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RESEARCH ARTICLE

Comparative analysis of choice reaction times with randomly variable foreperiods in normal individuals and schizophrenic patients

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ABSTRACT

Background: Reaction time (RT) is an index of brain's biological efficiency. RT can indicate sensorimotor variability with varying foreperiods (FPs) and can indicate mental dysfunction like schizophrenia. **Aims and Objective:** Objective was to analyze the effect variable FPs on RTs in controls and schizophrenic patients. **Materials and Methods:** The study was conducted at Topiwala National Medical College, Mumbai, on 80 normal controls and 80 schizophrenic patients in the age group of 20-50 years. Digital RT apparatus (RTM-608) manufactured by Bio-Tech., with a maximum resolution time of 0.0001 s was used. Auditory RT (ART) and visual RT (VRT) with randomly variable FPs (2, 4, and 6 s) were recorded in controls and schizophrenic patients. **Results:** Two-way ANOVA with replication in MS Office Excel was used to analyze results. ARTs and VRTs in schizophrenic patients were significantly slower than that in controls with P = 1.4336E-215 with F = 6779.53969 and P = 2.5966E-209 with F = 6161.152654, respectively. The condition effect was also significant with ARTs and VRTs, increasing in patients with increase in the FPs with P = 4.84285E-16 with F = 73.35131426 (ART) and P = 2.72532E-14 with F = 63.68037666 (VRT), respectively. The Group X condition interaction also was significant with P = 8.80207E-12 with F = 50.27084108 in case of ARTs and P = 1.21054E-10 with F = 44.36301991 in case of VRTs. **Conclusion:** This shows that variation in FPs results in slower RTs in schizophrenic patients than in controls.

KEY WORDS: Choice Reaction Time; Foreperiod; Variable; Cognition; Schizophrenia

INTRODUCTION

Reaction time (RT) is the time interval between application of stimulus and appearance of appropriate voluntary response. It can be considered as a reliable indicator of both the rate of processing of sensory stimuli by central nervous system and the speed of motor response.[1,2]

RT has been a proven index of brain's biological efficiency.[1] RT can indicate mental dysfunction in various mental disorders like schizophrenia.[3] Schizophrenia is a disorder of central nervous system with grossly decreased cognitive function, decreased psychomotor ability, decreased perceptual skill, and decreased response selection ability.[4] RT provides a useful procedure for assessing the severity of schizophrenia and for monitoring the effects of medication.

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MATERIALS AND METHODS

Study Population

The study was conducted at Topiwala National Medical College, Mumbai, on age-matched 80 normal healthy controls and 80 schizophrenic patients (males and females) in the age group of 20-50 years, who were selected randomly by simple random sampling technique.

Patients with a history of schizophrenia for more than 2 years and on medication and with no history of violence in the past 6 months were taken. In case of females (patients and controls), those in proliferative phase of menstrual cycle were selected for the study. Subjects with any neurological impairment or hearing or visual impairment or color blindness in control and patient groups were excluded from the study.

Patients on tranquilizers, barbiturates and long-acting sedatives throughout the period of testing and examination, those with history of smoking, alcohol consumption, depression, epilepsy, and diabetes were excluded from the study. Females in menstrual or secretory phase of menstrual cycle were also excluded from the study.

All subjects were explained in detail in the language understood by them and to their satisfaction about the procedure of the tests to be conducted on them. Voluntary written informed consent was taken from normal controls and guardians of schizophrenic patients.

The study was approved by Institutional Ethics Committee of Topiwala National Medical College and B.Y.L. Nair Charitable Hospital, Mumbai.

Materials

Digital RT apparatus (RTM-608) manufactured by Bio-Tech (India), Mumbai, which has got maximum resolution time of 0.001 s was used in this study.

