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Letter to the editor

Perampanel improved intractable myoclonus in two patients with myoclonus epilepsy

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Perampanel (PER) is a specific antagonist of the α-amino-3-hydroxy-5-methyl-4- isoxazolepropionic acid (AMPA) receptor, used to treat epilepsy [1], and its efficacy has been demonstrated in drug-resistant cortical myoclonus [2–8]. We describe two patients with myoclonus epilepsy whose intractable myoclonus was improved by low dose PER.

1. Case report

Patient 1. A 19-year-old woman presented with drug-resistant myoclonus that had persisted for 18 years. Her birth was uneventful. A febrile seizure occurred at 9 months of age, followed by a non-febrile seizure 5 months later. She was given a diagnosis of epilepsy based on electroencephalographic abnormalities, and was administered with valproic acid (VPA). At the same time, she was pointed out to have tremulous myoclonus of extremities diagnosed by surface electromyography (SEMG) findings of 100-msec muscle discharges that were synchronized between antagonistic muscles. Stimulating the median nerve for somatosensory evoked potentials (SEP) showed normal amplitude. Seizures were controlled by VPA (200) mg and levetiracetam (2000 mg) but the myoclonus persisted. At the time of presentation, she had facial tics, myoclonus of all limbs, chorea of the fingers, and limb ataxia. Adding clonazepam (CZP; 1 mg) somewhat relieved the myoclonus (Video S1). SMEG showed synchronization between the left extensor carpi radialis and left flexor carpi ulnaris muscles with a duration of 100–150 msec (Fig. 1A). She was initially started on PER (2 mg/day), then the dose was increased to 4 mg/day two months later, and this much improved the myoclonus (Video S2).

Patient 2. A 41-year-old man who was diagnosed with progressive myoclonus epilepsy at the age of 16 years, had intractable positive and negative myoclonus and ataxia in extremities. His daily medications included VPA (800 mg), zonisamide (300 mg), CZP (6 mg) and piracetam (15 g). SEP latencies of N20, P25 and N33 were 23.5 ms, 29.9 ms, and 44.7 ms. Amplitudes of N20-P25 and P25-N33 were 45.8 μV and 43.3 μV (giant SEP; Fig. 1B, left) before PER administration. After administration of PER (4 mg), the positive myoclonus diminished. SEP latencies were prolonger (N20; 23.2 ms, P25;29.4 ms, N33: 45.8 ms), and the giant SEP was diminished (N20-P25; 20.7 μV and P25-N33;16.4 μV) (Fig. 1B, right).

2. Discussion

Low doses of PER (2–6 mg/day) are effective against intractable myoclonus in patients with Lance-Adams syndrome, Unverricht-Lundborg disease (ULD), postsurgical cortical myoclonus and Lafora disease [2–8]. Oi et al. [8] reported decreased of giant SEP amplitude and prolonged latencies (P25 and N33), and the correlation with the degree of ADL improvement and PER concentration for patients with refractory cortical myoclonus after PEM administration. The generator of P25 and N33 arise from the crown of the postcentral gyrus, and P25 was partly located in the motor and sensory areas. In the patient 2, the improvement of myoclonus and the reduction in the SEP expansion amplitude after PEM administration were presumed to be due to the suppression of abnormal cortical hyperexcitability in the primary sensorimotor cortex.

Myoclonus originating in the cortex can be associated with various epilepsy syndromes, but it could also be a subcortical phenomenon associated with post-hypoxic brain damage as in Lance–Adams syn-

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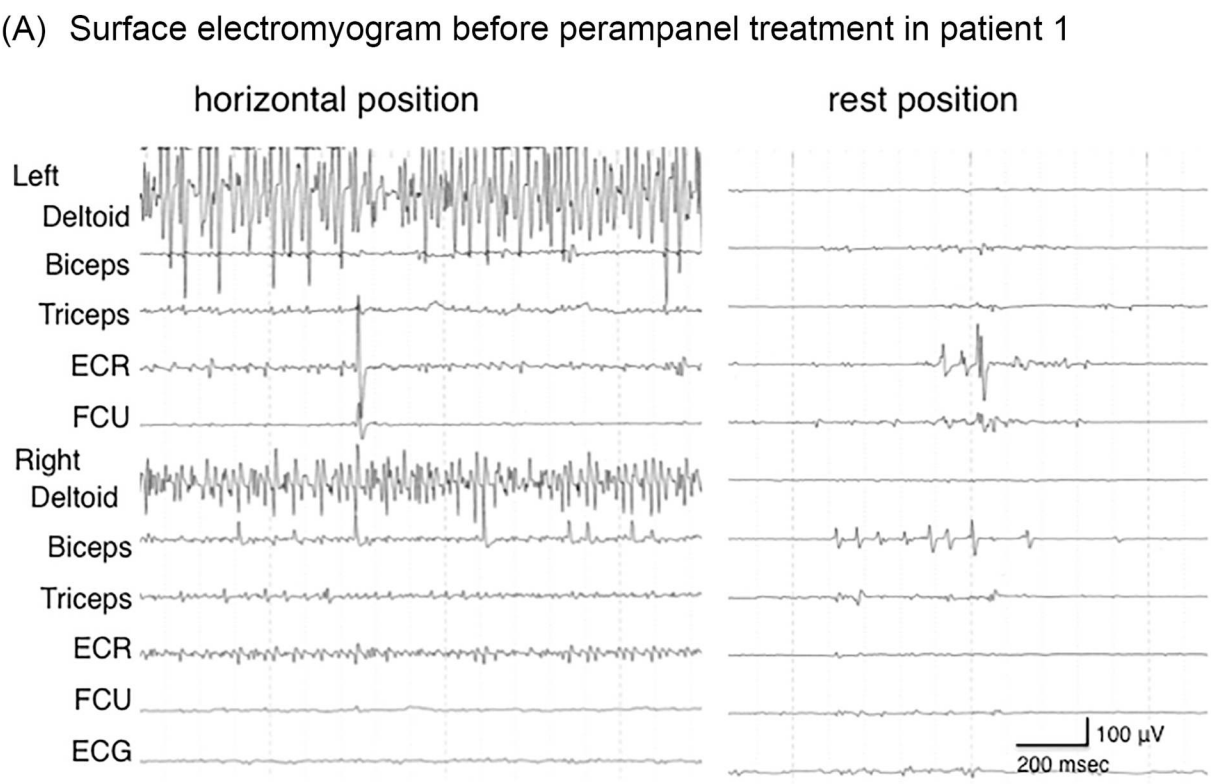

