Clinical Neurophysiology 130 (2019) 1499–1501

Contents lists available at ScienceDirect

Clinical Neurophysiology

journal homepage: www.elsevier.com/locate/clinph

Letter to the Editor

Is decremental modulation index on scalp EEG a sign of good seizure outcome? A Sturge-Weber syndrome case with epileptic spasms

Modulation index (MI) reflects the degree of pathological and physiological phase-amplitude couplings between high frequency oscillations (HFOs) and slow waves in electrocorticography (Canolty et al., 2006). Epileptic spasms (ES) are characterized by brief and sudden flexion, extension, or mixed movements, lasting for 0.3–2 s. The International League Against Epilepsy's 2017 classification of seizure types categorizes ES into focal, generalized, or unknown onset. Children with ES had high values of MI (HFOs & 3–4 Hz) in the intracranial video EEG (Iimura et al., 2018). We explored the MI of interictal epileptic discharges on scalp EEG of a patient with ES secondary to a posterior quadrant leptomeningeal capillary malformation (LCM) of Sturge-Weber syndrome (SWS), who underwent two-staged surgery. We tested the hypothesis that decremental MI on scalp EEG could predict good seizure outcome in this patient with SWS and ES.

We investigated a 7-year-old girl with SWS of the right posterior LCM. Her ES started when she was 8 months old and ES frequency developed to 20 times per day, refractory to carbamazepine, topiramate, and levetiracetam. Interictal scalp EEG at the age of 4 years showed left posterior predominant bilateral spike and slow waves (Fig. 1, left top). At the age of 5 years, we performed posterior corpus callosotomy. The interictal EEG subsequently showed only right hemispheric spike and slow waves (Fig. 1, left middle). Her ES frequency decreased to 1–2 times per day. At the age of 5.3 years, we performed right posterior quadrantectomy (PQT) (Sugano et al., 2014). She was seizure free at 2-years follow-up on levetiracetam (Fig. 1, left bottom).

We recorded scalp video EEG using NeuroFax (Nihon-Koden, Tokyo, Japan) at a sampling rate of 500 Hz according to the international 10–20 electrode system, with T1 and T2 electrodes. MI was automatically calculated at each electrode using EEGLAB Toolbox PACTv.0.17 as described previously (Iimura et al., 2017). We analyzed the MI of between gamma rhythm (30–70 Hz) with four delta slow bands (0.5–1 Hz; 1–2 Hz; 2–3 Hz; 3–4 Hz) using five 5-min periods of interictal EEG during non-REM sleep. We divided all electrodes into four areas: (1) left anterior quadrant, Fp1;F3;F7;T1 (2) left posterior quadrant, T3;T5;P3;O1 (3) right anterior quadrant, Fp2;F4;F8;T2 (4) right posterior quadrant, T4;T6;P4;O2. We excluded C3 and C4, because they were used for reference. We calculated the MI for 3 periods: before callosotomy, after callosotomy, and after PQT.

All statistical analyses were performed using SPSS Statistics 25 (IBM Corp, Chuo-ku, Tokyo, Japan). We performed a Mann-Whitney U test and Steel-Dwass test after testing for data normality using the F test. Statistical significance was set as $p < 0.05$. Written informed consent was obtained from her parents. This study was approved by the ethics committee of Juntendo University (No. 16-163).

Before callosotomy, the average MIs of gamma with 4 delta bands (0.5–1 Hz, 1–2 Hz, 2–3 Hz, 3–4 Hz) in the right posterior quadrant (3.28, 4.41, 4.44, 4.51, respectively) were significantly higher than those in the anterior quadrant (1.96, 2.37, 1.78, 2.48) ($p < 0.01$). MIs of gamma with 2 delta bands (2–3 Hz, 3–4 Hz) in the left posterior quadrant (3.96, 6.49) were significantly higher than those in the anterior quadrant (2.61, 3) ($p < 0.01$). The MI of gamma with 3–4 Hz in the left posterior quadrant was significantly higher than that in the right posterior quadrant ($p = 0.02$). The highest MI of gamma with 3–4 Hz was located in the left posterior quadrant among the four areas ($p < 0.01$).

