Decrease in cerebral ventricular volume in end-stage Huntington’s disease treated with purified eicosapentaenoic acid

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Introduction
Unsaturated fatty acids have been shown to slow the rate of progression of Huntington’s disease in open label studies1 and to prevent the movement disorders and neurodegeneration in mice transgenic for human Huntington’s disease. The omega-3 fatty acid eicosapentaenoic acid (EPA) is an intermediate in human metabolism which has been shown to inhibit phospholipase A2, an enzyme important in neurodegeneration.2 We tested 2g/day purified ethyl-EPA for six months against an identical appearing inert placebo in patients with end-stage Huntington’s disease who required 24-hour hospice care. 3D high-resolution MRI scans were carried out at baseline and six-month follow-up.

Methods
Eight patients were entered into the study after giving informed consent in association with their carers. The study was approved by the Riverside Research Ethics Committee. The patients were randomized on a double-blind basis in blocks of four by an independent computer program. One patient died before the study could begin. All the patients were evaluated at baseline and six months on the motor component of the Unified Huntington’s Disease Rating Scale (UHDRS).3 Owing to the movement disorder only four patients underwent successful MRI at baseline and six months. The MRI scans were assessed with accurate, positionally-matched, serially-acquired imaging using subvoxel image registration and segmentation.4 Sagittal 3D T1-weighted rf spoiled images (TR = 30 ms, TE = 3 ms, flip angle = 30 degrees, 15x256 image matrix, 114 slices, 1.6 mm slice thickness, 25 cm field of view) were acquired on a 1.5 T Marconi Medical Systems Eclipse scanner at each examination. To ensure consistency of brain position within the cranial cavity, care was taken to reposition the subjects to within 5 to 10 degrees of the initial baseline scan. Phantom measurements were also taken at each time of scanning to ensure that no changes in magnetic gradient strength had occurred. The volume scans were then accurately registered and subtraction images were obtained to demonstrate changes between baseline and follow-up images.5 The registered anatomical and subtraction images were then reformatted into the transverse plane with isotropic voxels of size 0.977 mm3.

Results
On the orofacial component of the UHDRS, three patients (who were all on EPA) improved and four (all on placebo) deteriorated (p = 0.04). On the other components of the motor scale, two patients improved and five deteriorated: both improvers were on EPA. Of the four patients who were successfully scanned at baseline and six months, two were on placebo and two were on EPA. The subtraction images showed that both patients on placebo had an increase in ventricular size. In contrast, the subtraction images from the two patients treated with EPA showed evidence of an overall decrease in ventricular size. It was not possible to quantify the amount of ventricular change owing to the gross cerebral atrophy.

Discussion
The assessments showed an improvement in both function and structure in patients on EPA, in contrast to the patients on placebo who followed the expected downhill course. EPA may offer a new approach to the management of Huntington’s disease.

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References