FDG-PET Study in A Case with Progressive Myoclonus Ataxia

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Sialidosis is a disorder caused by NEU1 gene mutation. The clinical manifestations consist of myoclonus, cerebellar ataxia and/or occasional seizure [1]. From the electrophysiological studies, the myoclonus of sialidosis is of cortical origin [1]. It is intriguing to know how the cerebral metabolic status of sialidosis patients may manifest and this may extend our understanding of cortical myoclonus.

A 39-year-old man developed jerks of four limbs since 9 years ago followed by gait unsteadiness 4 years later. During these years, he experienced two episodes of generalized seizure. Neurological examination revealed action and stimulus sensitive myoclonus in four limbs. Limbs and trunk ataxia was also noted. Fundi examination showed no cherry-red spot. Genetic studies confirmed homozygous missense mutation at nucleotide 544A to G in exon 3 of the NEU1 gene, a hot spot in Taiwanese ethnic patients [1], causing the amino acid substitution Ser182Gly. Levetiracetam in daily dose of 2000 mg was administrated and his symptoms were partially improved. The Unified Myoclonus Rating Scale score changed from 83 to 77. The short duration surface electromyography (sEMG) bursts(<30 ms) and the presence of an EEG event 15 ms prior to left first dorsal interosseous(FDI) jerks suggest the myoclonus is of cortical origin.(figure 1-a) 18F-deoxyglucose-positron emission tomography(FDG-PET) was conducted before and after levetiracetam. In 'drug off' state, the metabolism was increased of both anterior and posterior parts of the brain (Figure 1-b). The current findings were different from those one of sialidosis patient, in whom the posterior cerebral hypometabolism was the pivotal manifestation [2]. The present 'drug off' findings was in line with imaging findings in post-hypoxic myoclonus, which showed wide spreading increase of cerebral BOLD activities [3]. The brain metabolism was relatively escalated over the anterior half of the brain but was less robust of the posterior brain parts during 'drug on' as compared with the 'drug off' (figure 1-b). By subtracting the drug 'off' from the 'on' signals, figure 1-c illustrated that the enhanced metabolic spots allocated mainly of bilateral frontal and temporal regions and the cool spots distributed majorly of the occipital areas. Levetiracetam binds to synaptic vesicle protein 2A (SV2A), a protein relevant to neurotransmitter release, which is ubiquitously expressed throughout the brain [4]. The imaging changes caused by levetiracetam suggest that the effects of SV2A activation could be different in different brain regions as seen in animal study [5]. It implies that the circuitry balance between the anterior and posterior brain may be crucial for the generation of cortical myoclonus in sialidosis and this warrants further study.

Reference
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Figure 1

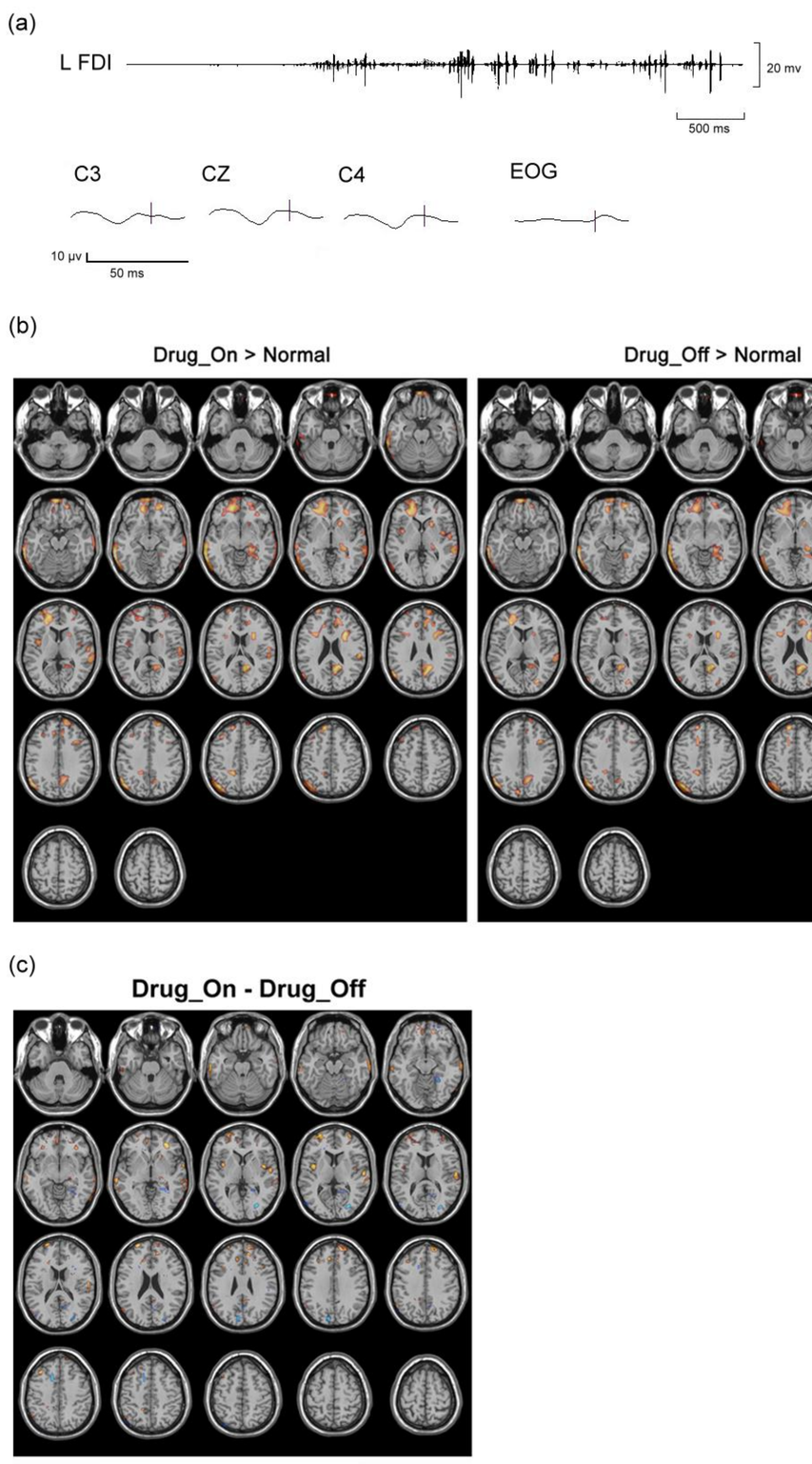

Figure 1-a: Surface EMG and Jerk-locked backaverage recording. (L FDI:left first dorsal interosseous)
Figure 1-b: FDG-PET before(Drug_Off>Normal) and after (Drug_On>Normal) levitiracetam. The orange color represents hypermetabolism.
Figure 1-c: FDG-PET by subtracting the drug-off signals from the drug-on signals. The orange color represents areas with higher metabolic rate in "drug-on" than in "drug-off" state and vice versa in blue color.