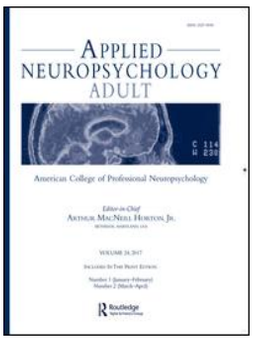

Routledge
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Applied Neuropsychology: Adult

ISSN: (Print) (Online) Journal homepage: https://www.tandfonline.com/loi/hapn21

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To cite this article: Moulika Mandal & Azizuddin Khan (2021): Attention switching deficit in patients of Parkinson's disease who experience freezing of gait, Applied Neuropsychology: Adult, DOI: 10.1080/23279095.2021.1951268

To link to this article: https://doi.org/10.1080/23279095.2021.1951268

APPLIED NEUROPSYCHOLOGY: ADULT
https://doi.org/10.1080/23279095.2021.1951268

Attention switching deficit in patients of Parkinson's disease who experience freezing of gait

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ABSTRACT

Attention switching is involved in postural adjustments for gait. A deficit in attention switching was expected among patients having Parkinson's disease and experiencing freezing. There was a deficit in attention switching abilities among the patients of Parkinson's disease, having episodes of freezing of gait. The task accuracy and reaction time of the freezing group was significantly reduced compared to the non-freezing group having Parkinson's disease and healthy control group on total AST task performance, congruent and incongruent trials. The non-freezing group with Parkinson's disease was also slower than the healthy control group, but its accuracy was not affected. The results suggest that patients with freezing of gait experienced a stronger deficit in attention-switching than the non-freezing group of Parkinson's disease. This attention switching deficit among freezers may imply inappropriate allocation of attention for postural responses required for stepping and resulting in freezing. Also, the non-freezing group may have prioritized accuracy over time as a compensatory strategy that may be slowing their gait but prevents freezing.

KEYWORDS

Freezing of gait; inhibitory control; attention switching; cognition; Parkinson's disease

Introduction

Parkinson's disease (PD) is characterized by progressive neurodegeneration and motor deficits like tremor, bradykinesia, postural instability and, abnormal gait. In the past few decades, cognitive dysfunction has also been considered a central feature of PD due to its contribution to reduced quality of life in PD patients (Davis & Racette, 2016).

Cognitive dysfunction is also known to exacerbate motor symptoms (Yamawaki et al., 2018). Cognitive underpinnings have been previously implied for freezing of gait (FOG) in PD (Peterson et al., 2016). Freezing of gait is an unnerving symptom characterized by the inability to move and feels "glued to the ground," despite their intention and effort to initiate movement. It affects about 50% of PD patients and up to 80% of PD patients in progressed stages (Tan et al., 2011). It is known to increase falls and dwindle quality of life, resulting in the patient's unwavering dependence on a caregiver (Bloem et al., 2001; Moore et al., 2007). Lewis and Barker (2009) proposed the integration of cognitive deficits and the motor and affective deficit as causal factors for FOG. Lewis and Barker (2009) model suggested a deficit in the ability to shift between response sets, which are required to keep up the alternate left-right stepping. Moreover, any situation that demands flexibility and adaptability of gait pattern elevate chances of freezing of gait episodes, such as turning, initiating gait or walking, narrow space, presence of obstacles, nearing the destination, or involvement of any other distraction (Cowie et al., 2012; Snijders et al., 2012). Such conditions often require heightened attentional resources. The risk of falls increased in dual-task conditions or when patients were required to perform another task while walking (Rahman et al., 2008). Therefore, attention deficits have been associated with the freezing of gait phenomena (Tard et al., 2015).

Jacobs et al. (2009) explained that freezing of gait occurs due to abnormal anticipatory postural adjustments before stepping, whether voluntary or involuntary. Timely and appropriately shifting of weight from one leg to another is required to maintain gait. Postural preparation is necessary for the initiation phase of stepping and the leg switching phase. Repeated inappropriate adjustments may lead to a delayed onset. A coupling/coordination of postural adjustments is needed to move from one phase to another. Zettel et al. (2008) reported that attention switching abilities are demanded an automatic postural response to change the phases of stepping. Minimal or no attentional resources are taxed to initiate gait in healthy individuals. They are required in the late phases of stepping and executing the stepping trajectory or the foot lift. Loss in automaticity among PD patients with freezing of gait may increase demands on attention switching abilities even at an early stage of stepping, before lifting the foot to initiate a step (Vandenbossche et al., 2012). In healthy individuals, this demand is relaxed, as the initial stage of stepping is automatic, leaving more attentional resources available.

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Few studies have been conducted to investigate task switching in PD. Based on Lewis and Barker (2009) model, it was postulated that set-shifting processes are primarily affected in patients experiencing the freezing of gait phenomenon (Naismith et al., 2010). Walton et al. (2015) observed that cognitive control is required for goal-directed behavior. The need to organize and prioritize appropriate information processing was involved in a flexible response to changes and was reflected in predicted behavioral outcomes. As the switching demands were introduced, self-monitoring abilities to cope with conflict-induced errors were taxed. When a high cognitive load was experienced, the cognitive resources were not adequately distributed to cater to the switching demands. An ineffective disbursal of attentional resources for switching may have contributed to freezing episodes.

Attention switching abilities in freezing patients have not been studied exclusively. The "cognitive" model of freezing of gait states that when response conflict processes deteriorate, it affects valid response switching (Vandenbossche et al., 2012). The ineffective response processing can induce a motor block, causing freezing of gait episodes. Smulders et al. (2015) also considered that deficit in responses in set-shifting might lead to motor blocks or problems in motor switching. However, the results of the study by Smulders et al. (2015) did not reflect cognitive switching deficits among the patients experiencing freezing. This contrast was attributed to the nature of the task, medication, and stage of the disease. When a cognitive switch accompanied the motor switch, the impairment in stepping response was aggravated among the patients experiencing freezing of gait. The rule-switching deficit seemed to be inducing a bias for the switch to operate generically.

This study is based on the relevance of attention switching in gait and its deficits, which may lead to freezing of gait. The switching of attention has been reported to dictate the postural adjustments for stepping responses. The present study attempts to infer the role of attention switching deficit in patients experiencing freezing of gait by comparing the performance of attention switching abilities between a group having PD with freezing of gait, a group having PD without freezing of gait, and the group of healthy control.

