Robotics-Based Characterization of Sensorimotor Integration in Parkinson's Disease and the Effect of Medication

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***Abstract*— Integration of multi-modal sensory inputs and modulation of motor outputs based on perceptual estimates is called Sensorimotor Integration (SMI). Optimal functioning of SMI is essential for perceiving the environment, modulating the motor outputs, and learning or modifying motor skills to suit the demands of the environment. Growing evidence suggests that patients diagnosed with Parkinson's Disease (PD) may suffer from an impairment in SMI that contributes to perceptual deficits, leading to motor abnormalities. However, the exact nature of the SMI impairment is still unclear. This study uses a robot-assisted assessment tool to quantitatively characterize SMI impairments in PD patients and how they affect voluntary movements. A set of assessment tasks was developed using a robotic manipulandum equipped with a virtual-reality system. The sensory conditions of the virtual environment were varied to facilitate the assessment of SMI. A hundred PD patients (before and after medication) and forty-three control subjects completed the tasks under varying sensory conditions. The kinematic measures obtained from the robotic device were used to evaluate SMI. The findings reveal that across all sensory conditions, PD patients had 36% higher endpoint error, 38% higher direction error in reaching tasks, and 43% higher number of violations in tracing tasks than control subjects due to impairment in integrating sensory inputs. However, they still retained motor learning ability and the ability to modulate motor outputs. The medication worsened the SMI deficits as PD patients, after medication, performed worse than before medication when encountering dynamic sensory environments and exhibited impaired motor learning ability.**

***Index Terms*— Sensorimotor integration, Parkinson's disease, KINARM endpoint robot.**

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I. Introduction

HUMANS rely on the integration of motor and sensory systems to optimally perform any voluntary movements. While the motor system is responsible for executing a set of motor commands, it cannot act independently and needs information from the sensory system about oneself and the surroundings to plan and modulate the motor output to suit the demands of the environment. The sensory system collects information through multiple sensory modalities, integrates this information (multi-sensory integration), and uses the integrated information to form an accurate perceptual estimate (a unified and coherent representation of the world). Multi-sensory integration is a vital process in SMI, as an estimate based on integrated sensory information in general will provide a more robust and accurate representation of the world than an estimate formed using information from a single modality [1], [2]. Perceptual estimates enable us to make sense of the environment and respond appropriately by generating or modulating motor commands [3]. The process of integrating inputs from multiple modalities and using the resulting perceptual estimates to generate or modulate the motor output is called Sensorimotor Integration (SMI) [4], [5]. Therefore, SMI encompasses functions related to multi-sensory integration and responding to changes in the environment through a set of motor commands in a meaningful and consistent manner. Our ability to produce accurate movements depends on two crucial facets of SMI: (i) multi-sensory integration and (ii) modulation of motor outputs based on perceptual estimates. Any deficits disrupting the SMI processes may adversely affect the ability to perceive the world and appropriately modulate the motor outputs to suit the demands of the environment, thereby causing difficulties in performing any motor movements.

Parkinson's Disease (PD) is a neurodegenerative disorder primarily characterized by motor symptoms. However, recent evidence indicates that Basal Ganglia (BG), the affected

