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Original Article

Effect of Parkinson's disease on audiovisual reaction time in Indian population

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ABSTRACT

Parkinson's disease is a progressive neurodegenerative disorder caused by loss of dopaminergic neurons in the basal ganglia. Objective : To evaluate sensorimotor processing in the CNS in patients with Parkinson's disease. Method : Reaction time serves as an index of psychomotor performance useful for estimating the severity of disease. Reaction time of 30 controls in age group 50-70 years and 30 age-matched Parkinson's patients on treatment was taken with the help of a reaction time apparatus. Results : An increase in both simple VRT and ART was found in Parkinson's patients when compared to controls ($p<0.001$). Conclusion : This increase in reaction time may be attributed to defect in motor programming and reduced signal-to-noise ratio due to dopamine deficiency. Emphasis is also laid on role of non-dopaminergic pathways mediating reaction time.

1. Introduction

Reaction time is the time from onset of a stimulus to the occurrence of response [1]. It has been recognized since the mid-nineteenth century as a potentially powerful means of relating mental events to physical measures. It plays a certain role in measurement of psychomotor performance and as an adjunct to tests of psychological functioning.

Parkinson's disease is a progressive neurodegenerative disorder characterized by its three cardinal signs i.e. rest tremors, rigidity and bradykinesia. Postural instability or impaired balance appears to be the 4th cardinal sign later in the course of the disease. Idiopathic Parkinson's disease can be diagnosed clinically by the presence of atleast two of the three cardinal signs [2]. The typical age of onset of idiopathic Parkinson's disease ranges between 35-85 years of age with peak in early 60s. It is estimated to occur in 1-2% individuals over age 65. The disease is caused due to loss of dopaminergic transmission within the basal ganglia as a result of neuronal loss in the substantia nigra.

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Reaction time studies can be used to analyse objectively pre-movement abnormalities in Parkinson's disease. Reaction time may provide a useful prognostic tool for estimating severity of Parkinson's disease [3]. Thus, though reaction time may not provide a substitute for the neuropsychological tests in Parkinson's disease, backed by clinical judgement, it does have important role as an index of psychomotor performance in various mental disorders including Parkinson's disease. Recently, attention has been focused primarily on the issue of programming of responses employing reaction time paradigms. Most of the studies on reaction time in Parkinson's disease are conducted on western population with variable results. This study was, therefore, conducted in Indian population to see effect of Parkinson's disease on reaction time.

2.Materials and Methods

The study was conducted in Department of Physiology in Topiwala National Medical College and B.Y.L Nair Charitable Hospital, Mumbai. 60 subjects in the age group 50-70 years participated in the study. They comprised of 30 controls including 18 males and 12 females and 30 patients including 21 males and 9 females. Controls included apparently healthy subjects who were spouses, relatives accompanying patients and laboratory staff. The subjects were briefed about the study protocol and informed consent was taken. The clearance from the ethical committee of the institution was taken for the study.

Cases included in the study were clinically diagnosed patients of idiopathic Parkinson's disease with disease duration upto 5 years recruited from Neurology OPD. Patients with atleast two of the three cardinal signs of Parkinson's disease, i.e rest tremors, rigidity and bradykinesia and currently on treatment were selected for the study. Each volunteer underwent a detailed neurological examination to clinically rule out any other impairment of the nervous system. Each subject was subjected to a thorough ophthalmological and ENT examination to rule out any visual or auditory defect. Alcoholics, smokers, diabetics, hypertensives and subjects with history of thyroid disorders, depression, dementia, schizophrenia or any other psychiatric disorder which can affect reaction time were not included in the study. Subjects with long term steroid therapy or psychotropic drugs, anti-hypertensives or anti-diabetic drugs were excluded from the study.

