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# Exaggerated startle in Post-Infectious Opsoclonus Myoclonus syndrome

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A thirty-year-old male presented with a three-day history of jerky movements involving all four limbs, trunk and face. One week before, he had a self-limiting illness with vomiting, myalgia and back pain. On examination, there was marked opsoclonus at rest that worsened with gaze. He had a broad-based gait and could not walk unaided. There was multifocal myoclonus, most prominent in facial muscles (see supplementary video), with an irregular tremor affecting arms, legs and head that enhanced during movement. He was diagnosed with opsoclonus myoclonus syndrome (OMS) and commenced on clonazepam for symptomatic management.

Extensive investigations including whole body PET-CT found no evidence of occult malignancy or infection. Structural MRI brain was normal but MR spectroscopy of the cerebellum was abnormal in the vermis with an area ratio of NAA to Creatine (NAA/Cr) of 0.89 (normal >0.95) (Fig 1D). Neurophysiology performed on day fifteen of his illness (see supplementary video) revealed prominent forearm myoclonus and jerk-locked back averaging (Fig 1C) revealed no cortical spikes confirming a sub-cortical origin. Four limb somatosensory evoked potentials were normal (the median and posterior tibial nerves were stimulated at the wrist and behind the medial malleolus, respectively). Further examination revealed exaggerated physiological startle responses to unanticipated loud auditory stimuli with no habituation (Fig 1A). Seven months later the patient was much improved, with very little myoclonus although tandem walk remained difficult. Repeat neurophysiological examination

demonstrated persistence of exaggerated physiological startle responses (both to unexpected auditory and tactile stimuli) (Fig 1B).

At 12 months, his examination was normal but his partner still noticed persistence of his tendency to exaggerated startle to unexpected noises. At 18 months, he was fully recovered, with no tendency to startle. Repeat MR spectroscopy at 18 months showed the NAA/Cr ratio from the vermis had increased from 0.89 to 1.01 (normal ratio).

Exaggerated physiological startle in OMS has previously been described in paraneoplastic OMS (Sotirchos et al., 2011). Post-infectious OMS is well described (Mustafa et al., 2015) but presence of exaggerated startle has not previously been demonstrated. Furthermore this case, with MRI spectroscopy shows clear evidence of reversible cerebellar dysfunction.

The most frequent presenting symptoms of OMS are dizziness (67%), imbalance (67%), oscillopsia (28%) and tremor (19%)(Klaas et al., 2012). Myoclonus is typically postural or movement induced and may affect the face, eyelids, head, neck, limbs or trunk, like in this case. There is controversy in the literature as to what extent the gait disturbance is a result of cerebellar ataxia or myoclonic jerks. In other case reports of OMS, functional metabolic imaging (including 18[F] fluoro-2-deoxyglucose positron emission tomography (FDG-PET) & SPECT) examination reveals cerebellar abnormalities, in particular involving of the vermis (Mustafa et al., 2015; Yakushiji et al., 2006).

In summary, we present a case of OMS associated with persistent exaggerated physiological startle responses (that resolved more slowly than myoclonus). We believe the OMS was post or para-infectious due to the preceding illness one week earlier with vomiting, myalgia and back pain. However no infectious agent was detected. As shown in the neurophysiological analysis, these are initiated in the lower brainstem, the commonly accepted generator of physiological startle (Bakker et al., 2006). Our spectroscopy findings show clear but reversible involvement of the cerebellum. Once cerebellar spectroscopy values had normalized, complete clinical recovery was reported by the patient, thus suggesting that the brainstem startle responses had been modulated, at least in part, by the cerebellum.

**Conflict of Interest:** None

**Disclosures**: The authors confirm that the approval of an institutional review board was not required for this work as it is a case review and the patient has provided written consent for publication.

## References

Bakker, MJ, van Dijk JG, van den Maagdenberg AM, and Tijssen MA, (2006). Startle syndromes. Lancet Neurol **5**(6): 513-524.

Klaas, JP,, Ahlskog JE, Pittock SJ, Matsumoto JY, Aksamit AJ,Bartleson JD, Kumar R, McEvoy KF, and McKeon A, (2012). Adult-onset opsoclonus-myoclonus syndrome. Arch Neurol **69**(12): 1598-1607.