region in PD, plays a vital role in sensorimotor functions [5]. Impaired BG may therefore give rise to sensory abnormalities in PD patients. Numerous studies have reported perceptual deficits pertaining to various modalities (proprioceptive [6], visual [7], haptic [8] and auditory perception [9]) in PD patients. A growing body of literature suggests that sensory deficits in PD may manifest before the onset of motor symptoms [10] and contribute to the motor impairments observed in PD [11]. An impairment in the central processing of sensory inputs, primarily SMI, may contribute to these wide-ranging perceptual deficits leading to motor abnormalities [12]. Earlier studies [13], [14] also hypothesized that increased visual dependence among PD patients may imply an impaired SMI as it indicates an inability to organize the sensory hierarchy and prioritize modalities based on its accuracy and relevance of information. Investigating the functioning of SMI in PD would enable us to understand the impairments in sensory processing that contributes to motor deficits. Further, it would inform us how sensory cues could be used during rehabilitation therapies considering their impaired SMI circuit, as studies [15] have reported benefits in motor performance if appropriate external sensory cues are used during therapies. Another facet that needs to be studied is if the dopaminergic medication alters the functioning of SMI. While it is well known that dopaminergic medication mitigates the cardinal motor symptoms of PD, adverse effects of medication on sensory perception have been reported [16], [17]. Understanding the changes in SMI functions during the ON and OFF state of medication is essential to determine when it is most beneficial for PD patients to undergo the rehabilitation program. As sensory cues play a vital role in the efficacy of rehabilitation programs, a patient may benefit more if they undergo rehabilitation therapies in a state where they can better integrate sensory inputs and modulate motor outputs as opposed to a state in which they experience worsening SMI functions. Currently, very little is known about SMI deficits in PD, and there are few experimental studies [18], [19], [20] that have investigated this domain. In recent times, studies have also explored altered SMI mechanisms in multiple PD subtypes [21], and the asymmetry [22] and the functional connectivity losses [23] in the SMI network due to PD. However, earlier studies have neither tested the patient's SMI performance with multi-modal sensory inputs nor explored the effects of medication on SMI. The lack of understanding about the SMI deficits may also be due to inadequate assessment techniques to quantitatively evaluate SMI. Studies [24], [25] have emphasized the need for objective methods to characterize the symptoms of PD. Therefore, there is a need to develop an objective SMI assessment method to characterize SMI deficits in PD patients and understand the impact of medication on SMI.

The study aims to quantify the abnormalities in SMI among PD patients before and after medication. Two assessment tasks (reaching and tracing) were developed using a robotic manipulandum comprising a virtual reality (VR) display to examine SMI. Participants from the three groups (PD patients in the OFF state (PD-OFF), PD patients in the ON state (PD-ON), and control subjects) performed the reaching and tracing tasks in the virtual environment. Evaluating SMI performance requires testing participants in varying sensory environments. Therefore, the participants completed the tasks under different sensory conditions (with/without Assistive Sensory Cues (ASC) and with/without sensory manipulation). Features that can evaluate the participant's ability to perform voluntary movements based on perceptual estimates were extracted using the upper-limb kinematic data for each group. Two comparisons were made: (1) within-group; (2) between-group. While these comparisons shed light on the abnormalities in SMI among PD patients, a trial-by-trial analysis [26] was performed to explore how deficits in SMI may affect motor learning. The findings from this study will help understand the SMI deficits in PD patients when encountering multi-modal sensory inputs, how it affects motor performance and the effects of medication on SMI. Further, the study's results could be used to determine when PD patients can benefit the most from rehabilitation therapies and the nature of sensory cues that are most effective in improving their motor performance.

II. Methods

A. Participants

The Office of Human Research Ethics in Western University's Research Ethics Board approved the study protocol (protocol numbers: 115770 (approved in August 2021), and 108252 (approved in July 2016)) for this work. Patients were recruited through the Movement Disorders Clinic at University Hospital in London, Ontario, Canada. All participants were informed of the study protocols, and written consent was obtained for their participation. The study has been carried out following the ethical standards laid down in the Declaration of Helsinki. A total of 100 patients diagnosed with PD and 43 healthy age-matched control subjects were recruited for the study. While all 100 PD patients performed the reaching task, only 71 performed the tracing task. Inclusion criteria for patients were diagnosis of PD, no injury-limiting upper-limb movements, and normal or corrected-to-normal vision. The PD patients were tested in their OFF state after overnight suspension of medication. The tests were repeated in their ON state the same day, one hour after intake of medication. Prior to the tests, each patient was assessed using the Unified Parkinson's Disease Rating Scale (UPDRS) and Montreal Cognitive Assessment (MoCA) test. No dyskinesia affecting the upper-limb movements was observed during the assessment.

