

Usually, rTMS-induced seizures start from a contralateral partial seizure and transfer to a secondary generalized seizure.³ Thus, contralateral evoked motor activity, such as right thumb twitch during rTMS, might indicate the onset of generalized convulsions. Here we report a case of sudden thumb twitch during rTMS for the treatment of medication-resistant depression after a usual dose (200 mg) of caffeine intake. Written informed consent was obtained from the patient for publication of this report.

A 48-year-old Asian woman with a 9-year history of major depressive disorder was admitted to our hospital. She had experienced four episodes of depression. In the current episode, antidepressants and augmentation therapies had had little effects on her depressive symptoms. She did not have a prior history of convulsion, neurologic disorder, or alcohol dependence. Laboratory test results were in the normal range. There were no abnormal findings in head magnetic resonance imaging or electroencephalogram. She was taking the following medications: mirtazapine 45 mg, diazepam 2 mg, and brotizolam 0.25 mg during rTMS. Her Hamilton Rating Scale for Depression 21-item (HAM-D 21) score was 23 at baseline.

The rTMS was administered at 120% resting motor threshold (MT) with 10 Hz, a 4-s stimulation time, a 26-s interstimulation interval, and 3000 pulses/day over the left PFC using a NeuroStar TMS system (Neuronetics, Inc., Malvern, PA, USA). A total of 30 sessions were delivered over about 6 consecutive weeks. We determined the resting MT (1.40 standard MT [SMT]) and the stimulation site (5.5 cm anterior to the MT location) according to the standard protocol of a NeuroStar TMS system.

After the initiation of the treatment, there were no adverse events except for minor scalp pain. However, when we started the 29th treatment session, her right thumb started to twitch consistently with the timing of stimulation. We interrupted stimulation immediately and at the same time, her thumb twitch disappeared. Two psychiatrists confirmed that the treatment parameters and position were the same as we had determined previously. There were no abnormalities in general neurologic or mental status examination. We found that she had had two cups of coffee 4 h earlier as well as an energy drink containing caffeine 2 h before the treatment (total caffeine intake was about 200 mg). She did not usually drink such caffeine. The resting MT and the treatment position were determined again on the following day, but they were almost the same as previously (1.36 SMT). She received the rest of the treatment sessions and there were no side-effects, including thumb twitch and seizure. Her HAM-D 21 score decreased from 23 to 10 after 30 treatment sessions.

We experienced the first case of sudden thumb twitch during rTMS over the left PFC after taking the usual dose of caffeine. Our patient had had a sufficient quality sleep and had taken her medications properly. To the best of our knowledge, she had no risk factors of lowering MT except for caffeine intake.

In the previous small sample study using single-pulse TMS,⁴ caffeine intake (200 mg, 400 mg) did not change the cortical threshold significantly. However, more than 90% of caffeine is metabolized by the enzyme cytochrome P450 1A2 whose activity is largely different among individuals.⁵ Therefore, it could be possible that 200 mg of caffeine could change MT substantially in specific populations. The limitations are that we did not measure resting MT immediately after the event and did not examine her genetic factors related to caffeine metabolism.

The findings suggest that caffeine is a potential risk factor of lowering MT and increasing the possibility of seizure during rTMS. Clinicians should evaluate daily caffeine intake before rTMS and redetermine MT when unusual events occur. A further study of how caffeine has an effect on MT during rTMS needs to be conducted.

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Disclosure statement

Dr Yamazaki reports personal fees from Inter-Riha, outside the submitted work; Dr Kito reports grants and personal fees from Century Medical,

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Intermittent psychotic symptoms in an adult with history of neonatal parasagittal injury: A case report

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Neonatal hypoxic ischemic encephalopathy is a brain injury caused by oxygen deprivation due to perinatal asphyxia and is a leading cause of neonatal mortality and chronic neurological disability. Parasagittal cerebral injury (PCI) is a relatively mild form of hypoxic ischemic encephalopathy involving intravascular watershed zones of three major vessels.¹ PCI symptoms are usually subtle and sometimes PCI is asymptomatic; however, the long-term outcomes of the disorder are unclear. Presently, reports are lacking on the relation between PCI and psychotic diseases.² Here, we report the case of an adult who developed schizophrenia-like psychotic symptoms of epilepsy with the seizure focus on the PCI scar. The patient's consent was obtained for reporting her case.

A 33-year-old Japanese woman with suspected schizophrenia was referred to our hospital. Her intrapartum course had been normal, and her newborn's Apgar scores had been 7 and 8 at 1 and 5 min, respectively.

The patient's early development had been typical. At the age of 10 years, she had experienced a tonic-clonic seizure episode, and magnetic resonance imaging (MRI) had identified a PCI from the parietal to the occipital lobe. She was diagnosed with multifocal epilepsy resulting from her PCI re-divided scars. Since then, she had received carbamazepine and had not experienced further seizures. At the age of 32 years, her carbamazepine dose had been reduced and replaced with lamotrigine (100 mg/day) to accommodate her desire for childbearing as carbamazepine has a relatively high risk of fetal malformation. Six months later, she had developed delusions of persecution, auditory hallucinations criticizing her behaviors, and elemental visual hallucinations.