Fig. 1. Findings of surface electromyography and somatosensory evoked potentials.
A. Patient 1 before perampanel therapy. Discharges are synchronized between left extensor carpi radialis (ECR) and left flexor carpi ulnaris (FCU) muscles with a duration of 100–150 msec in both postural and resting positions.
B. Somatosensory evoked potentials generated by stimulating the median nerve in patient 2 show high-amplitude N20-P25 (giant SEP; 51.4 μV) (left). Administration of PER (4 mg) decreased giant SEP by 63.8% to 18.6 μV (right).

drome. Since the patient 1 had no giant SEP, myoclonus might have originated from subcortical lesions. In conclusion, small amount of PER is useful for treating both cortical and subcortical myoclonus.

Supplementary data to this article can be found online at https://doi.org/10.1016/j.ensci.2019.100215.

Declaration of Competing Interest

The authors have no conflicts of interest to declare. Both patients provided written, informed consent to the publication of the video material.

References

[1] T. Hanada, The discovery and development of perampanel for the treatment of epilepsy, Expert Opin Drug Discovery 9 (2014) 449–458.
[2] M. Dirani, W. Nasreddine, F. Abdulla, A. Beydoun, Seizure control and improvement of neurological dysfunction in Lafora disease with perampanel, Epilepsy Behav. Case Rep. 2 (2014) 164–166.
[3] K. Schorlemmer, S. Bauer, M. Belke, A. Hermsen, R.M. Klein, P.S. Reif, et al., Sustained seizure emission on perampanel in progressive myoclonic epilepsy (Lafora disease), Epilepsy Behav. Case Rep. 1 (2013) 118–121.
[4] E. Santamarina, M. Sueiras, R.M. Lidón, L. Guzmán, J. Bañeras, M. González, et al., Use of perampanel in one case of super-refractory hypoxic myoclonic status: case report, Epilepsy Behav. Case Rep. 4 (2015) 56–59.

[5] B.J. Steinhoff, M. Bacher, C. Kurth, et al., Add-on perampanel in lance-Adams syndrome, Epilepsy Behav. Case Rep. 6 (2016) 28–29.
[6] H. Shiraishi, K. Egawa, T. Ito, et al., Efficacy of perampanel for controlling seizures and improving neurological dysfunction in a patient with dentatorubral -pallidoluysian atrophy (DRPLA), Epilepsy Behav. Case Rep. 8 (2017) 44–46.
[7] S. Bianchini, G. Bellantoni, A. AnAlbergati, L. Magrassi, Postsurgical cortical myoclonus responsive to perampanel, Neurol. Clin. Pract. 8 (2018) 159–161.
[8] Y. Oi, S. Neshige, T. Hitomi, K. Kobayashi, M. Tojima, M. Matsuhashi, et al., Low-dose perampanel improved refractory cortical myoclonus by the dispersed and suppressed paroxysmal depolarization shifts in the sensorymotor cortex, Clin. Neurophysiol. 130 (2019) 1804–1812.

Mutsumi Iijima[a,*], Hirokazu Oguni[b], Masaki Kobayashi[a], Kazuo Kitagawa[a]
[a] *Department of Neurology, Tokyo Women's Medical University School of Medicine, Japan*
[b] *Department of Pediatrics, Tokyo Women's Medical University School of Medicine, Japan*
E-mail address: iijima.mutsumi@twmu.ac.jp (M. Iijima).

* Corresponding author at: Department of Neurology, Tokyo Women's Medical University School of Medicine, 8-1 Kawada-cho, Shinjuku-ku, Tokyo 162-8666, Japan.