Material and methods

Participants

A total sample of 45 participants was recruited. Fifteen participants were having were experiencing freezing of gait (FOG), and fifteen participants were not experiencing freezing of gait (NFOG). A sample of fifteen healthy controls (HC) was also included. They were age-matched, education matched, culture matched, and household composition matched. The participants having PD patients were recruited from clinics in North India. A qualitative interview was conducted with the consulting neurologist to understand the diagnostic details and to exclude any incongruent participants. The diagnosis was done based on UK brain bank criteria (Hughes et al., 1992) and MDS Criteria full version (Postuma et al., 2015) along with the UPDRS scale (Goetz et al., 2008). The freezing episodes were reported in ON state. No alteration in their medication had been made in one month before data collection. The patients who were taking additional medications that may have affected gait or cognition were excluded. Those having any additional neurological disorders, psychiatric conditions, preexisting cognitive impairments, or any other physical disabilities interfering with gait were excluded from the study. This information was also recorded with confidentiality. Hoehn and Yahr staging ranged between stages 1 and 3. No significant difference between the H/Y staging between FOG and NFOG was reported ($p = 0.42$).

A trained neurologist from the host institute supervised the testing process to ensure their ethical standards toward the PD patients. Healthy control (HC) participants were recruited based on convenience sampling. All participants signed an informed consent form. The informed consent form and the administration procedure of the tests were reviewed and approved by the institute's research committee. The trials were randomized to minimize the effect of confounds. The participants were informed about the procedure and the voluntary nature of their participation. They were allowed to drop out if they were unwilling to continue participating at any point in time. Provision for urgent psychological intervention by trained professionals was also arranged for the participants, in case they felt any distress during or after the test administration. The assessments were done by the ethical standards of the hospital or clinics, giving access to the patients. Subjects' confidentiality was protected.

The number of participants was largely decided based on the allowance of the clinic to access their patients. Due to imposed methodological constraints, a *post-hoc* power analysis was done based on the effect size. All the variables from the MANOVA had power >80%. The age range for FOG was 56–82 years, NFOG was 55–70 years, and HC was 58–70 years. The range of PD (in years) after diagnosis for FOG was, and NFOG was matched. They were matched at levels of education (primary, secondary, and tertiary). In the Indian education system, primary education refers to schooling up to the fifth standard. Secondary refers to attending school till 12th standard and tertiary education if for graduate and above. The level of education (Primary: Secondary: Tertiary) among FOG was 3:3:9, NFOG was 1:6:8, and HC was 1:4:10. The gender ratio (Male: Female) for FOG was 8:7, NFOG was 9:6, and HC was 8:7.

All the participants were under their usual medication at the time of assessment. All PD patients (FOG and NFOG) were prescribed Levodopa (LD). Nine patients (60%) in the FOG group and seven patients(46.6%) in the NFOG group were prescribed Dopamine agonists (DA). Monoamine oxidase B inhibitor(MAO–Bi) was prescribed to eight patients (53.3%) in the FOG group and five patients (33.3%) in the NFOG group. Six patients in the FOG group(40%) and three patients in the NFOG group (20%) were prescribed Trihexyphenidyl (THP) also. The groups differed significantly on UPDRS II-motor experiences of daily living

($p = 0.03$) at <0.05 and III scale-motor examination ($p = 0.008$) at <0.008. No significant differences were reported between FOG and NFOG groups on Part I ($p = 0.43$) non-motor experiences of daily living and Part IV-motor complications ($p = 0.24$). The clinical details of the participants have been reported in Table 1.

Measure

MDS-Unified Parkinson's disease rating scale (UPDRS) was used to diagnose patients with Parkinson's disease (Goetz et al., 2007). It is a comprehensive battery of 50 questions to assess the symptoms of PD. The symptoms (motor and non-motor) associated with PD include the following sections: non-motor experiences of daily living, motor experiences of daily life, motor examination, and motor complications. A trained clinician did this assessment for the recruitment of patients with Parkinson's disease.

A Freezing of gait questionnaire (FOG-Q) is a self-report rating scale to assess freezing, festination, and gait symptom (Giladi et al., 2000). This questionnaire was also used to categorize the groups of PD. Participants with PD were assigned to the freezing of gait group (FOG) or the non-freezing of gait group (NFOG) depending on their score on the New Freezing of Gait Questionnaire (NFOGQ). Subjects with a score of 0–2 were assigned to the NFOG group, and subjects with a score of 7 or higher were assigned to the FOG group (Cohen et al., 2014). It yielded a high Cronbach alpha of 0.89, confirming the reliability of the questionnaire. Additionally, items 2.13 and 3.11 from the revised MDS-Unified PD disease rating scale were also used to assess the freezing of gait. The categorization based on freezing of gait was further verified with the patients' clinical history taken at the hospital and the interview conducted with the consulting neurologist for clinical details. The freezing was diagnosed clinically by instrumented timed up and go test (Mancini et al., 2012) and clinical evaluation was undertaken by a visiting movement disorder specialist, taking into account gait parameters, such as stride length, step length, cadence, progression line. We excluded the participants whose self-reported freezing of gait was not congruent with the neurologist's evaluation of their freezing.

The Montreal Cognitive Assessment (MoCA) is a standardized test with 30-points to detect mild cognitive impairment in elders (Nasreddine et al., 2005). A recent study suggested a revised MoCA cutoff score of 23. This cutoff score contributes to a more accurate diagnosis by lowering the rate of false positives (Carson et al., 2018). The MoCA was administered to screen cognitive impairment. Each participant was screened with a cut-off of 23. This assessment also yielded a coefficient alpha of 0.671, suggesting satisfactory reliability.

The frontal assessment battery (FAB) was also used, a tool with six neuropsychological tasks. Each task assessed different frontal lobe functions (Dubois et al., 2000). This tool has been validated to use in a clinic setting or bedside. This tool also aided in ruling out dementia by screening

Table 1. Clinical details for groups (FOG, NFOG, and HC).

Groups	Age	Duration of PD after diagnosis (in years)	Modified H and Y scale	UPDRS part I	UPDRS part II	UPDRS part III	UPDRS part IV	Medication			
								LD	DA	MAO-Bi	THP
	M ± *SD*	*M* ± *SD*	*M* ± *SD*	*M* ± *SD*	*M* ± *SD*	*M* ± *SD*	*M* ± *SD*	*M* ± *SD*	*M* ± *SD*	*M* ± *SD*	*M* ± *SD*
FOG	64.27 ± 6.53	4.93 ± 1.98	2.01 ± 0.5	4.93 ± 1.10	19.4 ± 4.82	35.93 ± 10.39	5.27 ± 2.38	322.54 ± 29.33	5.93 ± 5.12	0.3 ± 0.36	1.8 ± 2.93
NFOG	62.07 ± 4.79	4.73 ± 1.03	2.06 ± 0.45	4.87 ± 1.12	15.6 ± 5.47	26.86 ± 9.30	4.66 ± 2.06	308 ± 28.07	4.66 ± 5.25	0.23 ± 0.34	0.86 ± 2.03
HC	61.13 ± 2.95	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A