Methods

In this study, the examiner sat with the master (primary) controls on one side and subject sat on another side with secondary controls separated by the opaque partition, which prevents seeing which switch the examiner pressed. Below the digital time display, there was a press button for resetting the machine to zero timing. Headphone was provided to the subject for auditory ART (ART).[5]

Once the unit was switched on, the examiner presented either visual signals (red, green, or yellow lights) or auditory signals (high, medium or low frequency sounds) to the subject at random. The RT timer starts immediately and the corresponding signals occur on both sides. The subject immediately responded by pressing the appropriate switch on his / her side. The RT timer stops immediately and the RT was recorded on RT apparatus in seconds. In case a wrong button is pressed, the timer continues to run without stop. Only correct responses were recorded.[5]

The tests were carried out between 9.30 and 10.30 am in an isolated room to prevent any disturbance/distraction which can affect RT. The tests were conducted in the presence of a guardian in case of patients. In case of female patients, female guardian and female assistant were always present, and for female controls, tests were conducted in the presence of female assistant. All subjects (patients and controls) were thoroughly acquainted with the operating mechanism of RT apparatus. Subjects used their index finger to press the appropriate button immediately after receiving the visual or auditory stimulus.

For recording visual reaction times (VRT) red, green or yellow lights stimuli were presented to the subjects at random. For recording auditory reaction times (ART) high, medium or low frequency sound stimuli were presented to the subjects at random. Foreperiods (FPs) (time interval between “ready” signal and application of stimulus) were randomly varied in the form of 2, 4 and 6 seconds. Before taking readings, six to seven practice sessions were given to subjects. Before presenting any stimulus, a warning signal in the form of a verbal instruction “Ready” was given. For each subject, three test recordings were done for each of red, green, and yellow lights in case of VRTs and for each of high, medium and low frequency sounds in case of ARTs for each of the FPs of 2, 4 and 6 seconds. The average values of these recordings were calculated in each category (that is) red, green, and yellow in VRTs and high, medium and low frequencies in ARTs for each of the FPs. Finally, the combined average is calculated from the average values of three categories of VRTs and same is done for ARTs at each FP. For the final analysis of the results, these combined averages were used as final VRTs and ARTs for respective FPs.

Statistical Analysis

Statistical analysis was performed using Microsoft Office Excel 2007 software. Descriptive statistics, i.e., mean and standard deviation was used for numerical data. Statistical significance was set at a value of $P < 0.05$. Two-way ANOVA with replication was applied to analyze the group effect (control vs. patient group), condition effect (randomly varying FPs), and interaction effect (Group X condition) on VRTs and ARTs.

RESULTS

Table 1 shows the average of mean choice ARTs for all frequencies in controls and patients at randomly variable FPs of 2, 4 and 6 seconds.

As per the Table 2, the group effect was significant (controls vs. patients), $P = 1.4336E\text{-}215$ with $F = 6779.53969$, with patients of schizophrenia having slower ARTs than the controls.

The condition effect was also significant, $P = 4.84285E\text{-}16$ with $F = 73.35131426$ with ARTs increasing with increase in the FPs and the Group X condition interaction also was significant, $P = 8.80207E\text{-}12$ with $F = 50.27084108$. Figure 1 shows graphical representation of these results with ARTs increasing with increase in FPs from 2 seconds to 6 seconds in controls versus patients.

Table 3 shows the average of mean choice VRTs for red, green, and yellow lights in patients at randomly variable FPs of 2, 4 and 6 seconds.

As per Table 4, the group effect was significant (controls vs. patients), P = 2.5966E-209 with F = 6161.152654, with patients of schizophrenia having slower VRTs than the controls.

The condition effect was also significant, P = 2.72532E-14 with F = 63.68037666 with VRTs increasing with increase in the FPs.

The Group X condition interaction also was significant, P = 1.21054E-10 with F = 44.36301991. Figure 2 shows graphical representation of these results with VRTs increasing with increase in FPs from 2 seconds to 6 seconds in controls versus patients. This indicating that both the disease and the varying FPs affected RTs with slower RTs in schizophrenic patients compared to control group as FPs increased.

