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Resting-state hyperperfusion in the whole brain: A case of malignant catatonia that improved with electric convulsion therapy

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Dear Editors,

The first detailed description of catatonia dates back to the 19th century (Kahlbaum, 1874). Since then, catatonia has been recognized as one of the most severe forms among psychiatric conditions. It also causes fatal medical complications in some cases (Funayama et al., 2018; Mann et al., 1986). Therefore, understanding the mechanisms behind catatonia, which have not yet been fully elucidated, is extremely crucial. Although there have been several imaging studies that revealed abnormalities in the caudate, orbitofrontal cortex, parietal cortex, premotor cortex and motor cortex in catatonia, these results have not been consistent (Walther et al., 2017). Walther et al. (2017) suggested that this inconsistency was caused by the fact that catatonia includes several subtypes and various degrees of severity, and they also demonstrated an association between increased catatonia severity and higher perfusion in the supplementary motor area (SMA) using arterial spin labeling (ASL).

These studies were limited to cross-sectional ones and targeted only patients with mild catatonia rather than those with malignant catatonia, the severest form of catatonia, which is accompanied by autonomic instability and hyperthermia and frequently causes severe medical complications (Fink and Tayler, 2003; Mann et al., 1986). To date, however, there had been no neuroimaging study to investigate this condition. Therefore, we analyzed a patient with malignant catatonia using ASL in the period of before and after treatment.

A 61-year-old man with schizophrenia with an onset at age 20 was admitted to our hospital with a condition of psychosis and catatonic excitement, i.e., excessive and purposeless motor activities, impulsivity, frenzy and incoherent speech. At admission, his physical findings, laboratory data and head computed tomography (CT) scan were normal. Immediately after being hospitalized, his psychiatric conditions deteriorated into mutism and stupor. On the second day of his hospital stay, he developed malignant catatonia (Fink and Tayler, 2003), presenting with hyperthermia, tachycardia, muscle rigidity, and high levels of serum creatine kinase (5822 IU/L), which was treated with lorazepam (given orally, 3 mg/day). He had several medical complications, including urinary tract infection, deep vein thrombosis, megacystis and megacolon. Although his medical conditions improved with antibiotics and anticoagulant therapy, his malignant catatonia remained. Therefore, we administered electroconvulsive therapy (ECT). The score on the Bush-Francis Catatonia Rating Scale (69, worst; 0, best) (Bush et al., 1996) was 21 on the day of the first ECT session and decreased to 0 after he received 10 sessions of ECT.

We acquired whole-brain resting state cerebral blood flow (rCBF) measurements using magnetic resonance imaging (MRI) with ASL both before and 61 days after the 10 ECT sessions. ASL is the latest modality of measuring rCBF and provides an absolute measure of rCBF. This case study adhered to the declaration of Helsinki and was approved by the ethics committee of National Hospital Organization Shimofusa Psychiatric Medical Center. His family provided written informed consent as a deputy before the first MRI was conducted, and the patient provided written informed consent after treatment (before the second MRI) was conducted.

Images were acquired using a 1.5 T MR system (SIGNA Explorer, GE Medical Systems) and a 12-channel headcoil. ASL was performed using a three-dimensional spiral fast spin-echo sequence with background suppression for perfusion imaging, which covered the entire brain. The ASL sequence consisted of a three-dimensional, multi-delay pseudo-continuous ASL (PCASL), with a fast spin-echo acquisition with background suppression. The labeling plane was set at the base of the brain without information from MR angiography. The imaging protocol was as follows: repetition time (TR) = 4841 ms, echo time (TE) = 10.5 ms, locations = 36, FOV = 24 × 24 cm, voxel size = 4.08 × 4.08 × 4 mm^3, post-labeling delay (PLD) = 2.025 s, labeling duration = 1.5 s, number of excitations (NEX) = 2, acquisition time = 2 min 35 s.

MRI with ASL revealed a remarkable increase in the rCBF in the whole brain, especially in the bilateral SMA, the bilateral anterior cingulate cortex (ACC), the left insular cortex, the left amygdala, the hypothalamus and the left striatum (Fig. 1). This abnormal increase in rCBF was improved after completion of 10 sessions of ECT, and the symptoms of malignant catatonia remitted (Fig. 1).