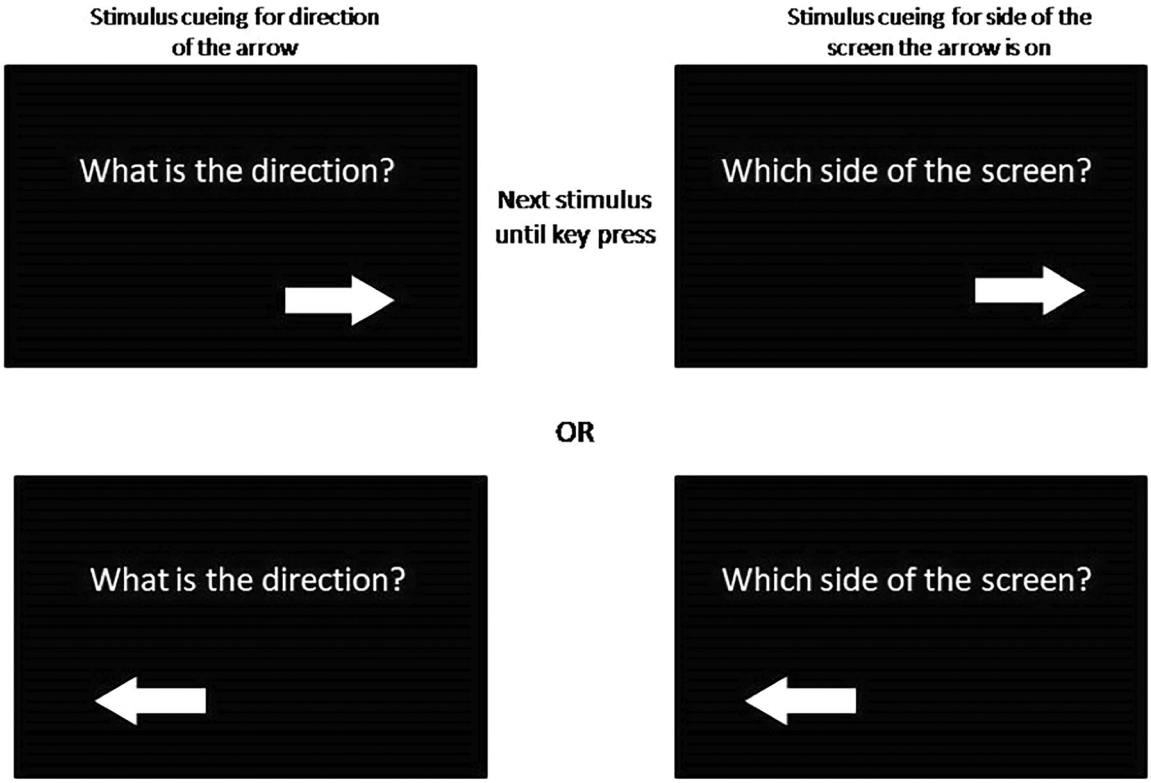

Figure 1. Stimuli for congruent trials.

each participant with scores higher than the cutoff of 12 (Slachevsky et al., 2004).

However, we did not include this assessment in our analysis as it yielded a low alpha of 0.379.

The attention switching task (AST) was administered to evaluate task-switching abilities (Cambridge Cognition, 1994). The Attention Switching task was programmed on open sesame. The test began with instructions to the participants. The instructions were, "An arrow will appear at the center of the screen pointing either to the left or to the right. You are required to respond by pressing a key indicating the direction to which the arrow is pointing, key 'A' for left arrow, and key 'L' for the right arrow." This practice session was intended to familiarize the participants with the keys. The practice session involved only familiarizing with the left and right response keys. The main task stimuli were not introduced in the practice session to bring more contrast between the rule changes among stimuli. Practicing on the main task was not preferred to avoid any practice effect since attention switching demands quick processing of the rules and responding to different stimuli. Any practice of the main task would have interfered with that. At the end of the practice session, feedback was given to the participants.

After this initial training, the participant was given further instructions for the main task. The instructions were, "An arrow might appear on the left or the right side of the screen. A new stimulus (arrow) would appear along with a cue on the top of the screen every time. The cue will either indicate the direction of the arrow or refer to the screen's side where the arrow had appeared. You will have to make the appropriate keypress according to the cue displayed on the screen. If the cue says, 'which side of the screen?' you will have to indicate the side of the screen the arrow appeared, irrespective of the direction of the arrow. If the cue indicates, 'which direction the arrow is pointing?' you will have to indicate the direction of the arrow, irrespective of the side of the screen it appears. The key choices are left (A) or right button (L) to indicate the side of the screen the arrow is displayed or the direction in which the arrow is pointing." The cues were congruent (Figure 1) and incongruent (Figure 2).

There was no timeout for stimulus presentation. The response window was the time required by the participants to respond to every stimulus, and the next stimuli would appear after they had responded to the previous one. The participants were instructed to provide their response using the keypress ("A" or "L") as accurately and quickly as possible to assess their speed and accuracy. Their responses would differ according to the cue given at the top of the screen at every stimulus. In this study, a total of 64 trials were done. The changes in the cues (side of the screen where the arrow appears X direction to which the arrow is pointing) demanded attention switching abilities. The participants were required to attend to the cue, and the response rules could change every time the stimulus changed. The congruency of stimuli determines the degree of task difficulty or demand on attention switching capacity.

Procedure

Data were collected from hospitals and clinics in Northern India, where the patients with PD upon consent from the