The test was carried out in a secluded room with subject sitting comfortably during morning hours after having light breakfast. 7-8 practice sessions were given to the subject before recording the actual readings. The instrument used for measuring reaction time was REACTION TIMER RTM-608 supplied by Bio-Tech India, which records both auditory and visual reaction time. Before presenting any stimulus, a warning signal in the form of a verbal instruction "READY" was given to the subjects. To record simple visual reaction time, RED colour stimulus was chosen and for recording simple auditory reaction time, HIGH frequency sound was selected. The subject was supposed to respond to the RED light presented to him by pressing a button on the subject's panel with index finger of the right hand as soon as possible. This would give simple visual reaction time of the subject in seconds over a digital display mounted on the examiner's panel. Similarly, subject was instructed to respond immediately to HIGH frequency sound presented to him by pressing the corresponding button on his side on hearing the sound with the help of headphones provided with the instrument. This would give a record of simple auditory reaction time in seconds over the same digital display. A set of three recordings of each i.e simple VRT and ART was taken and an average of these was taken.

2.1.Statistical analysis

The data were tabulated and evaluated using unpaired 't' test for comparison of means. Descriptive statistics i.e mean and standard deviation is used for numerical data. P-value less than 0.05 was considered statistically significant.

3. Results

Table 1 shows characteristics of subjects selected for the study. Table 2 shows that mean simple VRT for red colour was high in Parkinson's patients as compared to controls, the values being 0.4591 and 0.3125 seconds respectively.(Figure1)

Table 3 shows that mean simple ART for high frequency in Parkinson's patients is higher (0.3888 seconds) compared to controls (0.2563 seconds).(Figure 2)

Table 1 : Demographic characteristics of subjects

Variables	Controls	Patients
Number of subjects	30	30
Age(years)	59.2±5.53	59.8±5.38
Male: Female	18:12	21:09
Duration of disease(yrs)	_	3.68±0.79

Table 2 : Comparison of mean values of Visual Reaction Time (for Red colour) among Parkinson's disease patients and Controls

Group	Visual Reaction Time (Red) in sec				Unpaired t-test
	Mean	S.D.	t-value	p-value	Significance
Parkinson's patients (n=30)	0.4591	0.0400	17.0280	<0.001	Significant
Controls (n=30)	0.3125	0.0250			

Figure- 1. Comparison of mean values of visual reaction time (for Red color) in Parkinson's disease patients and Controls

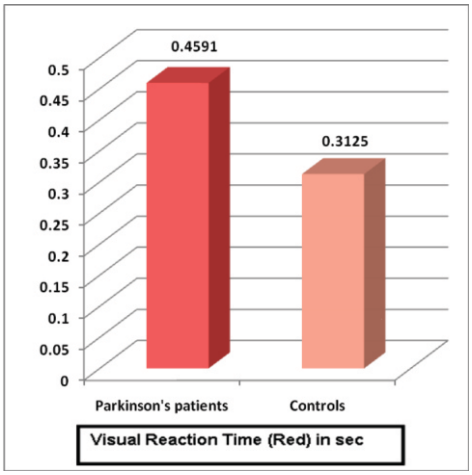
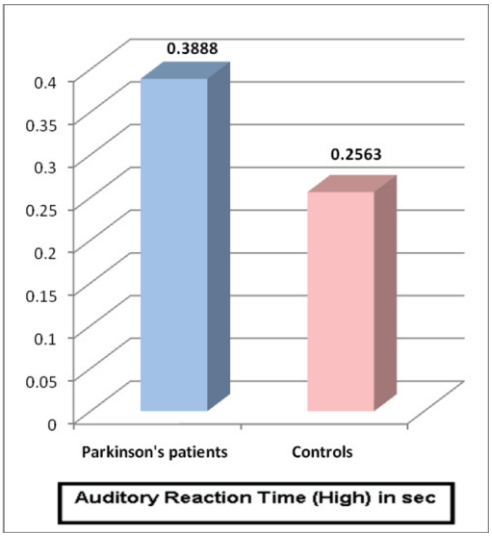


Table 3 : Comparison of mean values of Auditory Reaction Time (for High frequency) among Parkinson's disease patients and Controls

Group	Auditory Reaction Time (High) in sec				Unpaired t-test
	Mean	S.D.	t-value	p-value	Significance
Parkinson's patients (n=30)	0.3888	0.0361	16.0390	<0.001	Significant
Controls (n=30)	0.2563	0.0273			

Figure- 2. Comparison of mean values of Auditory Reaction Time (for High frequency) among Parkinson's disease patients and Controls.