B. Testing Apparatus

The KINARM endpoint robot [27] was used to assess the SMI in PD and control subjects. The device included a robotic handle coupled with a VR display. The display showed the real-time fingertip position of the participants (white dot) and the virtual objects related to the task. The view of the participant's arm was blocked using a black screen located between the subject's arm and the display. Figure 1 shows the KINARM endpoint robot.

C. Task Design

The study evaluated the subject's ability to integrate multi-modal sensory inputs and modulate the motor outputs to

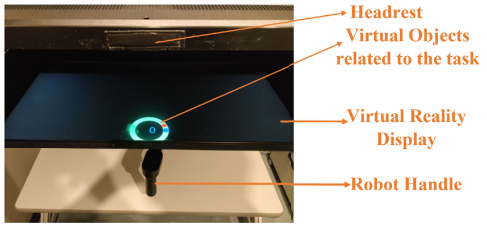

Fig. 1. A view of the KINARM Endpoint Robot comprising a VR display and a robot handle.

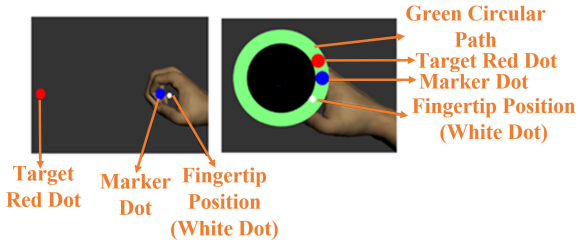

Fig. 2. Reaching task (on the left) and tracing task (on the right).

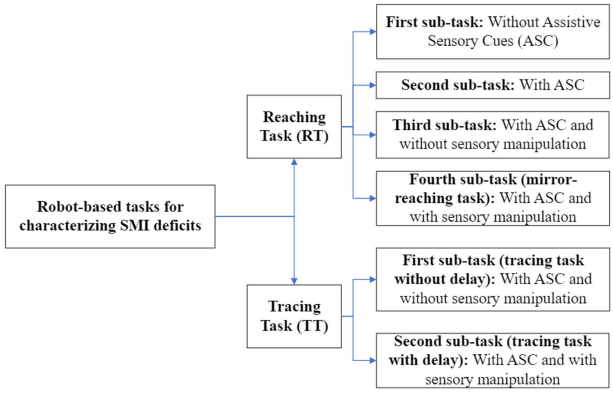

Fig. 3. Tasks used to characterize the SMI deficits and sensory conditions associated with each sub-task of the reaching and tracing task.

suit the demands of the testing conditions. To this end, the participants performed the custom-built reaching and tracing tasks under different sensory conditions. Earlier literature [28], [29] has specified reaching and tracing actions as a possible evaluator of sensorimotor performance. The participants were tested with and without ASC, and the ASC was provided through multiple modalities. This was done to understand if the PD patients could integrate the multi-modal inputs from the ASC and improve their motor performance. Secondly, the participants were tested with and without sensory manipulation (inaccurate sensory inputs) to understand if PD patients could adapt to unreliable or inaccurate sensory inputs. All participants were asked to perform each task with the right and left arms, and the PD patients performed these tasks in their OFF and ON states. Figure 2 shows an image of the reaching and tracing task. Figure 3 shows the sub-tasks of the reaching and tracing task used to assess the SMI deficits and their corresponding sensory conditions. A video showing the reaching and tracing task is also provided as supplementary material.