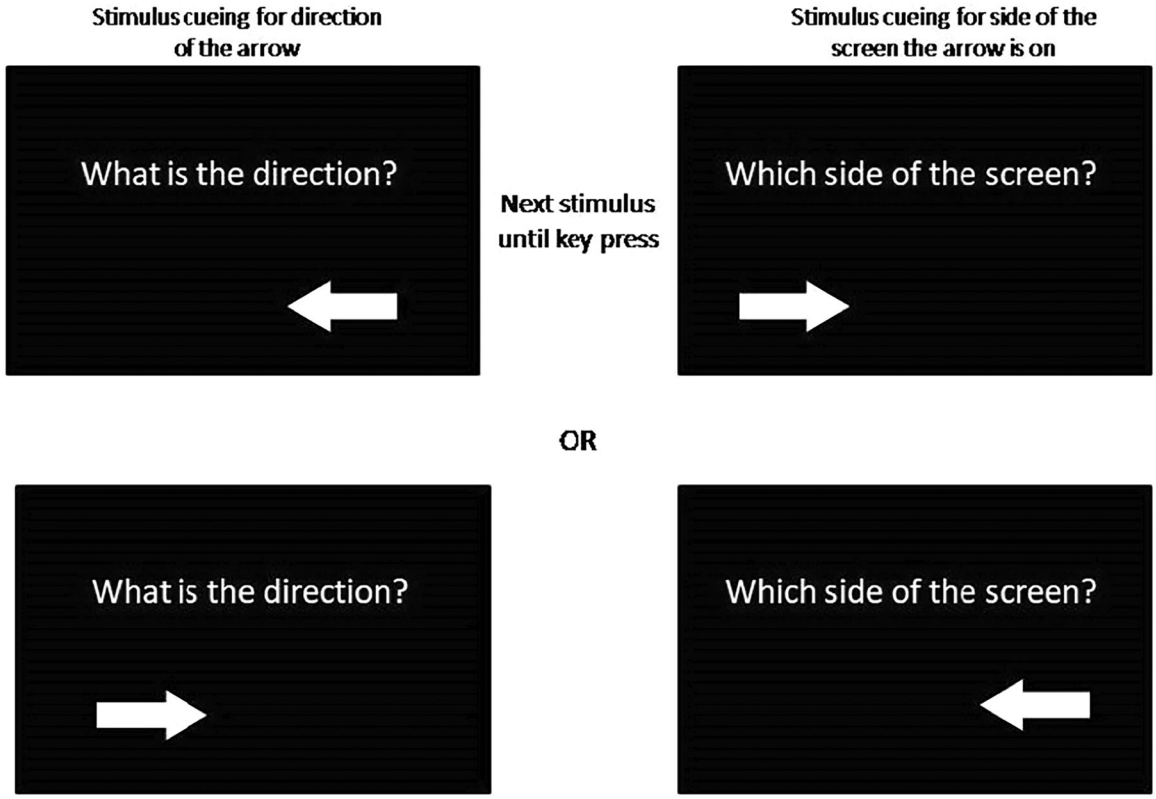

Figure 2. Stimuli for incongruent trials.

authorities. Professional neurologists referred the patients after screening for PD. The participants were tested individually under controlled laboratory conditions. They were attended to politely and seated comfortably. The participants were informed about the procedure and that their participation was completely voluntary. They were allowed to drop out if they were unwilling to continue participating at any point during the study. Provision for urgent psychological intervention by trained professionals was also arranged for the participants, in case they felt any distress during or after the test administration. The assessments were done instead of the ethical standards of the hospital or clinics, giving access to the patients. Subjects' confidentiality was protected. Upon their informed consent, the assessments were done. The instructions for each task were displayed just before the task was administered. Then the test administrations happened. Firstly screening for freezing of gait was done using the New Freezing of Gait Questionnaire. All the participants were screened for cognitive impairment using MoCA and screened for dysexecutive symptoms and dementia by FAB. After these paper-pencil screening tests, a computerized attention switching task was administered. Instructions were given in English as well as in Hindi on the computer screen. They were also briefed about the task verbally. They were also debriefed about the task verbally, "Here is are the instructions. Kindly give your response as quickly and as accurately as possible. If you have any queries, I am here to attend to them." An initial practice session was administered before the main task to get the participants acquainted with the task and the responses. A blank screen appeared for a brief period of 5 s between the practice session and actual trials, to avoid any carry-over effects. The end procedure took around 20 min, which was within the ethical regulations furnished by the host institute.

Table 2. Results of MANOVA for effect between groups (FOG, NFOG, and HC) on AST task accuracy.

Dependent measures	*F*	*p*	Effect size (η^2)
AST task accuracy	*34.30*	<0.01	0.62
Congruent stimuli accuracy	*7.59*	<0.01	0.27
Incongruent stimuli accuracy	*30.78*	<0.01	0.60

df for all analyses = 42; italicized *F*-ratios are significant.

Results

Multiple analyses of variance between subjects was calculated for accuracy (Table 2) and reaction time (Table 5) on total scores, congruent and incongruent trial scores of the attention switching task among the three groups: FOG, NFOG, and HCG, followed by Tukey for post-hoc analysis. Mixed ANOVA for accuracy and reaction time was also performed to understand the interaction effect between trials and groups.

Effect on attention switching task accuracy

Effect of freezing of gait on AST accuracy was significant [$F_{(2,\ 42)} = 34.30$, $p < 0.01$]. The results on congruent trials [$F_{(2,\ 42)} = 7.60$, $p < 0.02$] and incongruent trials $F_{(2,\ 42)} = 30.78$, $p < 0.01$] were significant (Table 2). Post-hoc comparisons using the Tukey HSD test (Table 3) indicated that the mean score for the freezing of gait condition ($M = 46.80$,

Table 3. Results of Tukey analysis for comparisons among groups (FOG, NFOG, and HC) on AST accuracy.

Dependent measures	Groups		Mean difference	Standard error	Significance (*p*-value)
AST accuracy (total)	FOG	NFOG	−12.64	1.74	<0.01**
	FOG	HC	−12.36	1.74	<0.01**
	NFOG	HC	0.28	1.74	0.99
Congruent trial accuracy	FOG	NFOG	−12.75	3.57	<0.01**
	FOG	HC	−11.22	3.57	<0.01**
	NFOG	HC	1.53	3.57	0.90
Incongruent trial accuracy	FOG	NFOG	−16.21	2.43	<0.01**
	FOG	HC	−16.78	2.43	<0.01**
	NFOG	HC	−0.57	2.43	0.97

**Indicates significant difference ($p < 0.01$).

Table 4. Pair wise comparisons for interactions between factors with mixed ANOVA for AST accuracy.

Interaction	*T*-value	*p*-Value
FOG_Con-FOG_Incon	4.89	<0.01**
FOG_Con-NFOG_Con	3.92	<0.01**
FOG_Con-NFOG_Incon	4.68	<0.01**
FOG_Con-HC_Con	4.57	<0.01**
FOG_Con-HC_Incon	2.70	0.02*
FOG_Incon-NFOG_Con	0.79	0.44
FOG_Incon-NFOG_Incon	7.01	<0.01**
FOG_Incon-HC_Con	1.51	0.14
FOG_Incon-HC_Incon	1.38	0.18
NFOG_Con- NFOG_Incon	5.81	<0.01**
NFOG_Con-HC_Con	0.67	0.51
NFOG_Cong-HC_Incon	2.06	0.40
NFOG_Incon-HC_Con	7.62	<0.01**
NFOG_Incon- HC_Incon	6.59	<0.01**
HC_Con-HC_Incon	2.55	0.02*

*, ** indicate significant difference at $p < 0.05$ and significant difference at $p < 0.01$.

Table 5. Results of MANOVA for effect between groups (FOG, NFOG, and HC) on AST task reaction time.

Dependent measures	*F*	*p*	Effect size (η^2)
AST task reaction time	*37.01*	<0.01	0.58
Congruent stimuli reaction time	*36.93*	<0.01	0.58
Incongruent stimuli reaction time	*44.84*	<0.01	0.58

df for all analyses = 42; italicized *F*-ratios are significant.