Mustafa, MJ, Levin F, Schöberl and Rominger A, (2015). Postinfectious Opsoclonus-Myoclonus Syndrome in a 41-Year-Old Patient-Visualizing Hyperactivation in Deep Cerebellar Nuclei by Cerebral [(18) F]-FDG- PET. J Neuroimaging **25**(4): 683-685.

Sotirchos ES, Dorsey ER, Tan IL, and Zee DS, (2011). Opsoclonus-myoclonus syndrome and exaggerated startle response associated with small-cell lung cancer. Mov Disord **26**(9): 1769-1770.

Yakushiji YR, Otsubo T, Hayashi K, Fukuchi N, Yamada Y, Hasegawa and Minematsu Y, (2006). Glucose utilization in the inferior cerebellar vermis and ocular myoclonus. Neurology **67**(1): 131-133.

**Figure 1 legend**

Electrophysiological analysis of the myoclonus with EEG/EMG polygraphy (A, B, C) and spectroscopy of the cerebellum (D, E).

A: Recorded during acute phase. Jerk-locked averaging (4 sweeps – the auditory startle was used as trigger) showing the exaggerated physiological startle responses elicited by unanticipated loud auditory stimuli at 100dB. No habituation was seen despite the procedure was repeated on numerous occasions over short intervals of time. Consistently the abdominal and lower limb muscles were activated during the startles.

B: Recorded 7 months after acute phase. Startle response to tactile stimulation of the forehead. The startles are also shown in the video submitted as supplementary material.

C: Jerk-locked averaging (774 sweeps) for the multifocal myoclonus affecting arms and legs. The myoclonic EMG discharges captured from the right ADM where used as trigger. Note absence of cortical spikes in the EEG traces.

D: Cerebellar spectroscopy of the vermis during the symptomatic phase. The NAA/Cr ratio is at 0.87 (normal range >0.95). The voxel of interest is indicated by the red box.

E: Cerebellar spectroscopy of the vermis after recovery. The NAA/Cr ratio is within normal limits at 1.01.

*ADM: abductor digiti minimi, APB: abductor pollicis brevis, BB: Biceps brachii, EDC: extensor digitorum communis, FCU: flexor carpi ulnaris, L Abs: lower abdominals,*

*Mass: masseter, OOc: orbicularis oculi, OOr: orbicularis oris, Ster: sternocleidomastoid, TB: triceps brachii, Up Abs: upper abdominals.*

**Video Legend**

Neurophysiology was performed on day fifteen of his illness and was dominated by non-habituating, exaggerated physiological startle responses precipitated by unanticipated loud auditory stimuli (See also Fig 1A). Clinically inconspicuous spontaneous myoclonus is captured from the surface EMG polygraphy recordings, mainly from the forearms (see also Fig 1C, where jerk-locked averaging shows the subcortical generator of the myoclonus). The right side of the screen shows at the top in black the EEG montage used (from the top raw moving downwards, the right and then left frontotemporal anteroposterior derivations are followed by the transversal frontal, centrotemporal and temporoparietal bipolar recordings). Below the EEG channels the surface EMG polygraphy recordings are shown in green with the abbreviations for each channel specified on the left side of the recordings.

The second half of the video is from a repeat examination, seven months later. The patient had significantly improved, to include much less significant spontaneous occurring myoclonus that can be appreciated on the EMG polygraphy recordings. Despite the marked clinical improvement, the exaggerated physiological startle responses persisted to some extent both to unexpected auditory and tactile stimuli (only tactile stimulation shown; See also Fig 1B).

*Accel: Accelerometers placed in the right and left hand and in the forehead area, ADM: abductor digiti minimi, APB: abductor pollicis brevis, BB: Biceps brachii, C5: cervical paraspinals at C5 level, EDC: extensor digitorum communis, FCU: flexor carpi ulnaris, L Abs: lower abdominals, Mass: masseter, OOc: orbicularis oculi, OOr: orbicularis oris, Para: paraspinals applied in the cervical region at C5, Ster: sternocleidomastoid, TB: triceps brachii, Trap: trapezius, Up Abs: upper abdominals.*