INTRODUCTION

Huntington’s disease (HD) is a neurological disorder caused by an expanded CAG repeat in the Huntingtin gene. The disease initially affects GABAergic neurons of the caudate and putamen and progresses to affect the entire fronto-striatal network and sensory cortices. HD is characterised by motor, psychiatric and cognitive symptoms.

Eye movements are impaired at an early stage, often long before other symptoms become clinically relevant. Patients demonstrate a marked delay in executing voluntary saccades and difficulties inhibiting saccades to irrelevant stimuli.

The primary aim in this study was to compare the effectiveness of three saccadic paradigms in distinguishing HD patients from presymptomatic carriers of the HD gene mutation. The combination of a cognitively-demanding task with an oculomotor response may offer a sensitive functional biomarker of HD.

METHOD

Eye-tracking and stimuli presentation were carried out using a Saccadometer Advanced (Ober Consulting). The saccadometer is an Infra red system that measures reflectance off the inner canthi of both eyes and averages them for a single value of horizontal eye position. Rate 250Hz, linearity +3.5 degrees. Stimuli were delivered by 4 head mounted lasers, projected 2 metres onto a blank wall.

Paradigms:
(A) Prosaccade - Step task: saccades to randomly presented stimuli on either left or right.
(B) Centrally cued - Single choice task: saccades to left or right target depending on colour of cue.
(C) Peripheral conflict - Double choice task: central cue informs subject whether to make a pro or anti saccade to a target that is randomly on the left or right.

RESULTS

1. Error rates
Saccadic error rate increased with HD status.

![Error rate graph](Image)

Error rates were highest in paradigm (C). The very high error rate in the Early group is mainly accounted for by errors in the anti-saccade condition (see 2.). Motivation is likely to account for the better-than-control performance of the Pre-1 group.

The peripheral conflict paradigm allowed error rates and latency calculations according to the nature of the preceding trial, i.e. same or different target side, same or different rule (central cue). This clearly differentiated the two subgroups of pre-symptomatic participants (pre-1 and pre-2).

2. Switch Cost
Task switching increased error rates.

![Switch Cost graph](Image)

![Error rate graph](Image)

CONCLUSION

Group differences in saccadic latency profiles suggest that the peripheral conflict task has the highest power in discriminating HD progression. This paradigm appears to be able to differentiate Pre-1 and Pre-2 which is important in considering its use as a marker of preclinical disease progression.

Increased error rates in the antisaccade paradigm may be indicative of saccadic inhibition deficits in Early HD participants.

Error rates and switch cost are both good indicators of cognitive function, and may be combined with saccadic latency measures to produce an index of HD progression.

A refined protocol based on the peripheral conflict task is being trialled in the Track-HD study, beginning January 2008.

References