Our results revealed that hyperperfusion was observed not only in the SMA, which was previously reported in mild catatonia (Walther et al., 2017), but also in the whole brain, particularly the ACC, insula, amygdala, hypothalamus, and striatum. The ACC, insula, amygdala, and hypothalamus are core components of the central autonomic network (CAN), which plays a prominent role in regulating the autonomic

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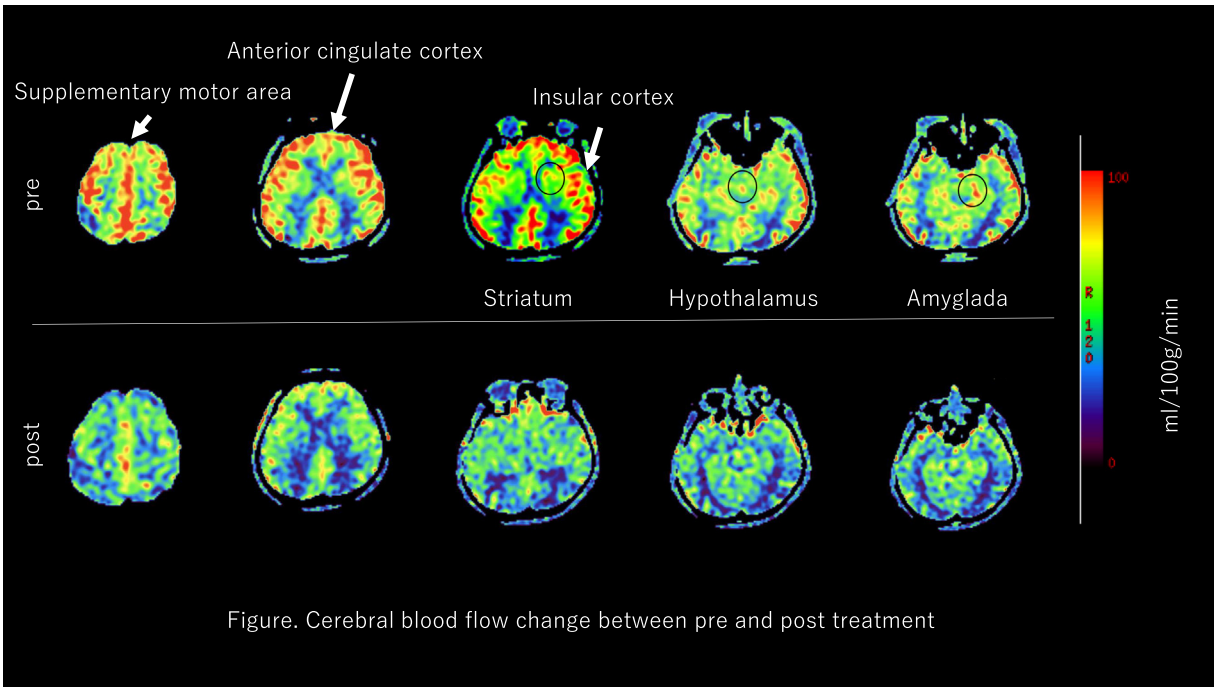

Fig. 1. Cerebral blood flow change between pre and post treatment.

nervous system (Beissner et al., 2013), and excessive activation of these areas can result in hyperactivity of the sympathetic nervous system (Beissner et al., 2013). Hyperactivity of the sympathetic nervous system is considered to be the most important feature of malignant catatonia because it can lead to various lethal complications (Funayama et al., 2018). Indeed, this patient showed various complications associated with hyperactivity of the sympathetic nervous system, such as tachycardia, hyperthermia, urinary tract infection and deep vein thrombosis (Funayama et al., 2018).

It is still unknown what caused hyperperfusion in malignant catatonia. One clue to these results may be neuroinflammatory reaction following malignant catatonia. In recent years, neuroinflammation has re-emerged as an important facet in pathophysiology of schizophrenia (Haller et al., 2014). In fact, neuroinflammation can lead to hyperperfusion and hyperexcitability in the central nervous system (Xanthos and Sandkühler, 2014). Our results that ECT improved increased rCBF in malignant catatonia support the possibility of neuroinflammation involvement because anti-inflammatory effect was regarded as one of the mechanisms of ECT (Kartalci et al., 2016).

In conclusion, in this patient with malignant catatonia, rCBF in the entire brain and particularly in regions involving the central autonomic network was markedly increased, and this abnormal rCBF was improved along with improvement of malignant catatonia. Our findings suggest that hyperactivity of the whole brain including the central autonomic network might represent the pathophysiological mechanism behind malignant catatonia, which most likely was caused by neuroinflammatory activation.

Contributors

Shin Kurose: clinical evaluation and treatment of the patient; interpretation of the data; execution of the case study; writing of the first draft and review and critique of the manuscript.

Akihiro Koreki: clinical evaluation and treatment of the patient; interpretation of the data; conception, organization, and execution of the case study; writing of the first draft and review and critique of the manuscript.

Michitaka Funayama: interpretation of the data; writing of the first draft and review and critique of the manuscript.

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Mitsumoto Onaya: preparation of the facilities; review and critique of the manuscript.

Masaru Mimura: supervision of the study; review and critique of the manuscript.

Competing interests

No competing interests to disclose.

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