DISCUSSION

In this study, all patients of schizophrenia were taking antipsychotic drugs. RT assessment in drug-free patients is not feasible in the studies for clinical reasons. Most existing studies have found no effect of neuroleptic medication on RTs.[6]

In choice RT tasks, the subject has to discriminate between various presented stimuli and make an appropriate choice among various available responses.[2,7]

Table 1: Effect of randomly variable FP on auditory reaction time

ART	Randomly variable FPs		
	2 s mean±SD	4 s mean±SD	6 s mean±SD
Control group	0.668±0.157	0.770±0.155	0.863±0.157
Patient group	4.546±0.789	5.503±0.768	6.488±0.792

RT: Reaction time, ART: Auditory reaction time, SD: Standard deviation, FP: Foreperiod

Choice RT include following processes:[2,7]

a. Reception of the signal by a sense organ and conveyance of data by afferent nerves to the brain,
b. Identification of the signal,
c. Choice of the corresponding response,
d. Initiation of the action that constitutes the response.

In choice RT, the correct response is first selected and prepared and then the response is initiated by the subject. Therefore, choice RT test has a cognitive element. Thus, response is given only after presentation of the imperative stimulus, as this condition is a purely stimulus-driven task.[8] In the choice RT tasks, state of cognitive peak readiness involves less motor activation but is established by optimizing the allocation of attentional capacity at an expected moment of imperative stimulus expectation. Naturally, since cognitive processing (i.e. stimulus categorization, response selection) cannot start before imperative stimulus presentation, a pure temporal anticipation strategy would prevent participants from temporally anticipating the imperative stimulus.[8,9]

To anticipate an incoming event is a cognitive process. In the particular process of anticipating the next incoming event, participants must use simultaneously the following: The knowledge of a repetitive sequence, the sequence of information stored in memory, the instructions provided to anticipate the stimulus and properly perceive the provided stimulus. All these components are integrated to produce motor representation which activates the motor command that initiates the response. Schizophrenics do not benefit from regular and predictable preparatory intervals in RT tasks and show deficiency in explicit and conscious modalities of processing for cognitive tasks where working memory is likely to be involved.[10]

In the studies of the effect of FP duration on RT, it has been shown that the process of time preparation is fatigue-sensitive. Time preparation is set according to the subject's expectation concerning the occurrence of the response signal and can be optimal for a few milliseconds only. When the duration of the FP is varied across blocks of trials, the subject times his (her) preparation so he (she) can be optimally ready at the onset of the response signal.[11]

In the RT tests with variable FP, the classical finding is that mean RT decreases as FP increases. This is because the force exerted on response buttons also decreases as FP increases

Table 2: Two-way ANOVA with replication for ART

Source of variation	SS	df	MS	*F* value	*P* value	*F* critical
Between groups	2145.481	1	2145.481	6779.53969	1.4336E-215	3.871054
FP	23.21306	1	23.21306	73.35131426	4.84285E-16	3.871054
Interaction	15.90891	1	15.90891	50.27084108	8.80207E-12	3.871054
Within	100.0026	316	0.316464			
Total	2284.605	319				

Values are given with±standard deviation (SD). $P < 0.001$.

which may indicate that the FP effect is located at a motoric level of processing.[12] When a subject has to make a rapid response to a signal, RT is shortened if the stimulus is preceded by a warning signal. As the FP duration between warning signal and stimulus decreases, the RT decreases until some optimal FP is reached.[13]

In the variable condition, there is not only one possible moment but also several critical moments at which the imperative stimulus may occur. In the variable FP condition, the imperative stimulus always occurs at random times after the warning signal; hence, reliable response strength cannot develop. In this situation, the individuals have been shown to prepare according to FP-length of the preceding trial. Reinforced response strength from the previous trial carries over to the next trial and elicits response-related activation at the moment which was imperative in the previous trial. Hence, especially short RTs are implied when the FP of the preceding trial is repeated.[8,9]

There are three possible FP sequences in the variable FP condition. First, a FP can be repeated in the subsequent trial. As mentioned before, RT is predicted to be short on the subsequent trial, because response strength was reinforced at the imperative moment in the preceding trial. Second, the FP can alter from long to short. In this case, a long RT should result because the imperative moment was not reinforced in the preceding trial. Finally, the FP can alter from short to long. Accordingly, response strength to an imperative stimulus should increase with FP-length and should be maximal at the latest imperative moment.[8,12] In this case RT will be short.

