Clinical Correlates of Eye Movements in Huntington Disease

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A. Background

Huntington disease (HD) is a genetic, neurodegenerative movement disorder characterized by chorea, behavioral co-morbidities, cognitive deficits, and eye movement abnormalities. The basal ganglia is adversely affected in HD and this, in turn, results in deficits in cognitive and eye movement functions (Peltsch et al., 2008). Therefore, we sought to evaluate whether eye movement tasks prove useful in characterizing disease severity in HD.

B. Clinical Assessment

Subjects

9 HD patients
- 4 Off-Medication
- 5 On-Medication (Tetrabenazine)

Diagnostic Tests

Montreal Cognitive Assessment Test (MoCA)
Unified HD Rating Scale (UHDRS) - Motor Subscale
Repetitions of C-A-G neucleotides

Table 1 - HD Population

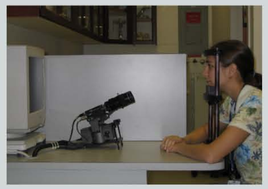
	All HD N=9		OFF N=4		ON N=5	
	mean (sd)	*range*	*mean (sd)*	*range*	*mean (sd)*	*range*
Age (years)	46.7 (15.7)	27-70	40.3 (20.0)	27-70	51.8 (10.9)	43-70
MoCA	26.2 (2.2)	22-30	27.8 (1.7)	26-30	25.0 (1.9)	22-27
UHDRS Motor	26.1 (20.8)	0-47	14.0 (22.1)	0-47	35.8 (15.4)	9-47
CAG Repeats	44.0 (3.7)	41-52	45.5 (5.1)	41-52	42.8 (2.1)	41-45

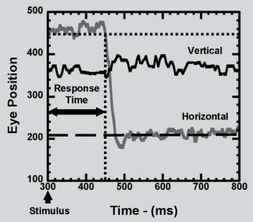
Table 2 - UHDRS Motor Components

		All HD N=9	
		mean (sd)	*range*
Total		26.1 (20.8)	0-47
Ocular Pursuit	**vertical**	0.33 (.50)	0-1
	horizontal	0.44 (.53)	0-1
Saccade Initiation	**vertical**	1.0 (.87)	0-2
	horizontal	1.0 (.87)	0-2
Saccade Velocity	**vertical**	.78 (.44)	0-1
	horizontal	.78 (.44)	0-1
Bradykinesia		.89 (.93)	0-2
Chorea (whole body sum)		10.8 (8.9)	0-21

C. Eye Tracking

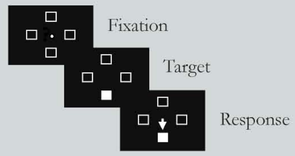
Using an infrared eye tracker, we measured HD patient response times (RTs) and directional error rates (ERs) of horizontal and vertical saccades using prosaccade and antisaccade eye movement tasks.





Tasks

Prosaccade
48 trial block



Antisaccade
48 trial block

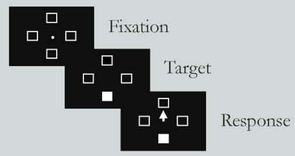


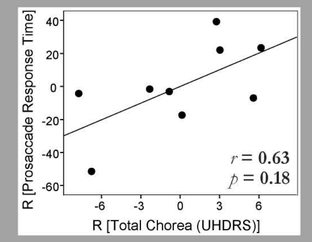
Table 3 - HD Results

		All HD N=9	
Prosaccade		*mean (sd)*	*range*
Error Rate (%)	**vertical**	8.0 (8.5)	0-23.8
	horizontal	1.9 (4.3)	0-12.5
	total	5.0 (3.9)	0-11.9
Latency (ms)	**vertical**	328 (70)	218-411
	horizontal	289 (63)	197-391
	total	308 (61)	207-374
Antisaccade			
Error Rate	**vertical**	49.2 (35.1)	8.3-85.7
	horizontal	54.5 (37.3)	4.2-91.7
	total	52.0 (36.1)	6.4-88.9
Latency	**vertical**	493 (137)	263-700
	horizontal	395 (138)	229-644
	total	457 (119)	247-591

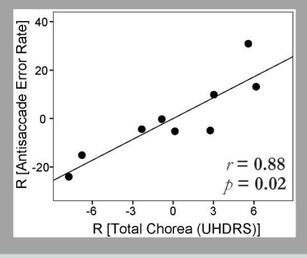
D. Correlations Between Clinical Assessments & Eye Tracking

Controlled for Age, CAG Repeats and Medication State
R [variable] = residual variable values after partial correlation

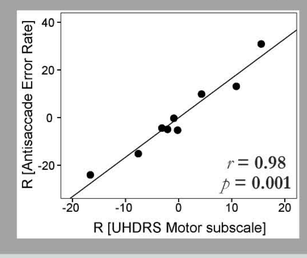
Prosaccade response times tend to increase with increased HD chorea severity.



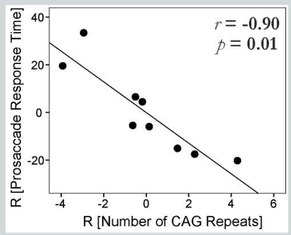
Antisaccade errors increase with increased HD chorea severity.



Antisaccade errors increase with increased HD motor severity.



Controlled for Age, UHDRS Motor Score and Medication State



Prosaccade response times decrease with increased HD CAG repeats.

E. Summary & Conclusions

- Infrared eye tracking is a quick, non-invasive, and objective method of characterizing disease severity in HD.
- Our results show that with increasing clinical severity, HD patients show a slowing in the initiation of reflexive eye movements and dysfunction of executive control (increased antisaccade errors).
- Controlling for Age, UHDRS Motor Score, and Medication State, there was a strong negative correlation between number of CAG repeats and reflexive prosaccade response time, suggesting eye movement measures may be a sensitive biomarker in HD.
- Thus, eye tracking has the potential to evaluate disease progression and treatment effects.

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