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

The autosomal dominant ataxias (ADA) are a genetically heterogenous 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-hydroxyindolacetic 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. Blood and cerebrospinal fluid were collected from patients with cerebellar ataxias with 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

Mean concentrations of HVA and 5-HIAA in CSF were calculated and statistical differences were determined by paired t test. The relation between the monoamine metabolites and cerebellar and pontine CSF area was examined by linear regression.

All 20 patients (12 male, eight female) had variable degrees of cerebellar ataxia without parkinsonian signs. Five study participants from two families showed a repeat expansion on chromosome 6p (spinocerebellar atrophy type 1; SCA1), nine patients from three families showed a repeat expansion on chromosome 14q (SCA3) and six patients from three families had neither genotype. In the entire group of patients with ADA, the mean (SD) pontine (315.9 (82.1)) and cerebellar atrophy (178.6 (25.3)) area were significantly larger (P < 0.01) than normal (pontine 393.5 (44.7); cerebellum 1120.0 (133.4)). The pontine area was linearly related to the decreasing concentrations of HVA in CSF (P = 0.05, r = 0.50, y = −23 + 0.09x) but the cerebellar area was not related to the concentrations of HVA or 5-HIAA in CSF. The concentration of HVA and the ratio of CSF HVA/5-HIAA were significantly lower in the entire group of patients with ADA than in normal controls (table). Although the cerebellar size was smaller (P = 0.01) in patients with SCA1 (670.5 (112.0)) than in patients with SCA3 (858.3 (126.0)), no differences in the concentrations of monoamine metabolites were found between these genotypes.

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

Because absorption and excretion of manganese is regulated by the hepatointestinal circuit, 3 advanced liver dysfunction may result in a reduction of manganese excretion and its accumulation in various organs including the brain. 4 A 58 year old housewife was referred to us because of left orbital pain but normal ophthalmological examination. She had liver cirrhosis due to hepatocellular carcinoma, which had developed after a blood
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