Validation of a Behavioral Approach for Measuring Saccades in Parkinson's Disease.

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Methodological Question

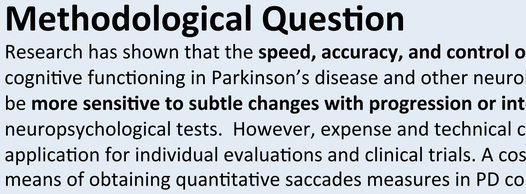
Research has shown that the **speed, accuracy, and control of saccades** is related to cognitive functioning in Parkinson's disease and other neurologic disorders, and may be **more sensitive to subtle changes with progression or intervention** than neuropsychological tests. However, expense and technical complications encumber application for individual evaluations and clinical trials. A cost effective and reliable means of obtaining quantitative saccades measures in PD could thus prove particularly useful to clinicians and researchers. To this end, a **behavioral battery of tests requiring only a PC laptop** was developed and validated in healthy adults (Turner 2007) and patients with Huntington's disease (HD, Turner et al., 2011).

Introduction

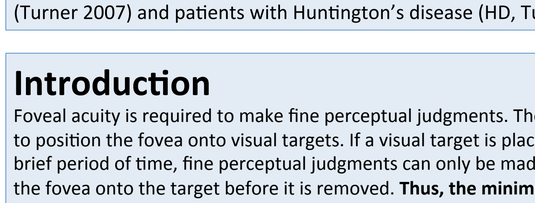
Foveal acuity is required to make fine perceptual judgments. The purpose of saccades is to position the fovea onto visual targets. If a visual target is placed in the periphery for a brief period of time, fine perceptual judgments can only be made if a saccade positions the fovea onto the target before it is removed. **Thus, the minimum presentation time wherein a fine perceptual discrimination can be made reflects the latency of the saccade to place the fovea onto the target.** This presentation time is considered the discrimination threshold and is directly correlated with minimum saccade latency. The entire battery takes about20 min to administer, and an automated scoring program provides immediate results for interpretation and databasing.

Screen Shots of Tasks

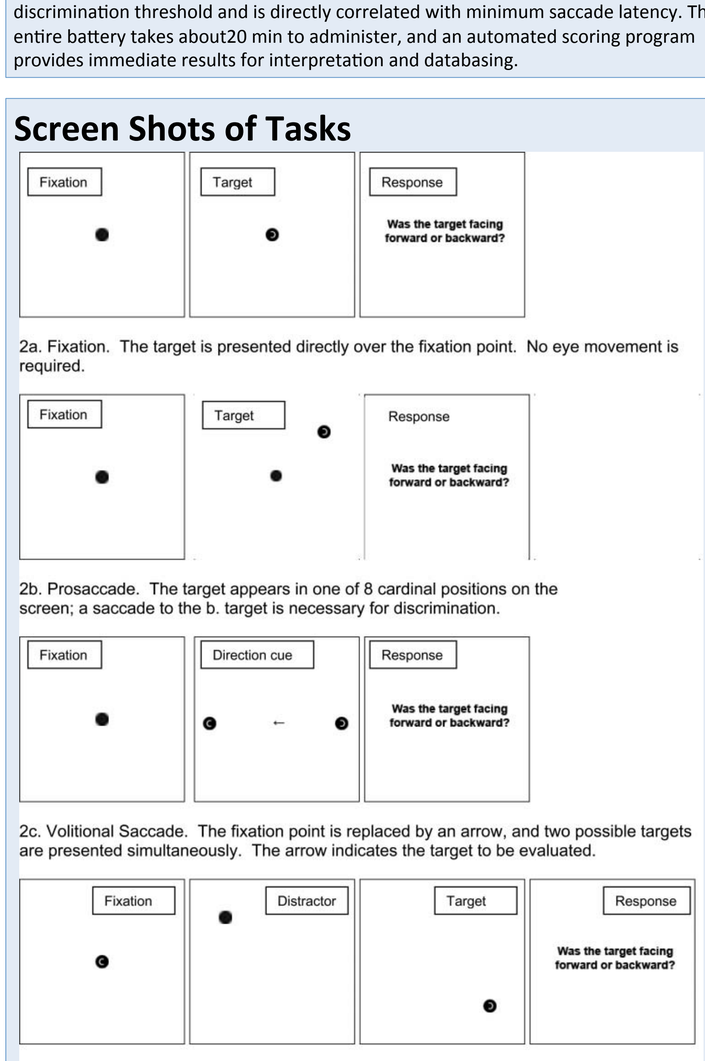
2a. Fixation. The target is presented directly over the fixation point. No eye movement is required.



2b. Prosaccade. The target appears in one of 8 cardinal positions on the screen; a saccade to the b. target is necessary for discrimination.



2c. Volitional Saccade. The fixation point is replaced by an arrow, and two possible targets are presented simultaneously. The arrow indicates the target to be evaluated.



2d. Saccade Inhibition. A distractor stimulus is presented in the opposite area of the screen from where the target will appear. Subjects are instructed to look for the target in the region opposite from the distractor. The target appears immediately after the distractor is removed.

Primary Aims

1. Examine influence of demographics, 30 day test-retest reliability, and practice effects of behavioral saccade measures in Parkinson's disease.
2. Examine validity of behavioral saccade measures with respect to corresponding indices from traditional eye-tracking in Parkinson's disease.

