white matter injuries, as compared to morphological MRI. However, these preliminary data need to be confirmed on a larger cohort of patients.

Conflict of interest

No conflict of interest.

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Brain H-MR spectroscopy in anti-GAD antibodies cerebellar ataxia

Spectroscopie protonique cérébrale dans l’ataxie cérébelleuse à anticorps anti-GAD

The patient was a 16-years-old boy, complaining of oscillopsia. There was no history of familial neurological disorder. Neurological examination revealed a bilateral down-beat nystagmus and ocular fixation instability, in absence of periodic alternating nystagmus. Other neurological tests were normal. Detailed sensory examination was normal. Blood laboratory studies showed anti-glutamic acid decarboxylase (GAD) antibodies (Ab) (titer: 6.7%; N < 2.6%), and anti-intrinsic factor Ab. Other blood immune tests were unremarkable. Genetic study for Friedreich ataxia and spino-cerebellar ataxia type 6 (SCA 6) was negative. The treatment using gabapentin (1.800 mg/day) improved nystagmus. Magnetic resonance (MR) imaging and proton-MR spectroscopy (MRS) of the brain were performed 13 months after the anti-GAD finding (year 2006) and repeated two years later on a 3 Tesla magnet (ACHIEVA 30 R2, Philips, Best, The Netherlands). For MRS, a single voxel (20 × 20 × 20 mm) technique at short echo time (TE/TR: 31/2000 ms; Nex: 144) was applied. The MRI remained unremarkable. Metabolite ratios were calculated (using an integrated Philips advanced spectrum post-processing software), in comparison to a control group (seven healthy subjects with normal neurological examination; mean age: 27.57 ± 2.88; F/M: 4/3),
Table 1  Metabolites ratios within the basal ganglia and the cerebellum as calculated from spectra and statistical z-test results (significant results in bold).

<table>
<thead>
<tr>
<th></th>
<th>NAA/Cr (SD)</th>
<th>NAA/Cho (SD)</th>
<th>Cho/Cr (SD)</th>
<th>ml/Cr (SD)</th>
<th>GlxT/Cr (SD)</th>
<th>GlxT/NAA (SD)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Basal ganglia</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Controls</td>
<td>1.54 (0.18)</td>
<td>2.39 (0.32)</td>
<td>0.65 (0.06)</td>
<td>1.08 (0.31)</td>
<td>1.01 (0.24)</td>
<td>0.67 (0.17)</td>
</tr>
<tr>
<td>Patient (2006)</td>
<td>1.63</td>
<td>1.86</td>
<td>0.88</td>
<td>0.53</td>
<td>0.69</td>
<td>0.68</td>
</tr>
<tr>
<td>z score1</td>
<td>0.461</td>
<td>1.619</td>
<td>3.573</td>
<td>1.729</td>
<td>0.491</td>
<td>0.1</td>
</tr>
<tr>
<td>Patient (2008)</td>
<td>1.72</td>
<td>2.33</td>
<td>0.73</td>
<td>0.69</td>
<td>1.15</td>
<td>0.67</td>
</tr>
<tr>
<td>z score2</td>
<td>1.017</td>
<td>0.187</td>
<td>1.467</td>
<td>1.232</td>
<td>0.604</td>
<td>0</td>
</tr>
<tr>
<td><strong>Cerebellum</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Controls</td>
<td>1.44 (0.30)</td>
<td>1.74 (0.29)</td>
<td>0.83 (0.09)</td>
<td>1.13 (0.25)</td>
<td>1.56 (0.44)</td>
<td>0.93 (0.34)</td>
</tr>
<tr>
<td>Patient (2006)</td>
<td>1.19</td>
<td>1.31</td>
<td>0.91</td>
<td>0.87</td>
<td>2.53</td>
<td>1.88</td>
</tr>
<tr>
<td>z score1</td>
<td>0.835</td>
<td>1.454</td>
<td>0.822</td>
<td>1.034</td>
<td>2.023</td>
<td>2.056</td>
</tr>
<tr>
<td>Patient (2008)</td>
<td>1.15</td>
<td>1.27</td>
<td>0.9</td>
<td>1.04</td>
<td>2.12</td>
<td>1.84</td>
</tr>
<tr>
<td>z score2</td>
<td>0.967</td>
<td>1.62</td>
<td>0.778</td>
<td>0.36</td>
<td>1.273</td>
<td>2.676</td>
</tr>
</tbody>
</table>

using a z score with values greater than 1.99 considered significant. Our patient showed a significant increase of choline-compounds (Cho)/Creatine (Cr) within the basal ganglia, total glutamine-glutamate complex (GlxT)/Cr and GlxT/NAA (N-acetyl-aspartate) ratios within the cerebellum (Table 1) at the first exam. The NAA/Cr and myo-Inositol (ml)/Cr ratios were decreased within the cerebellum. The control MRS showed a little variation compared to the first exam with a slightly decrease of GlxT/Cr and GlxT/NAA ratios (Table 1).