After callosotomy, all MIs in all areas decreased. The average MIs of gamma with 4 delta bands in the right posterior quadrant (1.4, 1.48, 1.52, 1.74) were significantly higher than those in the right anterior quadrant (0.67, 0.68, 0.59, 0.55) ($p < 0.01$). MIs of gamma with 3 delta bands (1–2 Hz, 2–3 Hz, 3–4 Hz) in the right posterior quadrant (1.48, 1.52, 1.74) were significantly higher than those (0.74, 0.73, 0.76) in the left posterior quadrant ($p < 0.01$). The highest MI of gamma with 3–4 Hz was located in the right posterior quadrant among the four areas ($p < 0.01$). After right PQT, all MIs of gamma with the 4 delta bands were in all areas <0.84. (Fig. 1, right)

We report the case of a 7-year-old girl with SWS and ES secondary to a right posterior LCM. After callosotomy, ES was less frequent. MI became highest in the right posterior quadrant corresponding with the interictal epileptiform discharges and the location of LCM. MIs in the other areas decreased. After PQT, all MIs of gamma with all 4 delta bands in all areas decreased along with seizure freedom and no interictal discharges.

The resection of the higher MIs (200–300 Hz & 3–4 Hz) on the intracranial EEG correlated with good seizure outcome in children with ES (Iimura et al., 2018). The high values of MI (200–300 Hz & 3–4 Hz) represented the epileptogenicity in drug-resistant ES. In this case, they were consistent with decremental MIs of gamma with 3–4 Hz in the left and right posterior quadrants after callosotomy and PQT, respectively. The decremental MI could indicate the success of posterior callosotomy and PQT for treatment of ES secondary to a posterior quadrant LCM.

Total corpus callosotomy (TCC) has been performed during initial diagnosis to lateralize and localize the epileptogenic hemisphere and foci for West syndrome patients with drug-resistant infantile spasms (Baba et al., 2018). After TCC, scalp EEG revealed no abnormalities in 6 (10.7%) without spasms, lateralized abnormalities in 19 (33.9%), and bilateral abnormalities in 31 (55.4%) of 56 patients. Fifteen of the 19 patients with lateralized EEG abnormalities achieved seizure freedom after further resective/disconnective surgeries. In our case, the highest MI and interictal