Study Design

Sample: Patients with formal diagnosis of idiopathic PD according to the UK Parkinson's Disease Society Brain Bank criteria. Diagnosis of PD-MCI, PD Dementia not preclusive

Exclusions:

- Prior history of neurosurgery (e.g., DBS)
- Other co-morbid neuropsychiatric disorder or injury
- Untreated myopia, exclusive use of bifocals, or significant visual impairment

All participants examined during subjective "on" medication state

Technical

- Participants were seated 57 cm away from 19" CRT monitor with 75Hz refresh rate
- Behavioral tasks programmed using E-Prime v1.2
- Digital video eye-tracking sampled at 250 Hz. Saccade metrics extracted using proprietary EyeLink II software

Visit 1

- Behavioral Saccade Tests
- Traditional Eye-tracking
- Neuropsychological evaluation (MDS Task Force Level II)
- Medical record review and clinical interview
- Cognitive testing
- Psychological measures

Visit 2 (+30 days):

- Traditional Eye-tracking
- Behavioral Saccade Tests
- Feedback from evaluation

Results

80 participants referred from within MUSC Movement Disorders Program

- Technical complications in eye-tracking data capture for first 4 participants
- 5 excluded because not idiopathic PD per neuropsychological evaluation (2 DLB, 2 FTLD, 1 co-morbid AD)
- Cognitive deficits interfered with completion of behavioral tasks in 5 participants
- 3 participants unable to complete traditional eye-tracking

Final sample n=65 PD patients

- 41 men; 24 women

Cognitive Status

- 41 PD Normal Cognition
- 22 PD-MCI
- 2 PD Dementia

	Minimum	Maximum	Mean (SD)
age	44	82	66.16 (8.35)
educ	7	20	16 (2.75)
Motor Duration	0.5	23	6.48 (4.24)
Cognitive Duration	0	15	1.34 (2.14)
HY Stage	1	4	2.12 (0.64)
DRS-2 Total	130	144	138.48 (3.52)

Demographics & Performance

- Age associated with Prosaccade DT
- **Education not related to performance**
- Duration of illness not strongly associated with DTs
- Disease state related to Volitional & Saccade Inhibition

	Prosaccade Discrimination Threshold	Volitional Discrimination Threshold	Saccade Inhibition Discrimination Threshold
age	.422**	-.139	-.068
education	-.102	.116	-.124
duration illness	.207	.313*	.185
Hoehn Yahr Stage	.225	.477**	.357**

Results - Reliability

Method	Measure	Test-Retest Reliability	Test-Retest Change	Standard Deviation of Difference
Behavioral	Prosaccade Discrimination Threshold	0.75	-12.75*	41.20
	Volitional Discrimination Threshold	0.70	-11.02	87.63
	AntiSaccade Discrimination Threshold	0.70	-19.36	104.60
Eye-Tracking	Reflexive Saccade Latency	0.84	-2.7	25.98
	Volitional Saccade Latency	0.70	-3.33	56.17
	AntiSaccade % Saccades to Distractor	0.70	-0.02	0.22
	AntiSaccade Latency Saccade to Target	0.87	-37.63**	99.97

Results - Validity

Eye-Tracking Measures

Behavioral Measures	Prosaccade Latency	Volitional Saccade Latency	AntiSaccade % Saccades to Distractor	AntiSaccade Latency Saccade to Target
Prosaccade Discrimination Threshold	**0.45** (.57)**	0.59**	0.12	0.49**
Volitional Discrimination Threshold	0.29*	**0.51** (.73)**	0.13	0.27*
Saccade Inhibition Discrimination Threshold	0.33**	0.67**	**0.27* (.39)**	**0.60** (.77)**

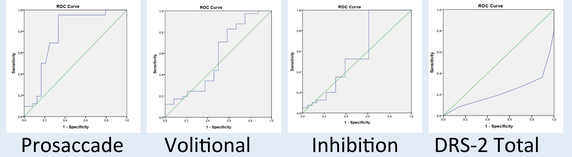
Results – Cognition and Performance

Method	Measure	PD No Cognitive Impairment (n=41)	PD Cognitive Impairment (n=24)	p-value
Behavioral	Prosaccade Discrimination Threshold	269 (56)	297 (56)	0.07
	Volitional Discrimination Threshold	389 (97)	460 (136)	0.022
	Saccade Inhibition Discrimination Threshold	526 (98)	646 (139)	<.001
Eye-Tracking	Prosaccade Latency	384 (38)	408 (45)	0.026
	Volitional Saccade Latency	490 (49)	542 (73)	0.001
	AntiSaccade % Saccades to Distractor	40 (25)	58 (25)	0.009
	AntiSaccade Latency Saccade to Target	686 (164)	844 (210)	0.001

Current Study – Normative Data Collection

Enrolling 80 healthy older adults

First 24 healthy adults compared to 41 PD normal cognition



Prosaccade Volitional Inhibition DRS-2 Total

Conclusions

The present findings support further development and use of behavioral tasks for assessing saccades in PD. The tasks are currently used in several clinical trials of interventions to enhance cognition in PD. Use of the tasks in clinical trials in other may provide incremental sensitivity to cognitive changes in other conditions as well.