$SD = 5.62$) was significantly worse than the non-freezing of gait condition ($M = 59.44$, $SD = 4.92$), and with the healthy control condition ($M = 59.17$, $SD = 3.54$). For congruent trials, the freezing of gait group ($M = 53.12$, $SD = 4.87$) performed significantly poorer than the non-freezing of gait condition ($M = 62.56$, $SD = 6.37$), and with the healthy control condition ($M = 61.04$, $SD = 6.12$). For incongruent trials also, FOG ($M = 40.51$, $SD = 9.29$) performed significantly poorer than non-freezing of gait ($M = 56.73$, $SD = 5.97$) and healthy control condition ($M = 57.29$, $SD = 3.48$). The mean scores of the NFOG condition did not differ from the HC condition on total AST accuracy. No difference was found for congruent and for incongruent trials. The trend of performance of FOG is more reduced than NFOG and HC, while no significant difference in accuracy between NFOG and HC (Figure 3).

A mixed ANOVA was calculated to understand the interaction effect between the groups (between-subjects factor) and the congruence of trials (within-subject factor) for accuracy. There was a significant effect main of the type of trial (congruent or incongruent), $F_{(1,\ 42)} = 20.6$, $p < 0.01$, $\eta^2 = 0.08$. There was a significant effect main of the groups (FOG, NFOG, HC), $F_{(2,42)} = 22.5$, $p < 0.01$, $\eta^2 = 0.05$. Also, There was a significant interaction between the type of trial and the group of participants, $F = F_{(2,42)} = 29.5$, $p < 0.01$, $\eta^2 = 0.22$. Post-hoc comparison have been made between interactions of FOG_Con ($M = 53.12$, $SD = 4.87$), FOG_Incon ($M = 59.44$, $SD = 4.92$), NFOG_Con ($M = 61.04$, $SD = 6.12$), NFOG_Incon ($M = 40.51$, $SD = 9.23$), HC_Con ($M = 62.58$, $SD = 6.37$), and HC_Incon ($M = 57.29$, $SD = 3.48$) and indicated in Table 4.

Effect on attention switching task reaction time

There was a significant effect for the overall AST reaction time [$F = F_{(2,\ 42)} = 37.01$, $p < 0.01$] and also for congruent [$F = F_{(2,\ 42)} = 36.93$, $p < 0.01$] and incongruent trials [$F = F_{(2,\ 42)} = 44.84$, $p < 0.01$] (Table 5). *Post-hoc* analysis revealed that the FOG ($M = 2{,}977.80$, $SD = 542.83$) performed significantly poorer than NFOG ($M = 2{,}288.60$, $SD = 238.02$ and HC ($M = 1{,}713.00$, $SD = 191.08$) on total AST (Table 6). The difference was significant between the NFOG and HC also, wherein NFOG slowed down significantly than HC. For the congruent trials HC ($M = 1{,}700.62$, $SD = 285.12$) performed significantly faster than FOG ($M = 2{,}789.90$, $SD = 471.77$) and NFOG ($M = 2{,}203.64$, $SD = 241.43$) at $p < 0.01$. For the incongruent trials also, HC ($M = 1{,}725.30$, $SD = 325.84$) performed faster and FOG ($M = 3{,}089.66$, $SD = 530.85$) and NFOG ($M = 2{,}373.60$, $SD = 373.52$) at $p < 0.01$. No difference was found for the speed between FOG and NFOG on overall AST, congruent and incongruent trials. The trend of reaction of FOG is slower than NFOG and HC. NFOG is also significantly slower than HC (Figure 4).

A mixed ANOVA was calculated to understand the interaction effect between the groups (between-subjects factor) and the congruence of trials (within-subject factor) for reaction time. There was a significant effect main of the type of trial (congruent or incongruent), $F_{(1,\ 42)} = 11.7$, $p < 0.01$, $\eta^2 = 0.004$. There was a significant effect main of the groups (FOG, NFOG, and HC), $F_{(2,\ 42)} = 39.1$ $p < 0.01$, $\eta^2 = 0.34$. Also, there was no significant interaction between the type of trial and the group of participants, $F = F_{(2,42)} = 0.56$, $p = 0.58$. Post-hoc comparison have been made between interactions of FOG_Con ($M = 2{,}789.90$, $SD = 471.77$), FOG_Incon ($M = 3{,}089.66$, $SD = 530.85$), NFOG_Con ($M = 2{,}203.60$, $SD = 385.89$), NFOG_Incon ($M = 2{,}346.98$, $SD = 372.76$), HC_Con ($M = 1{,}700.62$, $SD = 285.12$) and HC_Incon ($M = 1{,}891.97$, $SD = 379.77$) and indicated in Table 7.