1) Reaching Tasks (RT): In this task, the participants were asked to reach the targets within a specific time. The trial began when the participant's arm was placed at the center of the screen, which was indicated by a marker dot. When the participant reached the marker dot, a target red dot appeared somewhere on the screen. The trial ended when the participant reached the target red dot and stay on it for three seconds or if six seconds had passed. The location of the target was random. The reaching task was divided into four sub-tasks (see Figure 3).

a) First sub-task: In the first sub-task, the participants received no ASC and only received the visual inputs from the VR display, which showed their fingertip position and the targets. The participants performed 10 trials per arm of this sub-task. The target size ranged from 1 to 2.5 cm in radius, and the distance between the center of the screen to the target ranged from 7 to 12.2 cm.

b) Second sub-task: In the second sub-task, the participants received ASC and visual inputs from the display. The participants received a haptic (vibrotactile signal in the robot handle) and an auditory (beep sound) input when they reached the target. The participants performed a total of 10 trials per arm. The size of the target and its distance from the center of the screen was the same as in the first sub-task.

c) Third sub-task: The third sub-task included ASC but not any sensory manipulation. The participants performed a total of 33 trials per arm. The target size ranged from 0.6 cm to 2.6 cm in radius. The distance between the center of the screen and the target ranged from 20 cm to 40 cm.

d) Fourth sub-task (mirror-reaching task): This sub-task assessed the participant's performance when encountering sensory manipulations. In this sub-task, the fingertip position shown on the VR display moved in the direction opposite to that of the actual movement made by the participant. Therefore, the participant needs to move in the direction opposite to the target's location to reach the target. The participants received ASC and completed 33 trials per arm. The size of the target and its distance from the center was the same as the third sub-task.

2) Tracing Tasks (TT): In these tasks, the participants were shown a green circular path on the display. The width of the path was 2 cm. A marker dot appears inside the right half of the green path. The trial begins when the participant reaches this marker dot, and a target red dot appears above the marker dot. The participant must go around the entire circular path (clockwise direction) to reach the target dot while staying within the green path. Any deviations from the green path will result in an ASC, i.e., a beeping sound and haptic feedback pushing the participant's arm back to the path. This task was divided into two sub-tasks (see Figure 3). The participants completed 12 trials per arm in each sub-tasks.

a) First sub-task: In this sub-task, there was no sensory manipulation. All trials in this sub-task included ASC.

b) Second sub-task: In this sub-task, the visual input was manipulated. A time delay of 1000 milliseconds was added to the visual input. The fingertip marker (white dot) shown on the VR display moves or stops 1000 milliseconds after the

TABLE I
FEATURES EXTRACTED FOR EACH TASK DURING THIS STUDY

Features	Definitions
Reaching Task	
Target reach	Mean percentage of targets reached
Mean Endpoint error	Mean distance between the fingertip and center of the target when the subject reaches and stays at the target
Mean Direction Error	Mean distance travelled by the white dot indicating the fingertip position in the wrong direction, i.e., a direction in which there is no target.
Mean Deviation error (MDE)	Mean deviation between the ideal and the actual path taken by the participants was calculated using the K-Nearest neighbor (K-NNR). A higher MDE indicates a lower efficiency.
Maximum Endpoint error	Maximum distance between the fingertip and the center of the target when the subject reaches and stays on the target
Maximum Direction Error	Maximum distance traveled in the wrong direction
Mean Velocity	Mean velocity when performing the reaching task
Tracing Task	
Mean number of violations	Mean number of times the participant has moved outside the green track
Time spent under violation	Mean time spent by the participant outside the green track
Mean Violation Distance	Mean distance the participants have traveled outside the green track
Mean Deviation error (MDE)	Mean deviation between the ideal and the actual path. In tracing task, the ideal path is the center of the green track. A higher MDE indicates a lower efficiency.
Mean Velocity	Mean velocity when performing the tracing task

participants perform or stop the movement. All trials in this sub-task included ASC.