This is the third description of predominating ocu-lo-motor symptoms in a patient presenting anti-GAD Ab [1]. High titters of anti-GAD antibodies may be associated with disabling neurological diseases such as stiff-man syndrome and cerebellar ataxia, and patients may develop a slowly progressive insulin-dependent diabetes (SPIDDM) [2,3]. The pathogenesis of neurological involvement is not elucidated yet. Neuropathology studies show that the disorder can lead to a complete depletion of Purkinje cells in the cerebellum [2]. Recent in vivo experimental data show that the NMDA-mediated turnover of glutamate and the turnover of lipids are disturbed in the brain when NMDA is infused intracerebrally in vivo [3]. These findings might correspond to the initial steps of an excitotoxic cascade leading finally to cell death. MRS is the only non-invasive technique to provide in vivo biochemical information for the understanding and the management of cerebellar disorders, yielding information about the overall energy state, cellular membrane turnover, inflammation and glial cell status. Low concentrations

Figure 1  Spectroscopy of the cerebellum. A. Anatomical location of the single voxel (red square) including the dentate nucleus, in the patient as well as in the controls. B. Spectrum obtained in the patient (metabolite ratios are shown in the Table 1). C. Spectrum in one healthy control (means of metabolite ratios are shown in Table 1). D. Spectrum labelling.

Figure 2  Spectroscopy of the basal ganglia. A. Anatomical location of the single voxel (red polygon) including part of the caudate, the lenticular and the thalamus nuclei, and part of the internal capsule, in the patient as well as in the controls. B. Spectrum obtained in the patient (metabolite ratios are shown in the Table 1). C. Spectrum in one healthy control (means of metabolite ratios are shown in Table 1). D. Spectrum labelling.
of NAA (NAA/Cr ratio) within the cerebellum and the pons have been well correlated with disability scores in patients [4]. A recent study in ataxia-telangiectasia (A-T) patients has revealed significantly lower NAA/Cho and higher Cho/Cr ratios in the cerebellum as compared to controls, suggesting altered membranes turnover within the cerebellum [5]. In our case, the significantly higher Cho/Cr in the BG shows that the disease is not restricted to the posterior fossa and may affect supratentorial structures by impairing membranes turnover in areas corresponding to the cerebellar-thalamic pathways. Within the cerebellum, the significant increase of total glutamine-glutamate (GlxT/Cr, GlxT/NAA) suggest an imbalance between excitatory (Glx) and inhibitory (gamma-aminobutyric acid [GABA]) neurotransmitters. Our patient showed a clinical positive response to gabapentin. This drug acts upon the GABAergic pathways [6]. The positive response to this treatment and the abnormally high GlxT/Cr and GlxT/NAA ratios within the cerebellum support the hypothesis of a disorder involving the GABA neurotransmission and likely induced by anti-GAD Ab. MRS may be useful to detect and monitor specific changes in brain biochemistry in such cases while morphology remains unremarkable on MRI.

Conflicts of interest

We declare no conflict of interest.

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References


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Möbius syndrome and epilepsy

Syndrome de Möbius et épilepsie

A 3420 g infant girl was delivered through caesarean section at 39 weeks of gestation, with an Apgar score of 7 at 1 min and 10 at 5 min. On examination, bilateral facial nerve paralysis, right abducens nerve paralysis and craniofacial asymmetry with microretrognathia were noted. A diagnosis of Mobius syndrome was therefore suggested. Patient presented tonic seizures in the first 24 h of life, which were initially controlled with phenobarbital. Soon after, she started to have frequent focal and multifocal clonic seizures. Despite medication with clonazepam and phenobarbital, the child continued to have clinical seizures. A history of epilepsy in the family (the mother and maternal grandfather) was present. Also of note, the mother took misoprostol in the first trimester of pregnancy in an attempt to induce abortion. Brain MRI revealed alterations in brainstem morphology, including hypoplasia of the dorsal aspect of the lower pons with straightening of the fourth ventricular floor. The middle cerebellar peduncles were also hypoplastic and only their rostral segment was present. The rostral pontine tegmentum was protruding in the fourth ventricle. The superior cerebellar peduncles and the mesencephalon appeared normal (Figs. 1 and 2).

The hallmark of Mobius syndrome is facial diplegia and abducens nerve palsies, as described by Mobius in 1888. The aetiology is not well established. Most cases are sporadic, but there are reported familial cases, with the data indicating a gene for Mobius syndrome on chromosome 3, 10 and 13 [1,2]. It was proposed that sporadic cases are causally related with vascular impairment in a watershed zone of the brainstem, between the territories of the segmental paravascular penetrating arteries and the long circumferential arteries, branches of the basilar artery [3]. The abnormality of the brainstem that occurs in Mobius syndrome could be the result of a transient interruption in fetal blood.

Several teratogens have been implicated in the aetiology of Mobius syndrome. One of the most reported teratogenic agent is misoprostol [4]. When taken early in the pregnancy, misoprostol is a potent uterine stimulant that induces abortion. Induced uterine contractions can cause vascular disruption, resulting in fetal hypoxia and ischemia. MR imaging findings vary, according to the degree of rhombencephalic maldevelopment. Imaging study frequently shows a variable degree of pontine hypoplasia with straightening of the fourth ventricular floor [5].

We describe a neonate with Mobius syndrome presenting pontine and middle cerebellar peduncles hypoplasia. The differential diagnosis includes other brainstem developmental disorders. Ventral tegmental changes are similar to those found in pontine tegmental cap dysplasia, which also presents middle cerebellar peduncles hypoplasia [6]. However, in this case, we did not find an abnormal shape and orienta-