Behavioral deficits in Huntington's Disease correlate with tissue differences measured with MRI.

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Synopsis

In this study we present a non-biased approach to estimate the differences in tissue as measured in 3D high resolution MRI between Huntington's disease patients and healthy controls and to correlate these differences with Minimental Examination Test (MME), The University of Pennsylvania Smell Identification Test (UPSIT) and the Concurrent Visual Discrimination test (CVDT)

Introduction

Huntingto's disease (HD) is a neurodegenerative disorder in which gene mutation has been found and is caused by an unstable CAG trinucleotide expansion in the IT15 gene. It is characterized by involuntary motion, rigidity and mental deterioration resulting from degenerative processes, particularly in the basal ganglia [1]. MRI based morphologic studies have been used to characterize a variety of brain diseases and lesions. Age-related loss of brain tissue has been inferred from cross-sectional neuro-imaging studies, furthermore statistically oriented morphologic studies have proven precise and interesting in determining tissue brain changes during the ageing process [2]. Recent studies have correlated striatum single voxel MRS and cognitive performance in HD patients with age matched controls to estimate clinical significance of metabolic alterations in the striatum [3,4]. We propose that interesting results in correlation between MME, UPSIT and CVDT and statistical differences in tissue as measured with high resolution MRI can be found.

Methods

MR studies

High resolution three dimensional MRI images of 10 gene carriers HD patients and 10 age-matched control volunteers were acquired under the same controlled imaging conditions, after giving informed consent. All MR images were obtained in a G.E. 1.5 Tesla Signa LX (General Electric Medical Systems, Wilwaukee, WI) using 3D T1 weighted SPGR and standard quadrature headcoil, with; TR=24ms, TE=5ms and flip angle of 40°, two excitations over a FOV=24cm, slice thickness of 1.5mm and zero separation. Images were taken using a 256x192 matrix and reconstructed to 256 x256, in 124 coronal slices. The head was securely fastened to avoid movement. All HD patients were sedated during the MR scanning process, so they cope with motor disorders.

Subjects

All HD patients and controls were tested with MME, UPSIT and CVDT for image evocation, these tests were used as elements of memory and learning capabilities. HD patients can be divided in 5 older than 45 years and 5 younger than 35 years with small or no symptoms

Data analysis

Structural 3D MRI SPGR images were transferred to SPM (Wellcome Dept. of Cognitive Neurology, London UK (http://www.fil.ion.ucl.ac.uk/spm) were they were normalized and registered to 1.0 mm isotropic voxels and registered to a T1-weighted template in the standard Talairach anatomical space. All images were smoothed with a Gaussian kernel of 6.3 mm and the signal intensity between HD and controls was compared.

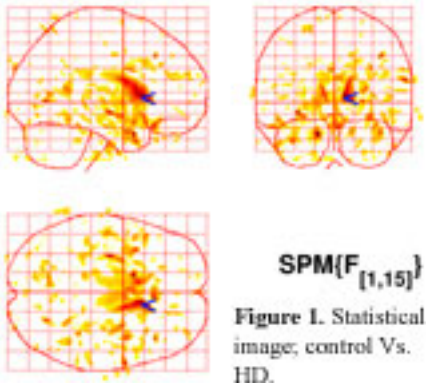

Figure 1. Statistical image; control Vs. HD.

Results and Discussion

Due to the 3D nature of the statistical analysis average difference maps were generated were volume of brain tissue was significantly lower in HD patients as group particularly in the caudate nucleus head, putamen and thalamus, as was expected (Figure 1). These results compare well with behavioral deficits in the MME where controls average score is 30.0 points while HD patients as group scores 24.4 (MME<24 is a signal of dementia). Significant tissue differences are well localized in the caudate nucleus and the thalamus regions. In addition a well localized significant difference was found at the inferior temporal lobe, following the hippocampus (figure 1). This result is interesting and may explain the results from the UPSIT were HD patients scored 21.7 while controls were in 40.0. It is known that the olfactory tract is localized in the temporal lobe as well as the center for smell memory. Statistical tissue difference maps for the HD patients older than 44 years and younger than 35, were projected over the average structural control image were the progress of the degenerative processes can be observed particularly in the putamen area.

Acknowledgments

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References

[1] P.S. Harper, "Huntington's Disease", W.B. Sauders Company ltd. London, 1996.

[2] S.M. Resnik, et al. *J. of Neuroscience*, 23(8):3295–3301, 2003.

[3] R. Sánchez-Pernaute, et al. *Neurology* 53(4):806-811,1999.

[4] F.A. Barrios, et al. *Porc. ISMRM 8th Scientific Meeting, 2000*, p1142.