Inverted saccade adaptation in Parkinson's disease

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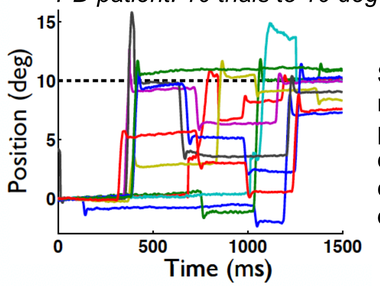
INTRODUCTION

Parkinson's disease (PD) can first present with visual or oculomotor pathology.

PD patients can have very hypometric saccades, attaining targets in multiple movements ('staircase saccades').

PD patient: 10 trials to 10 deg



Such severe saccadic dysmetria is more typically seen in cerebellar patients, whose cerebellar adaptive control mechanism that reduces consistent post-saccadic errors is damaged.

Adapting amplitudes upwards and downwards are known to involve different mechanisms.

Q1: Could the basal ganglia be preferentially involved in upward saccade adaptation (SA)?

Q2: Could PD hypometria be due to dysfunctional upward saccade adaptation?

The one previous study of upward reflexive saccade adaptation in PD (*MacAskill et al., Brain 2002*) reported normal upward adaptation.

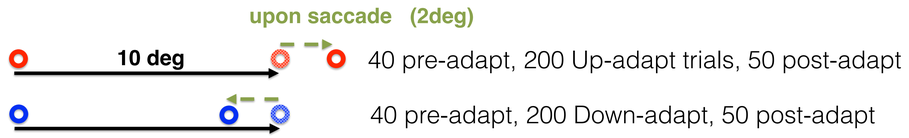
We tested 16 PD patients (ON-medication) and 16 age-matched controls in both upward and downward adaptation sessions, using rapid inter-trial intervals (0.35s; see *Gray et al., J Nphys 2014*).
A separate baseline experiment was also recorded (no adaptation).

PD Patients Table

Gender	Age	Hoehn & Yahr Scale	Duration	Medication	Expt
F	51	1	3	Pramipexole, Rasagiline	Adapt & Base
F	52	2	4	Pramipexole, Rasagiline	Adapt & Base
F	61	1.5	4	Carbidopa/levo, Pramipexole	Adapt & Base
M	66	2	8	Carbidopa, Rasagiline	Adapt & Base
M	67	1	4	Selegiline	Adapt & Base
F	67	2	18	Carbidopa/levo, Ropinirole	Adapt & Base
F	69	1	5	Carbidopa/levo, Pramipexole	Adapt & Base
F	71	1	4	Carbidopa/levo, Ropinirole	Adapt & Base
M	72	2	8	Carbidopa/levo	Adapt & Base
F	74	2	8	Carbidopa/levo, Ropinirole	Adapt & Base
M	77	2.5	3	Carbidopa/levo	Adapt & Base
F	80	2	2	Carbidopa/levo	Adapt & Base
F	54	2	1	Rasagiline	Adapt Only
F	66	1.5	2	Carbidopa/levo, Entacapone	Adapt Only
M	67	1	2	Rasagiline	Adapt Only
F	84	1	5	Carbidopa/levo	Adapt Only
M	58	1	3	Carbidopa/levo	Base Only
M	67	2.5	4	Carbidopa/levo, Pramipexole	Base Only
M	74	2	5	Carbidopa/levo	Base Only
M	77	2	2	Carbidopa/levo	Base Only
Mean	**67.5**	**2**	**5**		**20**

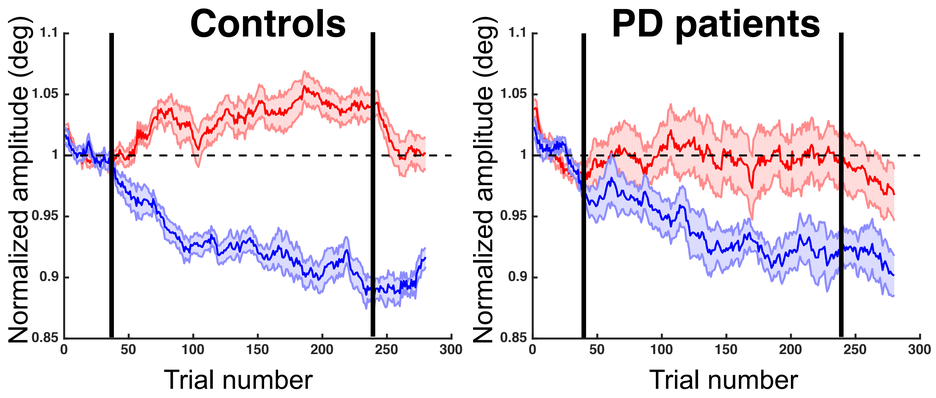
Controls age: 66.7 yrs (t=0.22, p =0.83)

