Dear Sirs,

Niemann–Pick disease type C (NP-C) is a rare autosomal recessive disorder with a wide clinical neuropsychiatric spectrum resulting from a disorder of intracellular cholesterol trafficking and synthesis caused by mutations in the NPC1 or NPC2 gene [1, 2]. We describe a 51-year-old man with a long disease course who showed a remarkable photomyogenic (photomyoclonic) response at photic flash stimulation during EEG recordings.

Thirty years after the initial presentation of symptoms, the patient was referred for the evaluation of an early onset dementia, progressive behavioural disturbances, tremors, and gait disturbances. Until puberty a normal intelligence and psychomotor development were reported. After puberty he gradually deteriorated in daily functioning and intelligence, and at the age of 46 his IQ score was below 70. He increasingly presented action tremors, gait disturbances, falls, myoclonic jerks in the limbs and the body, and an increased startle response. He showed severe obsessive traits and a sexual preoccupation towards young girls and women for which he was transferred to a psychiatric hospital. Neurological examination revealed poor facial mimic with a staring gaze. Speech was dysarthric and he had an aphasia. There were myoclonic jerks which increased on motor action and startle. Motor exam showed a severe ataxia of the extremities and muscle tendon reflexes were increased, but not pathologic.

Until that moment, laboratory tests, genetic counselling, and imaging studies never revealed a diagnosis. Brain MRI studies showed diffuse cerebral atrophy, most severely of the frontal and temporal lobes. Consecutive EEG recordings showed a background pattern of 8–9 Hz which slowed towards 7–8 Hz. These recordings increasingly showed repetitive runs of bilateral synchronous theta activity of 4–6 Hz frontotemporally, which lasted 1–3 s. Photic flash stimulation provoked a photomyogenic response (Fig. 1). Stimulation with repetitive flashes caused time-locked muscle artefacts at the rate of flashing with increasing amplitude on faster frequencies and a sudden ending on the cessation of flash stimulation. The muscle activation bursts started 48 ms after the flash and had a duration of approximately 150–200 ms. The posterior regions showed a normal photic driving response. NP-C was diagnosed when the accumulation of unesterified cholesterol by positive fibroblast Filipin staining and reduced LDL cholesterol esterification in fibroblasts was demonstrated.

At the age of 53 he succumbed from an aspiration pneumonia.

Myoclonic contractions are not a typical feature of NP-C and a photomyogenic reaction has been described only once before in NP-C [3]. Two cases of cortical myoclonus and one case on a progressive cortical action myoclonus on
motor activity have been described [4, 5]. The photomyo-
genic response results from stimulus time-locked rhythmic
contractions of periocular and facial muscles in phase with
the flash stimulus frequency which can extend to myo-
clonic jerking of the muscles of the upper body. It ceases
directly after flash stimuli are stopped. It is considered to
be a normal physiological response which can, however,
expand under emotional circumstances or metabolic or
toxic states. In our patient, EMG activity was mostly
dominant in the posterior regions. Its physiological mech-
anism was originally thought to be of muscular origin.
Myoclonus can have a cortical origin or it can be generated
by the brain stem showing mechanisms similar to the blink
reflex or in the reticular formation. A startle reflex induces
a facial muscle reaction comparable to the blink reflex with
a latency shorter than the latency we measured. Myoclonic
responses generated by the reticular formation typically
induce a motor reflex of the orbicularis oculi muscle 40 ms
after the stimulus. These EMG bursts typically show a rostro-caudal recruitment starting with activation of the
cranial nerves-innervated muscles and traversing down-
wards to the muscles of the arms and legs [6–9]. We did
not dispose of more extensive EMG recordings covering
muscles of face, neck, and limbs, so we cannot be con-
clusive about the generator mechanism. However, EMG
activity bursts in our patient were of a long duration of
150–200 ms. Moreover, the reticular reflex myoclonus is a
response typically induced by touch, noise, tendon reflex,
or muscle stretch. More recently, research findings suggest
a cortical origin of the photomyogenic reaction, which,
however, remains to be elucidated [9–11]. Myoclonic dis-
orders have repeatedly been associated with cortical hyperexcitability [10, 12, 13]. Such a mechanism is, for
instance, the case in the progressive myoclonic epilepsies.
This is a progressive neurodegenerative disease character-
ized by seizures which can be provoked by stimuli and
myoclonus of variable morphology. These patients show
exaggerated evoked potentials after somatosensory and
light stimuli as a result of cortical hyperexcitability. This
may also occur in NP-C cases as described in this report.
However, in our patient, evoked potential studies were not
performed. Our patient did not have seizures, making the
clinical state of our patient more consistent with a pro-
gressive myoclonic ataxia.

In the literature the neurophysiological findings of NP-C
are described in only a number of reports [2, 4, 5]. EEG
features reported consist of unspecific diffuse slowing of
background activity. Epilepsy is described sporadically [2].
The recognition of vertical gaze palsy by electro-oculogra-
phy has been described [14]. Neurophysiologic investiga-
tions may help to better understand the pathophysiological
mechanism of NP-C with respect to the nervous system, may
help to reveal a diagnosis, and may help to evaluate the
effects of treatment.
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