Slower RTs were observed with the longer FP, consistent with the view that (i) the precision of the time estimates of the response signal decreases with longer durations and (ii) a better level of preparation is attained for short than for long FPs. Time preparation increases neural activation during the particular FP. When the increase in preparatory neural activation bypasses a threshold, termed motor action limit, an overt response is triggered.[8,12]

Table 3: Effect of randomly variable FP on VRT

VRT	Randomly variable FPs		
	2 s mean±SD	4 s mean±SD	6 s mean±SD
Control group	0.667±0.156	0.775±0.158	0.861±0.153
Patient group	4.510±0.793	5.480±0.783	6.439±0.843

VRT: Visual reaction time, FP: Foreperiod, SD: Standard deviation

RT depends on the distance between the motor action limit and the level of neural activation attained during the FP. If this distance is large, the RT is long; in contrast, when the distance is short, the RT is short. When subjects expect the stimulus, they attempt to adjust neural activation close to the motor action limit. Given that the accuracy of this adjustment depends on the precision of time estimation, neural activation is on average higher at the time of occurrence of the stimulus when the FP is short than when it is long.[8,13]

Executive control involves planning, decision making, and error detection. The distinction between orienting, alerting and executive control is evident on the neuronal level. The orienting neural network selectively allocates attention to a potentially relevant area of the visual field, enhancing perceptual processing and involves the posterior parietal lobe, superior colliculus, and thalamus. The alerting network prepares for action by means of a change in internal state and comprises right thalamic, frontal, and parietal regions. This preparation for response can be triggered when a visual or auditory warning signal is presented. This is because orientation of attention, triggering an alert state and resolving response conflicts are processes involved in allocating proper motor response to any sensory stimulus.[14-16]

Executive functions are considered to be a product of various processes (information selection, inhibition, and maintenance), the coordination of which is assumed to be achieved by a mechanism called cognitive control. Thus, executive function deficits in schizophrenia could be accounted for by a specific impairment of the cognitive control mechanism. Working memory activates a network of interconnected cortical and subcortical areas including the prefrontal cortex and the hippocampus. Clinical studies in brain-lesioned subjects support this dissociation between the role of amygdalo-hippocampal regions in memory and that of frontal regions in executive functions. A deficient functional role of frontal cortex might also explain the problems met by schizophrenic patients during working memory tasks.[17,18]

Executive functions are considered to be associated with prefrontal cortex. Multiple executive functions have been shown to activate inferior parietal lobule along with

Table 4: Two-way ANOVA with replication for VRT

Source of variation	SS	df	MS	*F* value	*P* value	*F* critical
Between groups	2115.251	1	2115.251	6161.152654	2.5966E-209	3.871054
FPs	21.86279	1	21.86279	63.68037666	2.72532E-14	3.871054
Interaction	15.23074	1	15.23074	44.36301991	1.21054E-10	3.871054
Within	108.4893	316	0.343320			
Total	2260.834	319				

Values are given with±standard deviation (SD). $P < 0.001$.

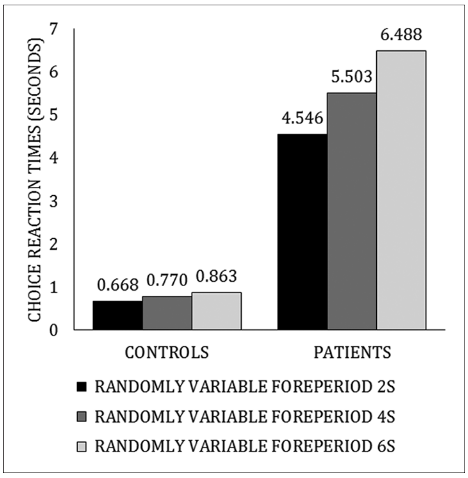

Figure 1: Comparison of choice auditory reaction times with randomly variable foreperiods (2, 4, 6 s) between controls and patients

