.0°C colder (range 1.1–1.6°C) than the unaffected leg.

This pain had been resistant to standard treatments, which included lumbar epidural block, lumbar chemical sympathectomy, and various medications (anticonvulsants, intravenous lidocaine, oral mexilitine, intravenous ketamine, and antidepressants) for more than 3 years. His pre-ECT pain severity was rated 7–8 on a visual analogue scale (VAS) that ranged from 0 to 10 (0, no pain; 10, maximal pain). Medications before ECT consisted of 30 mg amytriptyline.

The patient was referred to the Pain Clinic of the Department of Anesthesiology at Shiga University of Medical Science 3 years after the event, in order to receive a course of ECT treatment for the persistent pain. The patient was informed about the treatment protocol, which was approved by the Hospital Ethical Committee, and about the possible benefits and side-effects of ECT. Informed oral and written consent was obtained before ECT. His medical history was positive for hypertension and negative for psychiatric illness. The patient was not suffering from depression at the time of ECT referral. He was unable to work or enjoy hobbies, such as fishing, owing to persistent pain.

The ECT was conducted bilaterally, twice a week over 4 weeks, using a ThymotronTM DGX (SOMATICS), and seizure adequacy was ensured with electroencephalogram (EEG) monitoring and by viewing cuffed-limb seizures. Hypnosis was induced with thyamylal (125 mg), and muscle relaxation was achieved by administering succinylcholine (1–1.5 mg·kg^{-1} IV) be-

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fore the ECT procedure. Ventilation was assisted using a facemask with 100% oxygen, and nicardipin (1 mg) was injected to attenuate any acute cardiovascular side-effects. All medication was discontinued prior to the ECT course.

A course of eight bilateral ECT treatments resulted in a dramatic reduction in pain. After the fourth ECT, the spontaneous pain in his leg disappeared almost completely. After the complete ECT treatment, the allodynia in his leg disappeared and vasculature changes in CRPS resolved completely. From 1 week to 6 months after ECT, he rated the VAS levels of his pain as 0–2/10. After ECT, the skin temperature on the affected side rose to normal and the side-to-side symmetry became less than 1.0°C and then almost diasappeared. However, numbness in the lateral aspect of the lower extremity and the instep of the foot persisted. The allodynia in the lateral aspect of the lower extremity and the instep of the foot of the left leg diasappeared. The patient obtained a very satisfactory pain-relieving effect from ECT.

After ECT treatment, the patient still had some occasional light pain, but was able to tolerate it more satisfactorily and did not require medication such as antidepressants or nerve blocks for pain treatment. Temporary retrograde and anterograde memory impairments were observed, but these recovered within a month. After recovery of his memory, the reduction in pain persisted for 5 months.

A very satisfactory pain-relieving effect from ECT persisted, but the patient reported a gradual pain recurrence in his left leg 6 months after the treatment. A sensory examination 1 year after ECT revealed that VAS levels of throbbing, aching, and burning pain throughout his left leg, and allodynia and hypesthesia in the lateral aspect of the lower extremity and the instep of the foot of the left leg had returned to the levels experienced before ECT. Furthermore, vascular abnormalities, and marked atrophy of the muscle and skin of the lower extremity and nails of the foot, and bone atrophy in his left leg had also returned to the levels reached before ECT.

To investigate the possible mechanisms of the analgesic effect of ECT, we measured changes in the rCBF of the thalamus using xenon-CT before and 7 days after a course of bilateral ECT. rCBF values were measured using the conventional protocol (a wash-in, 5 min wash-out method with 3 min inhalation of 30% xenon gas) at a transverse slice 5 cm above the orbitomeatal line from a single CT slice at the level of basal ganglia, including the thalamus [5,6] (Fig. 1). rCBF calculations were semiautomatic, and performed with Xe/CT software.

Prior to ECT, the mean rCBF values of the right and left thalamus were 78.4 and 61.1 ($ml \cdot 100\,g^{-1} \cdot min^{-1}$), respectively. Xenon-CT revealed a significantly decreased