D. Feature Extraction

The performance of the participants was quantified by extracting features from the kinematic data collected by the KINARM end point robot. The robot collected the upper-limb kinematic data at a sampling frequency of 1000 Hz, which was filtered using a dual-pass digital filter at a cut-off frequency of 10 Hz. The features [30] that signified the participant's accuracy and efficiency in performing an voluntary movement were extracted. Table I indicates the features extracted and their corresponding descriptions. The performance of the participants in the right and left hands were averaged together [31].

Motor learning [32] is the ability to learn and improve the accuracy and efficiency of voluntary movements based on perceptual estimates. Hence, the process of motor learning depends on the optimal functioning of SMI. Therefore, a trial-by-trial analysis was performed to quantify the effect of SMI deficits on motor learning. In the trial-by-trial analysis, the performance of the participants was averaged for each trial, and this was done for selected features in all groups. Then the difference between the two groups in each trial was calculated. To understand if the difference between the groups for a specific feature increases or decreases as more trials are performed, a correlation coefficient was calculated between this difference and the trial number. A negative correlation indicates that the difference between the groups reduces, while a positive correlation indicates an increase in the difference.

TABLE II
CLINICAL AND DEMOGRAPHIC DATA FOR THE PARTICIPANTS

	PD Patients	Healthy Controls
Number of Subjects	100	43
Gender (M/F)	73/27	32/11
Age (years) (Mean (Range))	63(40)	54(49)
UPDRS Motor Subscale in OFF state (Mean (Range))	23.2(36)	N/A
UPDRS Motor Subscale in ON state (Mean (Range))	11.5(28)	N/A
MoCA (Mean (Range))	25.2(10)	N/A

This would show if the participants could improve their performance over time. For instance, a PD patient might have a higher mean violation distance than control subjects. However, if the difference between the two groups reduces as they perform more trials, that would indicate that the PD patients could use sensory inputs and reduce error over time. The trial-by-trial analysis was performed on four error metrics (direction error, mean number of violations, mean violation distance, and time spent under violation) obtained from tasks with sensory manipulation to understand if the participants could learn and adapt to the manipulation over time.

E. Statistical Analyses

Statistical analysis was used to determine if the groups had a statistically significant difference in the extracted features. A pairwise statistical analysis between PD-OFF and PD-ON was done using the Wilcoxon signed-rank test. PD-OFF and PD-ON were compared with the control participants using a Mann-Whitney-Wilcox test [33]. The Wilcoxon signed-rank test was also used for within-group comparisons. Both the statistical tests were non-parametric, as the extracted features were not normally distributed. To correct for multiple analyses, the Bonferroni correction was used to adjust the p-value. A p-value less than 0.05 were considered statistically significant.

III. RESULTS

A. Demographic and Clinical Information

The demographic and clinical information associated with the PD patients and control subjects is provided in Table II.

B. Within Group Comparison

This section compares the performance of each group in trials with ASC to their own performance without them. The within-group comparison between the tasks with and without sensory manipulation is not discussed here, as all groups performed better in tasks without sensory manipulation. Table III shows the performance of the groups. Table IV shows the significance value for the within and between-group comparisons.

1) PD-OFF: Comparing the performance of PD-OFF in the first (without ASC) and second (with ASC) sub-task of RT, PD-OFF reached fewer targets with ASC than without ASC, and the difference was also statistically significant. Concerning the mean endpoint and mean direction error, PD-OFF committed 6.8% and 36% higher errors, respectively, with ASC

