Low lumbar CSF concentrations of homovanillic acid in the autosomal dominant ataxia

The autosomal dominant ataxias (ADA) are a genetically heterogeneous group of disorders with similar phenotypes. There are few studies describing monoamine metabolites in CSF in patients with ADA. Low concentrations of the serotonin metabolite 5-hydroxyindoleacetic acid (5-HIAA) and the dopamine metabolite homovanillic acid (HVA) in CSF are found in patients with cerebellar cortical atrophy and Friedreich's ataxia. The low CSF concentrations of 5-HIAA may reflect a diminished contribution from the spinal cord and the cerebellar serotonergic pathways, whereas the low concentrations of HVA indicate involvement of the basal ganglia and other neural structures adjacent to the lateral ventricles. By contrast with other forms of ataxia, cerebellar signs did not improve in patients with ADA during trials evaluating the therapeutic efficacy of the serotonin precursor 5-hydroxytryptophan. 1 To determine the basis for this unresponsiveness, we measured CSF monoamine metabolites in patients with ADA with at least two different genotypes.

The Institutional Review Board of the National Institute of Neurological Disorders and Stroke approved this research. To study families with more than three consecutive generations of ataxia. After five days on a standard low monoamine diet and after eight hours of bed rest, a lumbar puncture was performed with the patient in the lateral decubitus position. Routine CSF studies were carried out on the initial 4 ml of CSF; for assay of HVA and 5-HIAA an additional 10 ml was collected in four 2.5 ml aliquots. All aliquots of CSF were frozen immediately on dry ice and stored at -70°C. To minimise the effects of CSF monoamine concentration gradients, the tube containing the fourth aliquot of CSF was used for analysis. Extraction, derivatisation, and measurement of HVA and 5-HIAA were performed as previously described. 2-3

<table>
<thead>
<tr>
<th>CSF monoamine metabolites in patients with autosomal dominant ataxia</th>
<th>HVA (ng/ml)</th>
<th>5-HIAA (ng/ml)</th>
<th>Ratio HVA/5-HIAA</th>
</tr>
</thead>
<tbody>
<tr>
<td>SCA1 (n = 5)</td>
<td>20-66 (3-05)**</td>
<td>12-89 (2-53)</td>
<td>1-67 (0-14)</td>
</tr>
<tr>
<td>SCA3 (n = 9)</td>
<td>20-23 (3-55)**</td>
<td>15-03 (1-28)</td>
<td>1-38 (0-21)**</td>
</tr>
<tr>
<td>Normal or SCA1 or 3 (n = 6)</td>
<td>36-81 (9-53)</td>
<td>16-78 (4-00)</td>
<td>2-10 (0-28)</td>
</tr>
<tr>
<td>Total SCA (n = 20)</td>
<td>25-31 (3-61)**</td>
<td>15-02 (1-42)</td>
<td>1-67 (0-14)**</td>
</tr>
<tr>
<td>Controls (n = 20)</td>
<td>39-08 (3-02)</td>
<td>17-26 (1-26)</td>
<td>2-30 (0-12)</td>
</tr>
</tbody>
</table>

Results are means (SEM).

*p < 0.01, paired two tailed t test.

Liver dysfunction and probable manganese accumulation in the brainstem and basal ganglia

Because absorption and excretion of manganese is regulated by the hepatointestinal circuit, advanced liver dysfunction may result in a reduction of manganese excretion and its accumulation in various organs including the brain. 6 A 58 year old housewife was referred to us because of left orbital pain but normal ophthalmological examination. She had liver cirrhosis due to hepatitis C virus infection, which had developed after a blood
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