

Reduced saccadic velocity and pupillary width in young onset Parkinson's disease

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ABSTRACT

Patients with Young onset Parkinson disease patients (YODP) are individuals with motor complications identical to late onset Parkinson's disease (PD) but onset in early age. YODP is a specific subgroup of PD and their performance on saccadic eye movements is not well established. This study evaluated saccadic eye movements in patients with YODP (< 40 years at onset of illness). Eye movements were recorded during saccadic eye movement tasks, induced by presentation of a visual target and reflexive saccadic task was administered. YODP patients showed reduced saccadic velocity on reflexive saccadic task (Gap task) as compared to their age matched healthy controls. Additionally, pupil width in gap period and at saccade onset was measured. Pupil width was significantly smaller in patients with YODP as compared to control subjects. Reduced saccadic velocity implies that Parkinson's disease affects saccadic circuitry in patients with YODP reflecting impaired circuitry at the brainstem level. The reduced pupillary response in gap condition is attributed to deficits in motor preparedness in patients compared to controls.

1. Introduction

Fast eye movements named saccades are very important eye movements involved in the processing of visual information in the environment. These saccadic eye movements are exogenously triggered (Reflexive) or endogenously triggered (Voluntary). Reflexive saccades mainly involve saccades towards a visual target (Krauzlis, 2008). Most of the previous studies have investigated saccadic performance in patients with late onset PD (Briand, Strallow, Hening, Poizner & Sereno, 1999; Briand, Hening, Poizner & Sereno, 2001; Chan, Armstrong, Pari, Riopelle & Munoz, 2005). Present study intends to contribute to the understanding of saccadic eye movement performance in patients with young onset Parkinson's disease.

Saccadic peak velocity is a very important saccadic parameter and any changes in this parameter could possibly reflect impairment of normal functioning of the saccadic circuitry in the structure like brainstem. Saccadic velocity as a saccadic parameter has been shown to be impaired in late onset PD in some reports (Shibasaki, Tsuji & Kuroiwa, 1979; White, Saint-Cyr, Tomlinson, & Sharpe, 1983; Nakamura et al., 1991; Lohnes & Earhart, 2011) and have been reported to be spared in others (DeJong & Jones, 1971; Bronstein & Kennard, 1985).

Visual information processing starts once the light enters pupil (Wilhelm, 2008). Changes in the size of the pupil are under the control of muscles (sphincter and dilator pupillae) and a well-established neural circuitry (Wang & Munoz, 2015). Parasympathetic and sympathetic system regulates pupil size and pupillary changes are a reflection of information processing in the cortex (McDougal & Gamlin, 2015). Pupillary size changes are mainly in response to light reflex and accommodation, but there are also some very small changes which are considered to be reflection of higher order cognitive processes (Beatty, 1982). Pupil dilation has been studied using eye tracking system when subjects perform on eye movement tasks. Pupil dilation has been reported to be a reflection of motor preparations. Greater dilation has been reported in gap trials (Jainta, Vernet, Yang & Kapoula, 2011). In Gap task, fixation point is removed 200 ms prior to target onset and this period is considered to be motor preparatory stage (Rolfs & Vitu, 2007; Moresi et al., 2008) and the pupil width dilation reflects motor preparation. Also, pupil size measurement at the saccadic execution reflects advanced motor preparations dependent on saccadic latencies. Wang and colleagues (Wang, Brien & Munoz, 2015) showed saccadic preparation modulated pupil size. Larger pupil dilation is reported for antisaccades as compared to prosaccades. Also, faster saccades for target had larger pupil dilations prior to target appearance. Pupillary

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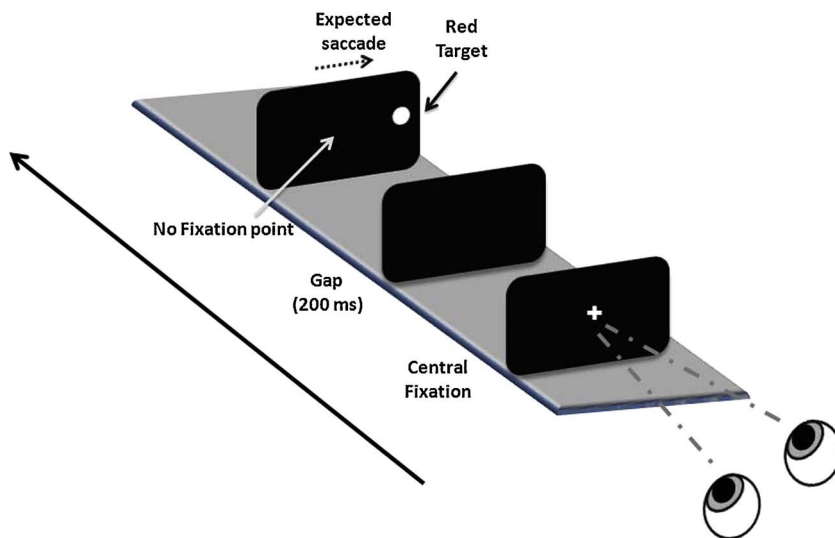


Fig. 1. Schematic representation of stimulus presentation in reflexive saccadic task.