4. Discussion

Reaction time is taken as an index of the brain's biological efficiency because it is a relatively straight forward means of subjectively evaluating the more complicated central executive machinery that controls sensorimotor coordination. It serves well to represent the functional changes in CNS indicating the deficit in sensorimotor processing. In the present study, mean simple visual reaction time and simple auditory reaction time both were found to be significantly increased in Parkinson's patients as compared to controls.

Similar results have been derived in some of the earlier studies. E.V.Evarts and his colleagues reported that mean simple visual reaction time in Parkinson's patients was significantly higher than controls with high statistical significance [4]. S. L. Pullman et al [5] found a statistically significant increase in simple VRT in Parkinsonians on treatment compared to controls. Nigel Jordan and his colleagues also observed significantly higher readings in mean simple VRT in both treated and untreated Parkinson's patients compared to controls [6].

Similar studies with increased simple auditory reaction time were also reported by some authors. Fusako Yokochi and his colleagues reported statistically significant increase in simple mean ART in patients compared to controls [7]. James A. Cooper et al [8] also found a prolonged latency in response to tone in Parkinsonians than controls. Also, C A Bloxham and his colleagues broadly supported that Parkinsonians have slower ART compared to normal elderly population [9].

Prolongation of both simple VRT and ART in Parkinson's patients could be a result of a defect with motor programming that leads to problems with motor execution. Evidence for a defect in motor programming in patients with Parkinson's disease comes from a number of studies which have shown a significant prolongation of simple reaction time (SRT) in Parkinsonians [10]. In simple reaction time tasks, a single response has to be produced every time the stimulus is perceived. The subject, therefore, has an opportunity to programme his response in advance of the stimulus. Thus, in SRT tasks, it can be assumed that the response has already been pre-programmed. The subject now requires only detecting the imperative stimulus in order to produce the response. The slowing of reaction time in Parkinsonians, despite this fact, indicates that patients with this disease are unable to take the advantage of this pre-programming . As a result of this, the programming takes place after the imperative stimulus with a consequent increase in reaction time [11, 12].

Also, evidence from Jahanashi et al [10] suggests that, when provided with spatial information about a forthcoming movement, patients with Parkinson's disease are slower than normal controls in using that information to prepare a response [13].

Deficits in programming the response in advance of the stimulus occurs due to degeneration of basal ganglia, which is involved in planning and programming a particular movement [14]. Degeneration of basal ganglia leads to dopamine deficiency. Dopamine deficiency leads to reduced transmission of information from basal ganglia to cortex. Before a particular movement can be executed, sufficient cortical motor excitability has to be built upto a certain level. Experiments using transcranial magnetic stimulation [15] have shown that this build up is slower in patients with Parkinson's disease.

The visual and auditory information perceived by the subject, via the visual and auditory pathways go to the visual and the auditory cortex respectively. This information is then carried to the motor cortex. Motor connections from the motor cortex, then project to the basal ganglia, mainly the putamen. Neurons in the striatum do not discharge before neurons in motor cortex are activated by sensory input [16]. This motor circuit, connecting the cortex and basal ganglia, projects almost exclusively back to the supplementary motor area (SMA). SMA has been found to influence motor planning, thus, affecting the cortical neuronal discharges. From the SMA, the information is relayed in the ventrolateral thalamus and from here, back to the cortex which sends commands to the appropriate effectors to perform the required voluntary activity. SMA has been found to contain a significant proportion of neurons exhibiting a preparatory-set related activity also known as motor readiness prior to a particular movement [17]. Also, positron emission tomography has demonstrated activation of SMA when normal subjects carry out a simple reaction task.

In Parkinson's disease, there occurs diminution in this preparatory-set related activity suggesting disruption of basal ganglia-supplementary motor area connections. This may be related to difficulties in preparing the instructions to move [18]. Thus, from above discussion, it can be concluded that reduced

activity of basal ganglia causes decreased activation of SMA. This leads to insufficient excitation of motor cortex, which is involved in execution of motor output in a simple reaction task in Parkinson's disease.