https://doi.org/10.1016/j.clinph.2019.06.002

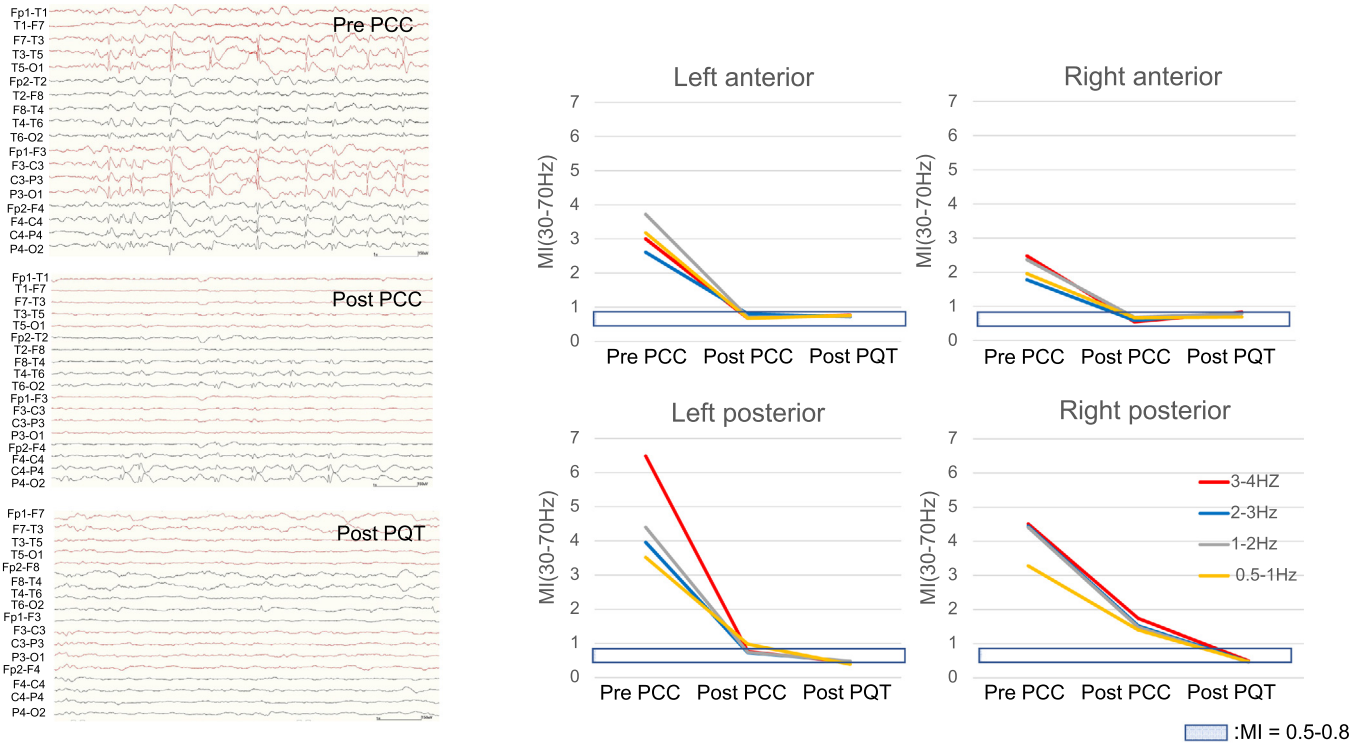

Fig. 1. (Left top) Interictal scalp EEG at the age of 4 years shows left posterior predominant bilateral spike and slow waves. (Left middle) After posterior corpus callosotomy (PCC), at the age of 5 years, the interictal scalp EEG subsequently shows only right hemispheric spike and slow waves. (Left bottom) After posterior quadrantectomy (PQT), at the age of 5.3 years, the patient became seizure free on levetiracetam at 2-years follow-up and showed a normal EEG. (Right) Before PCC, MIs of all 4 delta bands in the right posterior quadrant were significantly higher than those in the right anterior quadrant ($p < 0.01$). MI of gamma with 3–4 Hz in the left posterior quadrant was significantly higher than that in the right posterior quadrant ($p = 0.02$). The highest MI of gamma with 3–4 Hz was located in the left posterior quadrant ($p < 0.01$). After PCC, the MIs of gamma with all 4 delta bands in the right posterior quadrant were significantly higher than those in the right anterior posterior quadrant ($p < 0.01$). The highest MI of gamma with 3–4 Hz was located in the right posterior quadrant ($p < 0.01$). After PQT, MIs of gamma with all 4 delta bands decreased in all areas below 0.84.

EEG abnormalities shifted from contralateral to ipsilateral posterior quadrant and decreased after callosotomy. Although MI itself could not detect the epileptogenicity on the scalp EEG in this SWS patient with ES, MI clarified the dynamic changes of interictal EEG abnormalities by disconnection of corpus callosum.

In patients with SWS, interictal epileptiform discharges originate from the contralateral hemisphere. The mechanism of this apparently paradoxical EEG abnormality might be occupation of the brain surface by the LCM to obscure epileptiform discharge projections onto the scalp electrodes. The contralateral highest MI and epileptiform discharges on EEG might correlate with the paradoxical EEG change. We are recruiting further patients with ES, who require callosotomy, to investigate the predictive value of MI for treatment efficacy.

Acknowledgements

This research was supported by Japanese Science and Technology, CREST (JPMJCR 1784) and KAKENHI (18H06264).

Declaration of Competing Interest

The authors have no financial interest or conflict of interest to declare.

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Yasushi Iimura *
Department of Neurosurgery, Epilepsy Center, Juntendo University, Tokyo, Japan
* Corresponding author at: Department of Neurosurgery, Epilepsy Center, Juntendo University, 2-1-1, Hongo, Bunkyo-ku, Tokyo 113-8421, Japan. Fax: +81 3 5689 8343.
E-mail address: yasuyasu0104@gmail.com

Hidenori Sugano
Department of Neurosurgery, Epilepsy Center, Juntendo University, Tokyo, Japan

Madoka Nakajima
Department of Neurosurgery, Epilepsy Center, Juntendo University, Tokyo, Japan

Takuma Higo
Department of Neurosurgery, Epilepsy Center, Juntendo University, Tokyo, Japan

Hiroharu Suzuki
Department of Neurosurgery, Epilepsy Center, Juntendo University, Tokyo, Japan
Division of Neurology, The Hospital for Sick Children, Toronto, Canada

Takumi Mitsuhashi
Department of Neurosurgery, Epilepsy Center, Juntendo University, Tokyo, Japan

Tetsuya Ueda
Department of Neurosurgery, Epilepsy Center, Juntendo University, Tokyo, Japan

Kostadin Karagiozov
Department of Neurosurgery, Epilepsy Center, Juntendo University, Tokyo, Japan

Ayuko Igarashi
Department of Pediatrics, Epilepsy Center, Juntendo University, Tokyo, Japan

Hiroshi Otsubo
Division of Neurology, The Hospital for Sick Children, Toronto, Canada

Hajime Arai
Department of Neurosurgery, Epilepsy Center, Juntendo University, Tokyo, Japan

Available online 22 June 2019