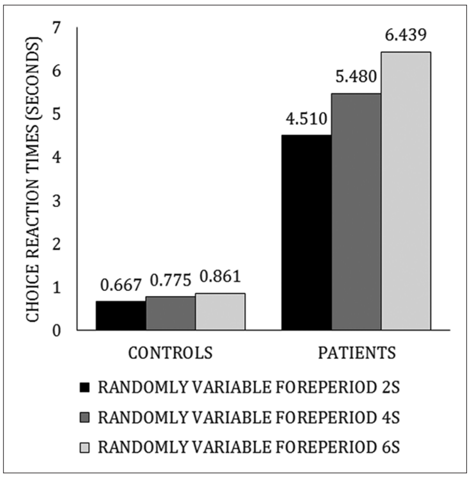

Figure 2: Comparison of choice visual reaction times with randomly variable foreperiods (2, 4, 6 s) between controls and patients

prefrontal cortex. It is thus possible that executive functions are impaired in schizophrenia due to dysfunction in inferior parietal lobule in addition to prefrontal cortex.[19]

The schizophrenia pattern of intermittency of fixed and random choice sequences is best conceptualized as a coexistence of highly predictable and highly unpredictable sequences (dysregulation) within the reservoir of behavioral patterns in an individual schizophrenia patient. Although healthy subjects mainly develop their various strategies in performing this test from the previous one (transitions), schizophrenic patients will persist for a long time in strategies, they have chosen and then will abruptly switch from the old to the new strategy. The response sequences of the schizophrenia patients are characterized by the reduced utilization of possible strategies in attempting to correctly predict the stimulus. This switching between the right and the left button irrespective of the outcome associated with the response can best be described as response perseveration, which may reflect a combination of pressure to act and inability to generate alternative response sequences.[20]

As shown in a neuropsychological study conducted by Stuss et al. 2005, the patients with lesions in the right dorsolateral prefrontal cortex (right DLPFC) fail to show the typical FP effect, unlike both control participants and other subgroups of prefrontal patients. Stuss et al. 2005 suggested that the right DLPFC is likely to be the region responsible for the strategic process producing the FP effect, which controls the state of preparedness by checking the conditional probability of imperative stimulus occurrence. The right DLPFC seems to be the location of a process critical for the FP effect because patients with lesions of this region do not show the typical FP effect.[21,22]

Dysregulation of DLPFC is thought to be central to the neurophysiology of schizophrenia. The link between DLPFC dysfunction and disrupted working memory is a prominent feature of leading cognitive neuroscience models of schizophrenia, which propose that working memory disturbances disrupt guidance of ongoing behavior and lead to the cognitive fractionation and psychiatric symptoms characteristic of schizophrenia.[23]

The schizophrenics experience in performing any task is described as an inability to sustain an intentional focus to attention. The patient's inability to direct a train of thoughts prevents full access to long-term memory so that early components of perception, which are designed to give early warning of stimulus, are overly influential and unmodulated by further mental processing.[24] Neuroscientific models of schizophrenia link structural and functional neuroimaging abnormalities with cognitive and behavioral impairments to suggest that schizophrenia is associated with disruption of the frontal cortex (including the anterior cingulate gyrus), the temporal cortex and the basal ganglia.[25]

It is the coordinated activity of the dorsal parietal and dorsolateral prefrontal cortices that is disturbed in schizophrenia. Since the dorsolateral prefrontal and dorsal parietal cortices are involved in a frontal-parietal executive system, it may be possible that the primary deficit in working memory among individuals with schizophrenia involves a disturbance of central executive function.[26]

An magnetic resonance imaging study of schizophrenic patients using continuous performance test as measure of sustained attention by Pineda et al., 2003, showed significant correlations between continuous performance test and gray matter volume in left supramarginal and angular gyri and it was concluded that these regions were possibly involved in attentional impairment in patients with schizophrenia.[27]

Strengths and Limitations

Instead of using choice RT with fixed FP, we used randomly variable FPs to eliminate any chance of predictability. However, there were limitations too, as we used combined average of average values of red, green, and yellow lights in case of VRTs and high-, medium-, and low-frequency sounds in case of ARTs at each of the randomly variable FPs of 2, 4 and 6 s for analysis.

CONCLUSION

The choices ART and VRT at randomly variable FPs of 2, 4, and 6 s increased more in schizophrenic patients than in normal controls with increase in FPs.

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