Also, it is important to note that the SMA and its connections are non-dopaminergic. Findings of several studies [19] showing simple reaction time not being significantly affected by dopamine replacement further provide some proof of the possibility that the SMA may serve as a substrate for processing simple reaction time tasks. In addition, Parkinson's disease is known to involve several neurotransmitter systems, and it has been suggested that a widespread decrease of norepinephrine (NE) may contribute to clinical deficits such as slowness in response initiation. A study conducted by Yaakov Stern, Richard Mayeux and Lucien Cote [20] reported a significant positive relationship between simple reaction time and cerebrospinal fluid levels of the NE metabolite 3-methoxy-4-hydroxyphenethyleneglycol (MPHG) in Parkinson's patients. They observed that as the MPHG concentration increased in Parkinson's patients, the simple reaction time also prolonged. This suggests that NE might play an important role in the clinical manifestations of Parkinson's disease.

Bradykinesia observed in Parkinson's disease is due to a deficit in execution which leads to problems in recruiting appropriate levels of muscle force sufficiently fast as to produce a response. Bradykinesia appears to be one of the causes that contribute to the magnitude of reaction time impairment. Apart from bradykinesia, other factors like tremors and rigidity may also contribute to increased reaction time.

An increased reaction time in Parkinson's disease could also be attributed to a reduced neural signal-to-noise ratio. For a sensation to be perceived, the neural impulses resulting from the sensory stimulation have to be distinguished from a background of random neural activity i.e neural noise. This neural noise is present in the sense organs, pathways to brain and structures within brain. If the neural impulses arising from the sensory stimulation are weak, it will be necessary to accumulate them over an appreciable period of time before they can be reliably distinguished from the neural noise. As they become stronger, the signal-to-noise ratio increases and the amount of accumulation needed becomes less [21].

In Parkinson's disease, a depletion of dopamine in the basal ganglia leads to an increase in neuronal noise, the behavioural consequence of which is that the patients always perform as if they had a secondary task demand. The pathophysiological basis of this reduction in signal-to-noise ratio could be due to role of dopamine in stimulating neural activity in direct pathway from striatum to GPi, which disinhibits thalamus. At the same time, it diminishes activity in indirect pathway, which normally inhibits thalamus. Lack of dopamine may lead to loss of amplification of cortically initiated signals and difficulty in distinguishing signal from noise.

Findings of a study conducted by C. A. Bloxham, D.J. Dick and M. Moore [9] has led to the interpretation that basal ganglia plays an important role in increasing the signal-to-noise ratio of information processing within this system and transmits this information to the cortex. Dopamine deficiency in the basal ganglia, as occurs in Parkinson's disease leads to a reduced transmission of information through the basal ganglia to the cortex. The motor consequences of this dysfunction could be a reason for the prolonged reaction times seen in Parkinson's patients.

Apart from the above studies, there have been a few studies that do not show consistent deficits in reaction time in Parkinson's patients when compared to the normal individuals.

William P. Goldman et al [22] compared simple auditory reaction time in controls with age matched patients of Parkinson's disease. The findings of the above study showed no slowing of reaction time in the patients when compared with the controls.

George. A. Talland compared simple visual reaction time of 25 Parkinsonian patients with varying degrees of motor incapacity with age and sex-matched controls in age group of 30-69 years. His findings suggested no loss of speed in reaction time as compared to controls in patients with mild to moderate disability. However, reaction time was significantly prolonged in those who were severely incapacitated [23].

Reaction time differences observed among the various Parkinson's patients across different studies lies in the wide range of symptomatology which can exist within any group of Parkinsonians. Also, differences in severity and progression of disorder in the patients selected in a particular study must be kept in mind. Since, it is virtually impossible to have comparable severity of illness across different studies reaction time impairments may have been detected in some studies, while some studies fail to do so. Variations in magnitude of slowing of reaction time may also be attributable to variations in procedure and patient sampling as well as the duration of the disease.

5. Conclusion

A deficit in motor programming and reduced signal-to-noise ratio due to degeneration of basal ganglia leading to dopamine deficiency is responsible for increased simple VRT and ART in Parkinson's disease. Also, disruption of basal ganglia-SMA connections leads to diminution of preparatory-set related activity occurring in SMA. Apart from dopaminergic neurotransmission, SMA and its connections which are non-dopaminergic might also be held responsible for increase in reaction time observed in Parkinson's patients.

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