TABLE III
TASK PERFORMANCE OF EACH GROUP IN REACHING AND TRACING TASKS

Parameters		PD-OFF Median (Range)	PD-ON Median (Range)	Control subjects Median (Range)
Reaching Task				
Target Reach (%)	w.o. ASC	100(25)	98(33)	100(0)
	w. ASC	97(75)	99(50)	100(0)
	w.o. SM	95(87)	98(100)	100(25)
	w. SM	92(100)	90(100)	100(75)
Mean Endpoint error (cm)	w.o. ASC	0.465(1.72)	0.423(2.58)	0.390(0.56)
	w. ASC	0.498(3.94)	0.412(1.79)	0.345(0.75)
	w.o. SM	0.502(13.5)	0.445(10.1)	0.319(4.04)
	w. SM	0.744(17.1)	0.635(22.3)	0.478(7.49)
Mean Direction Error (cm)	w.o. ASC	0.009(1.49)	0.008(1.23)	0.004(0.63)
	w. ASC	0.013(1.68)	0.005(0.74)	0.001(0.01)
	w.o. SM	0.058(10.6)	0.049(5.93)	0.030(4.74)
	w. SM	1.298(14.4)	1.628(19.1)	0.901(9.44)
MDE (cm)	w.o. ASC	0.430(1.44)	0.442(1.23)	0.366(1.03)
	w. ASC	0.436(4.15)	0.409(2.37)	0.336(1.06)
	w.o. SM	0.462(12.2)	0.418(4.04)	0.352(1.45)
	w. SM	0.604(10.8)	0.647(8.68)	0.469(6.04)
Maximum Endpoint Error (cm)	w.o. ASC	4.971(4.74)	6.712(6.75)	1.576(1.34)
	w. ASC	2.034(12.0)	3.035(6.53)	1.400(1.83)
	w.o. SM	2.212(26.1)	1.884(27.6)	1.074(19.8)
	w. SM	4.322(28.5)	5.476(29.2)	2.677(16.3)
Maximum Direction Error (cm)	w.o. ASC	2.421(4.48)	3.875(4.89)	1.588(2.53)
	w. ASC	1.067(2.20)	2.959(2.91)	0.427(0.30)
	w.o. SM	1.588(21.5)	2.613(20.8)	1.009(7.82)
	w. SM	4.051(22.4)	5.289(25.2)	3.612(12.5)
Mean Velocity (cm/s)	w.o. ASC	0.036(0.13)	0.038(0.06)	0.040(0.02)
	w. ASC	0.035(0.10)	0.037(0.05)	0.039(0.02)
	w.o. SM	0.058(0.12)	0.060(0.10)	0.065(0.08)
	w. SM	0.050(0.09)	0.055(0.13)	0.060(0.09)
Tracing Task				
Mean Number of Violations	w.o. SM	0.60(9.6)	0.35(8)	0.25(1.10)
	w. SM	2.33(12.1)	2.57(7.17)	1.63(4.36)
Time Spent under Violation (s)	w.o. SM	0.08(2.31)	0.19(2.80)	0.02(0.33)
	w. SM	1.12(5.66)	1.32(4.73)	0.53(3.47)
Mean Violation Distance (cm)	w.o. SM	0.0009(0.35)	0.001(0.24)	0.0004(0.007)
	w. SM	0.018(0.44)	0.025(1.06)	0.008(0.157)
MDE (cm)	w.o. SM	0.431(1.20)	0.494(1.79)	0.298(0.588)
	w. SM	0.691(1.65)	0.700(2.25)	0.607(1.367)
Mean Velocity (cm/s)	w.o. SM	0.055(0.08)	0.060(0.05)	0.063(0.06)
	w. SM	0.050(0.07)	0.057(0.07)	0.066(0.04)

Note: w.o. ASC = without assistive sensory cues; w. ASC = with assistive sensory cues; w.o. SM = without sensory manipulation; w. SM = with sensory manipulation.

than without ASC. Further, PD-OFF was less efficient when provided with ASC, as indicated by a 1.3% increase of MDE in the second sub-task compared to the first sub-task.

2) PD-ON: PD-ON reached more targets in the second sub-task. In error metrics, PD-ON had 2.6% and 46% less mean endpoint and mean direction error, respectively, in the second sub-task compared to the first sub-task. Further, PD-ON had improved efficiency in the second sub-task, as indicated by a reduction of the MDE. However, no statistically significant improvement was seen in PD-ON due to ASC.