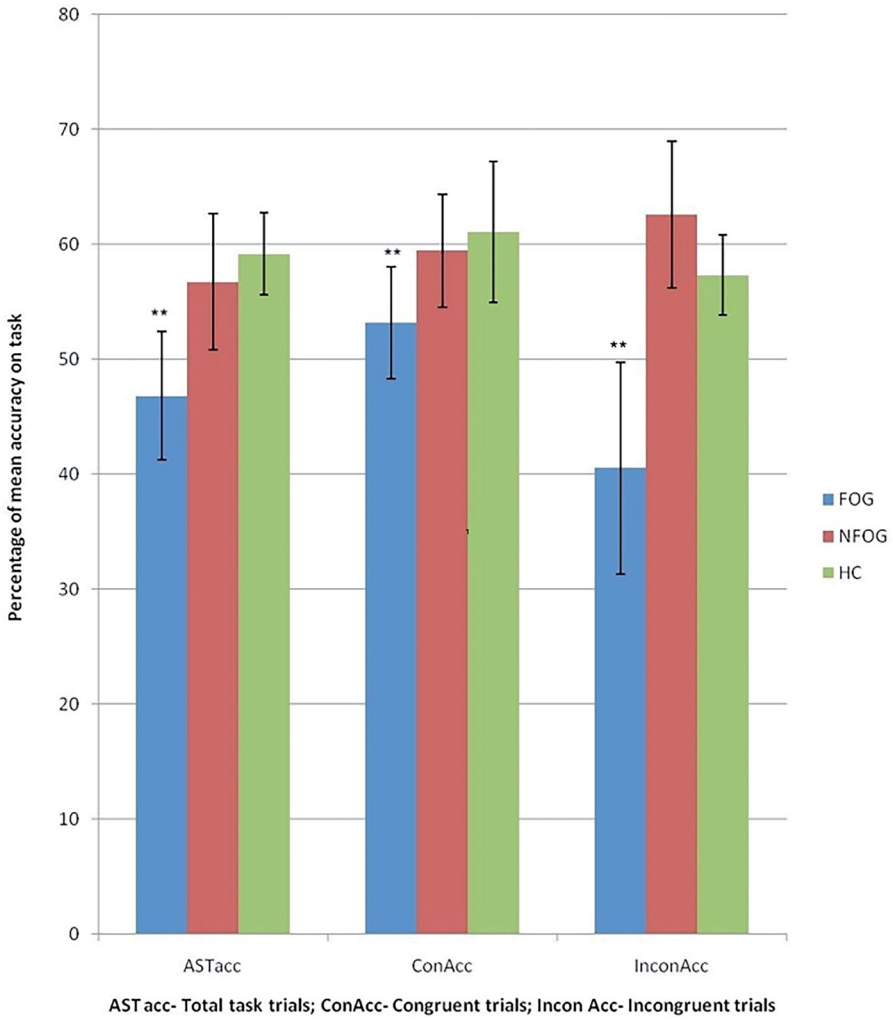

Figure 3. Graphical trend of the groups: FOG, NFOG, and HC on AST accuracy. FOG values are significantly (**$p < 0.01$) higher than NFOG and HC groups.

Table 6. Results of Tukey analysis for comparisons among groups FOG, NFOG, and HC on AST reaction time.

Dependent measures	Groups		Mean difference	Standard error	Significance
AST accuracy (total)	FOG	NFOG	626.69	151.39	<0.01**
	FOG	HC	1,138.33		<0.01**
	NFOG	HC	511.64		<0.01**
Congruent trial accuracy	FOG	NFOG	586.30	141.86	<0.01**
	FOG	HC	1,089.28		<0.01**
	NFOG	HC	502.98		<0.01**
Incongruent trial accuracy	FOG	NFOG	742.68	158.46	<0.01**
	FOG	HC	1,197.69		<0.01**
	NFOG	HC	455.01		0.02*

*, ** indicate significant difference at $p < 0.05$ and significant difference at $p < 0.01$.

Analysis of performance on cognitive batteries

Frontal assessment battery (FAB)

FAB was not included in the analysis because of its weak Cronbach alpha of 0.45. However, it is a standardized tool to screen for dementia if the score is <12. All our participants were screened accordingly to be included for a non-demented sample.

Montreal cognitive assessment (MoCA)

ANOVA was performed to identify any difference in mean scores of MoCA assessment among the FOG ($M = 24.40$, $SD = 0.99$, range = 23–26), NFOG ($M = 25.47$, $SD = 1.36$, range = 23–28), and HC ($M = 26.13$, $SD = 1.06$, range = 25–28) (Table 6). A significant effect was observed on the total MoCA score [$F_{(2,\ 42)} = 8.75$, $p < 0.01$], visuospatial function [$F_{(2,\ 42)} = 4.20$, $p < 0.01$], and attention [$F_{(2,\ 42)} = 13.90$, $p < 0.01$]. The tests for the subscales of memory, abstraction, language, and orientation were not significant. A *post-hoc* analysis was performed to identify the groups, which were different (Table 8).

Tukey analysis (Table 9) revealed that FOG ($M = 24.40$, $SD = 0.99$) scored less than NFOG ($M = 25.47$, $SD = 1.36$) and HC ($M = 26.13$, $SD = 1.06$) $p < 0.05$ and $p < 0.01$,

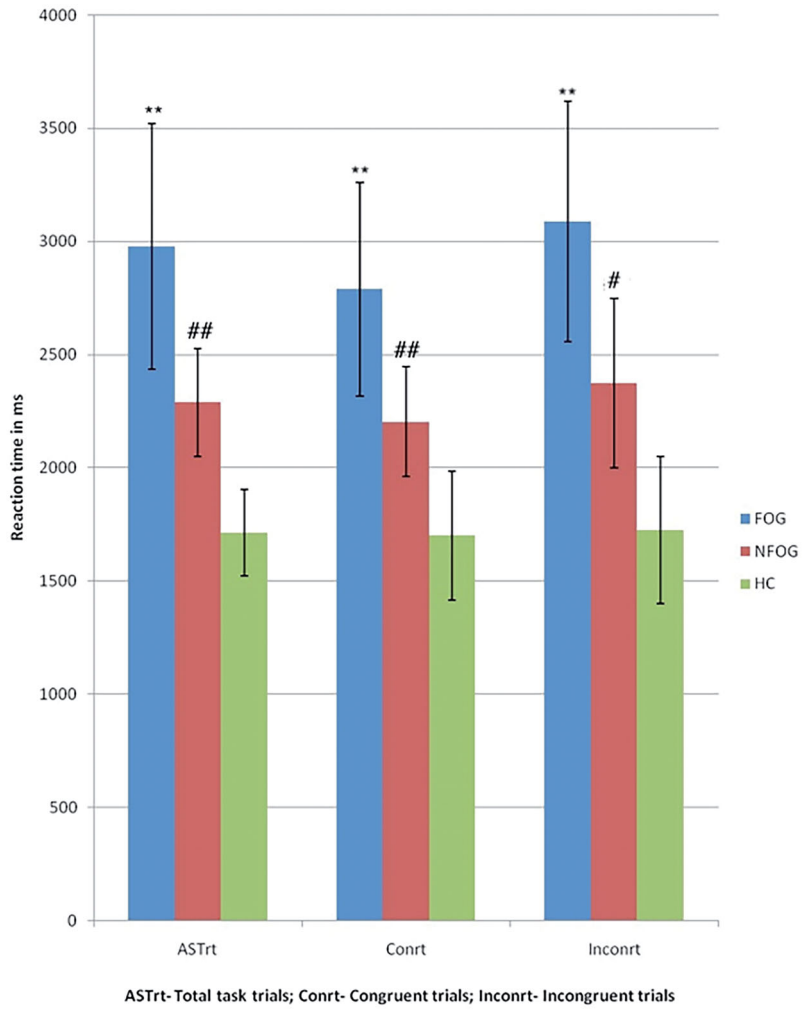

Figure 4. Graphical trend of the groups: FOG, NFOG, and HC on AST reaction time. FOG values are significantly ($^{**}p < 0.01$) higher than NFOG and HC groups and NFOG values are significantly ($^{\#\#}p < 0.01$; $^{\#}p < 0.05$) higher than HC group in AST trials and in congruent and incongruent trials.

respectively. No cognitive difference came up for NFOG and HC. For attention abilities, FOG ($M = 3.87$, $SD = 0.52$) differed with NFOG ($M = 4.40$, $SD = 0.51$) at $p < 0.05$ but no difference between NFOG and HC ($M = 4.33$, $SD = 0.62$).