Participants executed saccades in response to the onset of a red peripheral target, 200–300 ms after the disappearance of the fixation point

changes have been reported in PD when compared to age matched controls (Micieli et al., 1991; Giza, Fotiou, Bostantjopoulou, Katsarou & Karlovasitou, 2011).

In this study, the saccadic eye movements were investigated under gap condition in reflexive saccadic tasks to further our understanding of control of saccades in patients with young onset Parkinson's disease (YOPD). YOPD patients are individuals with motor complications identical to PD but onset in early age (Schrag & Schott, 2006). YOPD tends to have more gradual progression of Parkinsonian signs and symptoms (Golbe, 1991). Patients with YOPD progress more slowly in terms of motor features and have a longer disease course when compared to late onset PD. As the pathology in PD and YOPD is similar (Gibb & Lees, 1988), we expected abnormal saccadic performance in patients with YOPD. However, there are not many published reports, which have quantified saccade performance in YOPD cases. Present study aims to determine saccadic eye movement abnormalities in patients with YOPD during reflexive saccade task.

Saccadic velocity and pupil width were assessed at saccade onset and in gap period in reflexive saccadic task in YOPD. Saccadic changes have been reported in patients with late onset PD in various parameters. To the best of our knowledge there are no reports on saccadic velocity or on pupil size at the time of saccade execution in young onset Parkinson's disease. In the present study, we have recruited patients with Young onset Parkinson's disease and their age matched participants to investigate pupil width and saccadic velocity in reflexive saccadic task to get an insight into deficits in motor preparation and allocation of attentional resources in YOPD.

2. Materials and methods

Study participants consisted of YOPD (12 male, Age: 37 ± 4 year) and age matched control group (10 male, Age: 35 ± 3 years). The mean disease duration was 5.17 ± 1.27 years with mild to moderate PD (Hoehn and Yahr stages: 1–3). Patients with YOPD were recruited from Movement disorder clinic of Department of Neurology, All India Institute of Medical Sciences (AIIMS), New Delhi, India. Healthy controls were students/employees of the institute and spouse/attendants of patients. Patients with YOPD were diagnosed by Board Certified Neurologist at AIIMS specialized in movement disorder. Patients with YOPD diagnosed on the basis of standard diagnostic criteria. Patients with YOPD with age of onset < 40 years were included in the study. Patients with co-morbid neurological illness i.e. stroke, dementia etc were excluded from the study. Patients with known history of coexisting mental illness and subjects with visual impairment were also excluded from the study. Patients were tested on “On medication” at best motor

response time. Saccadic eye movements were recorded by an infrared based Arrington Viewpoint eye tracker system (Arrington Research, Inc. USA). Sampling rate of the eye tracker was 60 Hz. Images of the dark pupil created by the reflection of the infrared light from the eye were captured. Monitor control was adjusted to maximize contrast and screen was made dark in the setting of a dark room. Participants sat 70 cm from the screen of the monitor and their head was immobilized by chin and forehead rest. Calibration feature was used before each experiment. Saccadic start point and end point were determined by the experimenter manually for each saccade.

Each participant was asked to report in the morning session in the lab. The study was approved by ethical committee for human participants of All India Institute of Medical Sciences (AIIMS), New Delhi. All the patients and controls were informed about the aims and objectives of the study and were asked to duly fill the written consent form. They were asked to take their medication as usual on the day they were to be tested. Before the testing, procedures were explained followed by a short interview to gather information related to medication, disease history, education and their daily routine. Testing was done only when the participants were comfortable with the procedure and to avoid fatigue participants were instructed to take break whenever they felt tired or uncomfortable during the study. Testing was withdrawn if the participant reported inability to perform on the task.

Stimulus presentation was done using command function of the Arrington viewpoint eye tracker. All the participants performed the reflexive saccade task as explained below. Task was designed to elicit horizontal saccades to the left or to the right of the central fixation point.

2.1. Reflexive saccadic task (Gap task)

In the reflexive saccade task, participants were instructed to make horizontal saccades with the onset of peripheral target to the left or to the right of the central fixation point. The central fixation stimulus was green (plus shaped) and target stimuli was red (circular in shape) (Fig. 1). Target appeared 200–300 ms after central fixation point disappearance. They were instructed to fixate on the green plus sign in the centre of the computer screen and to move their eyes as quickly as they can towards the red circles in the periphery when they appear. Time duration of the fixation cross varied between 1000 ms–3000 ms during the task. Participants were instructed to move their eyes accurately towards the red circles (Fig. 1). Training trials were given to participants to make them comfortable with the tasks. Verbal feedback was given to participants in case of any confusion with the task procedure during training trials.

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