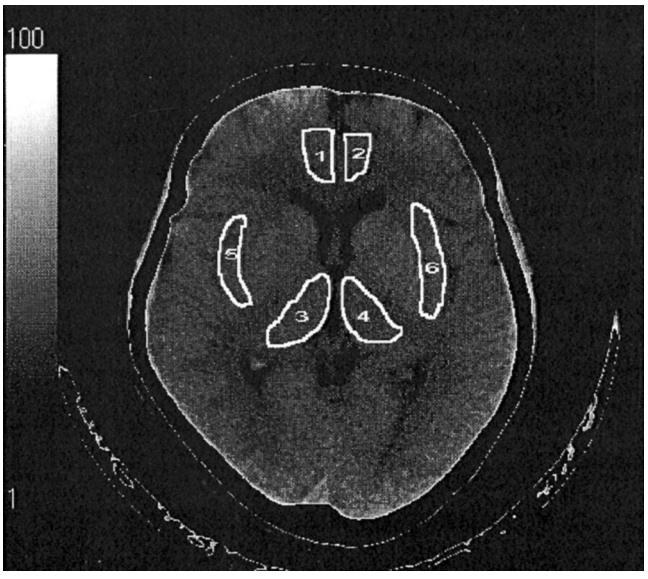

Fig. 1. Xenon-CT section for rCBF measurement 7 days after ECT. The xenon transverse CT slice was taken 5 cm above the orbitomeatal line (OM line) at the level of basal ganglia. The right (*1*) and left (*2*) subgeniculate part of the anterior cingulate cortex (Brodmann's areas 32), right (*3*) and left (*4*) thalamus, and right (*5*) and left (*6*) insula

rCBF in the thalamus ipsilateral to the side of the pain. After ECT, the mean rCBF values of the right and left thalamus were 72.3 and 70.3 ($ml \cdot 100\,g^{-1} \cdot min^{-1}$), respectively. The rCBF of the left thalamus rose and the significant right–left difference in thalamus rCBF was abolished when the pain subsided.

Discussion

Shibata et al. [7] reported a case of refractory reflex sympathetic dystrophy (CRPS type 1) whose symptoms were resolved after suffering a traumatic cerebral contusion in the left lobe. This case also suggests that the symptoms of chronic CRPS patients may largely be sustained by a complex network involving the brain. Based on a positron emission tomography (PET) study, Iadarola et al. [3] suggested that decreased thalamic activity contralateral to the symptomatic side may be a clinical feature which is common to a wide variety of chronic pain disorders. The central mechanism in the pathogenesis and maintenance of chronic neuropathic pain suggests that the brain itself may be a primary target when treating chronic CRPS. Considering our single photon emission computed tomography (SPECT) results, PHN resistance to standard therapies may involve some central mechanisms.

Although the mechanism of remission is unclear, several reports have suggested mechanisms for the analge-

sic action of ECT. (1) That ECT activates inhibitory pathways via the activation of serontonergic, noradrenergic, and dopamine neurotransmission systems in the brain [8]. (2) Electrophysiological studies showed that ECT has a deleterious effect on a form of synaptic plasticity (long-term potentiation, LTP), which is involved in pain memory, by inhibiting wind-up in a manner similar to *N*-methyl-D-aspartate (NMDA) receptor antagonists [9]. (3) An improvement in the patient's mental state with ECT may affect the pain threshold [10]. (4) ECT may block a localized pathological corticothalamic reverberatory loop that is involved in chronic neuropathic pain [11]. (5) Consistent with the findings of other brain-imaging studies [2,3], we observed a decreased rCBF in the thalamus before ECT. However, contrary to previous reports [2,3], the reduction in thalamus rCBF was seen on the ipsilateral side of the initial pain. A recent report suggested that pain projection from the spinal cord to the brain is organized in a complicated manner [12,13]. The affected thalamus might have caused differential pain pathways and varying amounts of ipsilateral corticospinal projections, which might be the reason why the reduction in thalamus rCBF in the present case was seen on the ipsilateral side of the initial pain [12,13]. It may be difficult at present to specify the brain site responsible for CRPS. From the xenon-CT data, it is suggested that normalization of the balance of rCBF in the thalamus may be attributed to the pain relief in this kind of chronic pain. Our results suggested that rCBF changes in the thalamus are related to at least past of the transient analgesic efficacy of ECT.

Compared with SPECT, xenon-CT used as a method for the measurement of rCBF offers the advantages of much higher spatial resolution, allowing a more precise flow reference, and providing quantitative information on rCBF in deeper regions of the brain. Furthermore, the values calculated by xenon-CT are quantatative, unlike SPECT, which produces only relative ratios [5,6].

Our case suggests that chronic pain in CRPS type I patients who are resistant to multiple therapies may respond to ECT. Our rCBF results using xenon-CT suggest that ECT normalizes the abnormal balance of rCBF in the thalamus in chronic CRPS.

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