FOG ($M = 3.80$, $SD = 0.94$) scored significantly less than NFOG ($M = 4.40$, $SD = 0.83$) at $p < 0.05$ and HC ($M = 5.40$, $SD = 0.74$) at $p < 0.01$ in visuospatial subscale. NFOG also scored significantly less than HC at $p < 0.01$. Regression analyses were performed to confirm that the difference in cognitive impairment did not affect the AST performance of the participants. Binary logistic regression analysis suggested that the effect of MoCA scores on the FOG and NFOG group was insignificant ($\chi^2 = 6.22$, $p = 0.42$). Also, results of the multiple linear regression indicated that there was no significant effect of MoCA scores on AST accuracy [$F_{(1,\ 28)} = 0.45$, $p = 0.51$, $R^2 = 0.016$] and AST reaction time [$F_{(1,\ 28)} = 0.02$, $p = 0.95$, $R^2 = 0.001$].

Discussion

The purpose of the present study was to investigate attention switching deficit among PD patients experiencing freezing of gait. Therefore, three groups were compared: the group having PD and freezing of gait episodes (FOG), the group having PD but no freezing of gait episodes (NFOG), and the healthy control group (HC) based on their performance on attention switching the task. Attention Switching Task (AST) paradigm involved trials of responding to the stimuli according to the cues provided. The difficulty of the trials was manipulated with congruent or incongruent stimuli. The results suggested more severe attention switching deficits among the FOG group than NFOG and HC groups. The accuracy of attention switching tasks remained intact among the NFOG and HC groups, and there was a significant interaction effect between the trials and the groups. The MoCA subscales analysis also suggested a deficit in the attention of FOG compared to NFOG and HC. The NFOG and HC groups did not differ significantly on the attention subscale.

Another important finding of the study is that the HC group's reaction time in the attention switching task was significantly lesser than the NFOG group even though there was no difference in accuracy between those groups. Also, the NFOG was significantly faster than FOG in all trials. The NFOG could compensate for the performance by taking more time and maintaining the task score for congruent and

Table 7. Pair wise comparisons for interactions between factors with mixed ANOVA for AST reaction time.

Interaction	*T*-value	*p*-Value
FOG_Con-FOG_Incon	3.06	<0.01**
FOG_Con-NFOG_Con	3.73	<0.01**
FOG_Con-NFOG_Incon	2.85	<0.01**
FOG_Con-HC_Con	7.65	<0.01**
FOG_Con-HC_Incon	5.74	<0.01**
FOG_Incon-NFOG_Con	5.23	<0.01**
FOG_Incon-NFOG_Incon	4.43	<0.01**
FOG_Incon-HC_Con	8.93	<0.01**
FOG_Incon-HC_Incon	7.11	<0.01**
NFOG_Con- NFOG_Incon	0.98	0.34
NFOG_Con-HC_Con	4.06	<0.01**
NFOG_Cong-HC_Incon	2.23	0.03*
NFOG_Incon-HC_Con	5.33	<0.01**
NFOG_Incon- HC_Incon	3.31	<0.01**
HC_Con-HC_Incon	3.13	0.02*

*, ** indicate significant difference at $p < 0.05$ and significant difference at $p < 0.01$.

Table 8. Results of MANOVA for between groups (FOG, NFOG, and HC) comparisons on MoCA score and its subscales.

Dependent measures	*F*	*p*	η^2
MoCA total	8.75	<0.01**	0.29
Visuo spatial	4.20	0.02*	0.40
Naming	1.00	0.38	0.05
Memory	0.73	0.49	0.03
Attention	13.90	<0.01**	0.17
Language	0.48	0.64	0.02
Abstraction	0.32	0.73	0.02
Orientation	0.00	—	—

df for all analyses = 42; italicized *F*-ratios are significant.

Table 9. Results of Tukey test for between groups (FOG, NFOG, and HC) comparisons on MoCA score and its subscales.

Dependent measures	Groups		Mean difference	Standard error	Significance
MoCA total	FOG	NFOG	−1.07	0.42	0.04*
	FOG	HC	−1.73	0.42	<0.01**
	NFOG	HC	−0.67	0.42	0.26
Visuo spatial	FOG	NFOG	−0.60	0.31	0.13*
	FOG	HC	−1.60	0.31	<0.01**
	NFOG	HC	−1.00	0.31	<0.01**
Naming	FOG	NFOG	−0.07	0.54	0.44
	FOG	HC	−0.07	0.54	0.44
	NFOG	HC	0.00	0.54	1.00
Memory	FOG	NFOG	0.33	0.54	0.55
	FOG	HC	0.33	0.54	0.55
	NFOG	HC	0.00	0.54	1.00
Attention	FOG	NFOG	−0.53	0.20	0.03*
	FOG	HC	−0.47	0.20	0.06*
	NFOG	HC	0.07	0.20	0.94
Language	FOG	NFOG	−0.20	0.24	0.70
	FOG	HC	0.00	0.24	1.00
	NFOG	HC	0.20	0.24	0.70
Abstraction	FOG	NFOG	−0.67	0.17	0.91
	FOG	HC	0.67	0.17	0.91
	NFOG	HC	0.13	0.17	0.70

*, ** indicate significant difference at $p < 0.05$ and significant difference at $p < 0.01$.

incongruent trials. The mixed ANOVA results also revealed no significant interaction effect between the groups and trials. MoCA revealed a significant effect of the total score on the groups. However, ultimately, NFOG could overcome their attention switching deficit by taking a longer reaction time but not affecting the accuracy.

The findings of this study suggest that a failure of attention switching among the freezers. The ability to switch or shift attention can be associated with the clinical severity of freezing and is worse in people with PD disease and freezing of gait. This phenomenon can be attributed to inappropriate recruitment of attentional sources (Tard et al., 2015). Switching from one response to another response was required by the attention-switching task. In this task, the participants needed to allocate the attentional resources to the appropriate stimuli by withdrawing the attentional sources and reallocate the attentional sources to a more relevant task. This ability is required to engage and disengage the left and right leg for alternate stepping. The deficit remained constant for the congruent and incongruent trials suggesting that attention switching is happening even with lower task difficulty. These findings can be explained in light of the existing literature. The attention switching process has been defined as "selection and maintenance of context-appropriate response" (Ravizza & Carter, 2008). Ravizza and Carter (2008) concluded that the ability to procure the correct set of rules of the newer task is required to switch response to another task, during the changes in anticipatory postural adjustments. The finding of FOG's reaction time longer than the NFOG and HC group is consistent with previous research (Shine et al., 2013; Walton et al., 2015). Shine et al. (2013) confirmed that the attentional set-shifting deficit does not correlate with PD severity and proposed that this might be a part of the pathophysiological mechanism to explain the freezing of the gait mechanism.