ADAPTATION



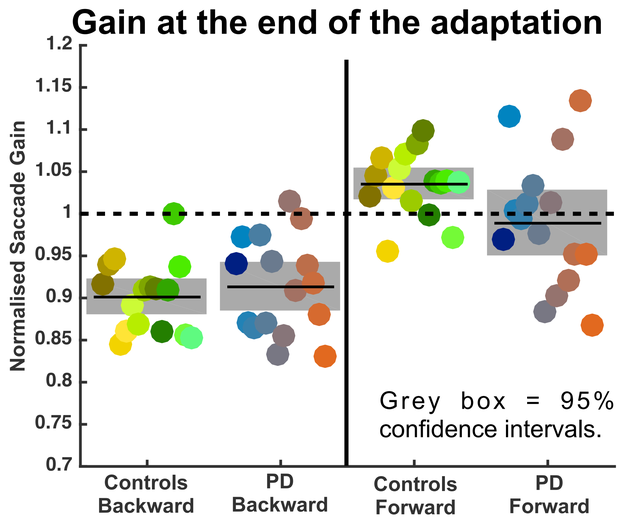
40 pre-adapt, 200 Up-adapt trials, 50 post-adapt

40 pre-adapt, 200 Down-adapt, 50 post-adapt



Novel finding: PDs did not adapt up (p > 0.54), and a proportion showed an inverted (downward) amplitude change to onward target steps.

PDs adapted down strongly (p << 0.001), and were not significantly different from age-matched controls in the down direction (p > 0.4).

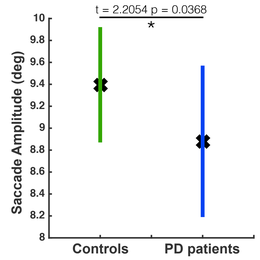


There were more individual differences in the Upward adaptation PDs.

We tested if individual differences in adaptation magnitudes correlated to baseline gain in a second non-adaptation experiment.

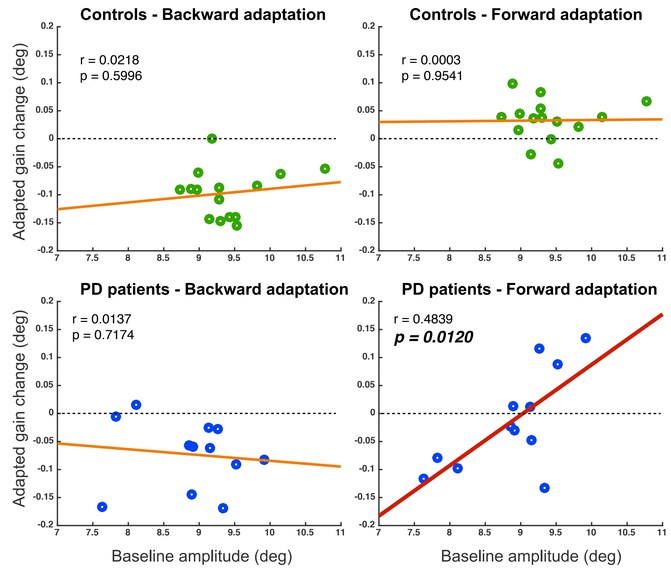
BASELINE AMPLITUDES

Alternating blocks of short (0.35s) and long (1.1s) inter-trial intervals (ITI) were used to measure baseline amplitudes of 10 deg saccades (n=224) in each subject. Twelve subjects completed both Baseline & Adaptation experiments.



Inter-trial interval did not affect amplitude, and neither did block number (p > 0.05).

PDs were more hypometric (p < 0.05)



Baseline amplitude was correlated with upward adaptability alone, and only in the patients.

CONCLUSION

Specific PD deficit in upward adaptation suggests a role for the basal ganglia in SA, perhaps via reinforcement.

PD staircase saccades might be causally linked to upward SA deficit. Conjecture:

Basal Ganglia lesion → Forward Adaptation Deficit → Saccade Hypometria (staircase)

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