3) Control Subjects: The control subjects reached 100% of the targets with and without ASC. However, compared to the first sub-task, their mean endpoint and mean direction error were reduced by 12.2% and 120% in the second sub-task, with the difference being statistically significant in direction error. The efficiency also improved due to ASC as they reduced their MDE by 8.5% in the second sub-task compared to the first sub-task.

C. Between Group Comparison

In this section, the groups were compared with each other based on their performance in trials with and without ASC and in trials with and without sensory manipulation. Figure 4 compares the error metrics between the groups. This section also discusses the trial-by-trial analysis, shown in Figure 5.

1) PD-OFF Vs. Control Subjects:

a) With and Without ASC: In the first sub-task of RT, the control subjects had 17% and 76% lesser mean endpoint and mean direction error, respectively, than PD-OFF. The control subjects were also statistically significantly more efficient, as their MDE was 16% less than PD-OFF. In the second sub-task of RT, when provided with ASC, the control subjects reached more targets than PD-OFF. The control subjects committed 36% and 171% lesser mean endpoint and mean direction error, respectively, than PD-OFF, with the difference being statistically significant. Finally, the control subjects were also more efficient than PD-OFF as their MDE was 25% lower than for PD-OFF.

b) With and Without Sensory Manipulation: A between-group comparison in the third sub-task of the RT showed that the control subjects reached 5.1% more targets than PD-OFF. Additionally, the control subjects also committed statistically significantly lesser mean endpoint and mean direction error than PD-OFF. The control subjects were also more efficient, as shown by their 27% lower MDE than PD-OFF. In TT without delay, PD-OFF committed 82% more violations than the control subjects, and the difference was statistically significant. Further, the mean violation distance and time spent under violation for PD-OFF were 76% and 120% higher than for control subjects, with the difference being statistically significant. Lastly, the efficiency of the control subjects in the first sub-task of TT was statistically significantly higher than that for PD-OFF.

Moving to the between-group comparisons in tasks with sensory manipulation, the control subjects again outperformed PD-OFF across all features. In the fourth sub-task of RT, the control subjects reached statistically significantly more targets than PD-OFF, with their mean endpoint error being 43% lesser than PD-OFF. The most important feature for this sub-task, which is the mean direction error (as it indicates if the participants have adapted to the mirrored vision), was 36% less for control subjects than for PD-OFF. PD-OFF was also less efficient than control subjects, with the difference being statistically significant. In TT with delay, the control subjects committed 35% fewer violations than PD-OFF. In the error metrics, the control subjects have 76% lesser mean violation distance and 71% lesser time spent under violation than PD-OFF, with the difference being statistically significant. The MDE in control subjects was also 12% lower than PD-OFF, indicating that the control subjects were more efficient. Control subjects were also much faster than PD-OFF as their mean velocity was statistically significantly higher than PD-OFF across all sensory conditions. In trial-by-trial analysis between the two groups, a positive correlation was observed in direction