However, Cohen et al. (2014) reported no difference between the freezing and non-freezing group concerning task switching. This difference could be attributed to the nature of tasks used by Cohen et al. (2014), which were broader and represented a global switch measure (rule and perceptual shifts) rather than an attention switch. The task switching tapped into other cognitive constructs, such as visuospatial abilities, memory, working memory, and language (Allen et al., 2012). Our research is focused on the attention switching component. The attention switching task used in this experiment involves cues and every stimulus eliminating the requirement to recall the rules and loading of working memory. Only the stimulus-response association needs to be changed for every response making it a relatively purer form of attention switch measure. Another difference was that no significant difference was no reported between FOG and NFOG on aggregate MoCA scores for the sample recruited by Cohen et al. (2014). The sample in our study was screened to exclude cognitive impairment in all participants, but the total score of MoCA of FOG was significantly less than NFOG. Detailed *post-hoc* analysis of the subscales revealed the domain mainly affected in FOG was attention, which confirms the more severe attention switching deficit in FOG.

During an ongoing walk or when the walk space involves obstacles and requires turning, the need for lateral weight shifts to coordinate forward stepping becomes crucial. The ability to disengage the weight on the current leg and then shift it onto a stepping leg and then again shift back to the other leg is required. This process of alternating postural adjustment needs to be repeated as long as the walking

continues. A lag in this process leads to a delayed step onset. PD patients with FOG have abnormal postural preparation before a voluntary or involuntary postural step initiation (Jacobs et al., 2009). Therefore, attention switching may be required for proactive control, which should be exercised at the stimulus level for postural preparation.

An alternative understanding of the role of attention switching can be considered to its involvement with the inhibitory control process. An inhibitory control deficit has been suggested in the freezing of gait (Bissett et al., 2015; Cohen et al., 2014). Attention switching has been reported as an underlying cognitive process of rule inhibition (Diamond, 2013; Xie et al., 2017). Coordination of forwarding stepping with lateral weight shifts continues to be necessary for forwarding locomotion (and maybe even more salient when passing through tight spaces or turning). An integrated, cohesive motor program operates for smooth gait (Cohen et al., 2014). Demands for adequate and effective allocation of more attentional resources to the new task-set are initiated when inhibitory control is exercised. Attention switching is required for shifting weights to the alternate legs controlled by the central executive. Attention switching deficit indicates a failure in the allocation of attention, and the top-down attention switching for incoming stimuli is affected (Hagen et al., 2006). Xie et al. (2017) observed that when there are changes in task requirements (such as the postural adjustment changes in gait), actions are reorganized according to the new task set rules reflecting attention switching ability as a part of the inhibition process. Hence, attention switching may be required for successful shifting of lateral weight for efficient gait.

The second finding showed a higher reaction time in FOG than NFOG and HC. Also, NFOG was slower than HC. Not only freezers but non-freezing PD patients also experience slow gait (bradykinesia), which is suggestive of a slower cognitive mechanism. NFOG exhibited a slower reaction time than HC but maintained a healthy level of accuracy and faster response time than FOG on attention switching abilities. A compensatory mechanism to prioritize accuracy over response time may be implied. This can be supported by a previous study, which explains this kind of compensatory mechanism in NFOG. A study by Bissett et al. (2015) observed that the group of PD patients without freezing experienced, proactive slowing, but their performance was unaffected after a change in their stimulus-response set was introduced. However, the freezing patients' accuracy drooped significantly than the NFOG, and reaction time slowed down. The task was prioritized after the shifting of the stimulus-response set, and the slowing happened without compromising the accuracy.

Our results showed a similar pattern. The accuracy and speed of the attention switching task were affected in the FOG group. The participants having PD disease may have prioritized accuracy over speed. Strategies are employed based on the resources available to overcome the deficits in cognitive control. In this case, priority was shifted to response while the speed or the need to perform quickly was underplayed. Therefore our results may not indicate complete intactness of attention switching abilities in NFOG. However, the disability is more profound in FOG as their accuracy and response time, and both were affected. A delay in carrying out attentions switching that is to reorient attention to relevant stimuli may bring out a slowness in the gait of non-freezing PD patients. The possibility of a compensation strategy could prevent freezing. Considering this ability is more depleted in FOG, it may result in the complete inability of forwarding locomotion.

A few inconsistencies arose from the graphical trends. Firstly, the NFOG group seemed to perform slightly more accurately than HC on incongruent trials (Figure 3). However, the difference in means is not significant. Secondly, the NFOG group is slower on the congruent trials, which are expected to be less demanding than the incongruent trials and also more accurate on the incongruent trials (Figure 4). Outliers were not detected using Grubbs' test for reaction time and accuracy on the congruent and incongruent trials. This effect can be investigated further with a larger sample size for compensatory cognitive mechanisms because the NFOG is significantly slower than HC on incongruent trials. The slowing is more for incongruent trials than the congruent trials, while the accuracy improves in incongruent trials, suggesting that prioritization of accuracy over speed increases as task difficulty increases. This trend can also be attributed to other external conditions, such as momentary distraction or inattention.

This study poses a few limitations that can be further investigated for more conclusive results. The first limitation is that the results are more implicative than conclusive. The relationship that has been established was not assessed in real-time, and a temporal coupling was not evident. The inference has been made based on the existing literature of how attention switching affects gait, and its deficit can lead to freezing. This relationship can be further investigated with methods that can establish a stronger temporal coupling. A second limitation of this research is the restricted number of trials on the task due to ethical constraints established by the host institute. Future studies can increase the trial numbers in each condition and observe their effects separately. A third limitation is the gait wasn't assessed using computerized instruments for better accuracy. For maximum control, we combined the patient's subjective assessment and clinical evaluation by a movement disorder specialist. The fourth limitation is that the criteria chosen for cognitive impairment screening using MoCA were not specifically standardized for cognitive impairment in PD and/or in the Indian population. Even though the regression analyses indicated that attention switching ability was independent of MoCA scores, the significant difference in cognitive function between the groups needs to be studied. Our results reflect that patients experiencing freezing of gait exhibited a stronger deficit in attention switching than non-freezing patients of PD, which may explain the uncoordinated postural adjustments in freezing. Also, the attention switching deficit may contribute to a rule inhibition failure, which could result in inappropriate lateral weight shifts during a stepping response. A loss in automaticity among

freezers may further overload the demands on attentional resources resulting in freezing. Further investigation can address the above-mentioned limitations and in the direction of cognitive rehabilitation or cognitive training for patients who freeze.

Acknowledgments

I would like to thank Prof. Deepika Joshi, MBBS, MD, DM (neurology), who extended uninhibited support in the recruitment of participants with Parkinson's disease and for a smooth data collection. I would also like to express my gratitude toward the neurologists who supervised the data collection. My doctoral scholarship by the Indian Council of Medical Research has helped me resolve the financial knots of this experiment.

Disclosure statement

No potential conflict of interest was reported by the authors.

Funding

This work was supported by the Indian Council of Medical Research, New Delhi, India.

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