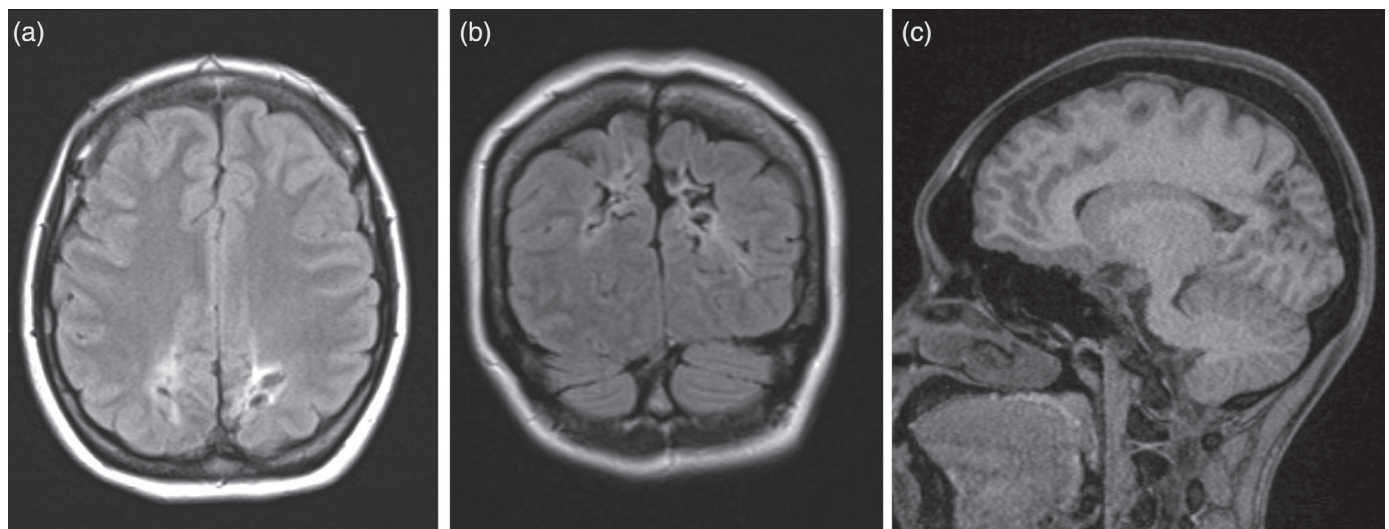


Fig.1 Magnetic resonance imaging (MRI) shows an atrophic scar bilaterally on the occipital and parietal lobes, corresponding to the watershed zone of the anterior, middle, and posterior cerebral arteries. (a,b) Fluid-attenuated inversion recovery MRI. (c) Magnetization-prepared rapid acquisition gradient-echo MRI.

Contrary to her medical history, when she first visited our hospital she showed no psychotic symptoms or negative symptoms (e.g., reduced motivation, emotional flattening, or disruptive thoughts). She also had no symptoms or history of depression or mania. However, according to family observation, she intermittently developed consciousness impairment, automatism, and psychotic symptoms at home. No abnormalities were found in the physical examination or laboratory test results, including in her thyroid function, and she was not pregnant. Her electroencephalography (EEG) showed multifocal spikes and slow waves mainly focused in the occipital and parietal lobes. Her MRI scans revealed ‘mushroom gyri,’ a region of brain atrophy mainly involving the deeper portions of the gyri, but not the gyrus surfaces, and located in the watershed areas of the anterior, middle, and posterior cerebral arteries.³ Given these MRI findings and a lack of other plausible pathologies, the patient was diagnosed with PCI (Fig. 1). We suspected that the patient’s psychotic symptoms were secondary, caused by symptomatic localization-related epilepsy. Accordingly, we prioritized treatment for epilepsy rather than for psychosis and gradually increased the dose of lamotrigine up to 300 mg (trough blood concentration, 4.1 µg/mL). During the course, her psychotic symptoms and automatism gradually disappeared without the prescription of antipsychotics. Currently, the patient has been in remission for 2 years.

This is the first report of a patient with epilepsy due to PCI who developed intermittent psychotic symptoms in adulthood. PCI affects full-term infants and sometimes newborns with PCI have normal perinatal stages and normal Apgar scores.⁴ Thus, early PCI diagnosis is difficult without MRI and is often overlooked. Notably, brain abnormalities in this case had first been detected at the age of 10 years.

Although our patient developed psychotic symptoms in adulthood and was initially suspected to have schizophrenia, she had developed intermittent psychosis and elemental visual hallucination following withdrawal of carbamazepine. MRI and EEG findings led to the suspicion of secondary psychotic symptoms due to epilepsy. Specifically, we speculate that focal impaired-awareness seizures accompanied by consciousness impairment and automatism, with the focus site on the PCI scar, resulted in postictal psychosis. Her good responsiveness to antiepileptic drug treatment, that is lamotrigine, without concomitant use of antipsychotics supports this diagnosis.

Several lines of evidence suggest that delivery complications related to hypoxic–ischemic events are associated with later development of various neurological/psychiatric conditions, such as schizophrenia.^{5,6} Our patient had no apparent neonatal asphyxia, but at the age of 10 years MRI had revealed that she had sustained a PCI during the perinatal period that

had caused EEG abnormalities and symptomatic localization-related epilepsy as well as later development of psychotic symptoms in adulthood. This case suggests the need for careful long-term follow-up of patients with PCI, even if they display no major symptoms in the short term. We also emphasize that the first diagnosis of psychosis requires obtaining detailed medical history, especially for obstetric complications, as well as EEG and MRI findings to consider the possibility of latent cerebrovascular disorder and presumed perinatal ischemic stroke, such as PCI.

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Disclosure statement

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