TABLE IV
SIGNIFICANCE VALUE FOR WITHIN AND BETWEEN-GROUP COMPARISONS

		Significance for within-group comparison			Significance for between-group comparison		
		PD-OFF	PD-ON	Control Subjects	PD-OFF vs. Control Subjects	PD-OFF vs. PD-ON	PD-ON vs. Control Subjects
Reaching Task							
Target Reach	w.o. ASC	$p = 0.0032$*	$p = 0.6090$	$p = 1$	$p = 0.5320$	$p = 0.0313$*	$p = 0.0711$
	w. ASC				$p = 0.0177$*	$p = 0.5625$	$p = 0.0765$
	w.o. SM	$p < 0.0001$*	$p < 0.0001$*	$p = 0.0260$*	$p < 0.0001$*	$p = 0.2101$	$p < 0.0001$*
	w. SM				$p < 0.0001$*	$p = 0.1343$	$p = 0.0001$*
Mean Endpoint Error	w.o. ASC	$p = 0.2959$	$p = 0.8777$	$p = 0.0775$	$p < 0.0004$*	$p = 0.0621$	$p = 0.1946$
	w. ASC				$p < 0.0001$*	$p = 0.1233$	$p = 0.0009$*
	w.o. SM	$p < 0.0001$*	$p < 0.0001$*	$p < 0.0001$*	$p < 0.0001$*	$p < 0.0001$*	$p < 0.0001$*
	w. SM				$p < 0.0001$*	$p < 0.0001$*	$p < 0.0001$*
Mean Direction Error	w.o. ASC	$p < 0.0001$*	$p < 0.0001$*	$p = 0.0382$*	$p = 0.0622$	$p = 0.5785$	$p = 0.1055$
	w. ASC				$p < 0.0001$*	$p = 0.7135$	$p = 0.0018$*
	w.o. SM	$p < 0.0001$*	$p < 0.0001$*	$p < 0.0001$*	$p = 0.0021$*	$p < 0.0001$*	$p = 0.0018$*
	w. SM				$p = 0.4306$	$p < 0.0001$*	$p = 0.0408$*
MDE	w.o. ASC	$p = 0.4690$	$p = 0.7830$	$p = 0.6035$	$p = 0.0017$*	$p = 0.1315$	$p = 0.0030$*
	w. ASC				$p < 0.0001$*	$p = 0.0459$*	$p = 0.0004$*
	w.o. SM	$p < 0.0001$*	$p < 0.0001$*	$p < 0.0001$*	$p < 0.0001$*	$p < 0.0001$*	$p < 0.0001$*
	w. SM				$p < 0.0001$*	$p = 0.3095$	$p < 0.0001$*
Maximum Endpoint Error	w.o. ASC	$p = 0.9729$	$p = 0.3591$	$p = 0.3021$	$p = 0.0013$*	$p = 0.5725$	$p = 0.2343$
	w. ASC				$p < 0.0001$*	$p = 0.2042$	$p = 0.1292$
	w.o. SM	$p < 0.0001$*	$p < 0.0001$*	$p < 0.0001$*	$p < 0.0001$*	$p < 0.0001$*	$p < 0.0001$*
	w. SM				$p < 0.0001$*	$p < 0.0001$*	$p < 0.0001$*
Maximum Direction Error	w.o. ASC	$p = 0.0001$*	$p < 0.0001$*	$p = 0.0278$*	$p = 0.0902$	$p = 0.9650$	$p = 0.1245$
	w. ASC				$p = 0.0037$*	$p = 0.6149$	$p = 0.0036$*
	w.o. SM	$p < 0.0001$*	$p < 0.0001$*	$p < 0.0001$*	$p = 0.0020$*	$p = 0.0023$*	$p = 0.0014$*
	w. SM				$p = 0.2309$	$p < 0.0001$*	$p = 0.0063$*
Mean Velocity	w.o. ASC	$p = 0.5143$	$p = 0.1349$	$p = 0.2910$	$p < 0.0001$*	$p = 0.0114$*	$p = 0.0174$*
	w. ASC				$p < 0.0001$*	$p = 0.0494$*	$p = 0.0013$*
	w.o. SM	$p < 0.0001$*	$p < 0.0001$*	$p < 0.0001$*	$p < 0.0001$*	$p < 0.0001$*	$p = 0.0026$*
	w. SM				$p < 0.0001$*	$p < 0.0001$*	$p = 0.0017$*
Tracing Task							
Mean Number of Violations	w.o. SM	$p < 0.0001$*	$p < 0.0001$*	$p < 0.0001$*	$p = 0.0060$*	$p = 0.0411$*	$p < 0.0001$*
	w. SM				$p = 0.0605$	$p = 0.1316$	$p = 0.0054$*
Time Spent under Violation	w.o. SM	$p < 0.0001$*	$p < 0.0001$*	$p < 0.0001$*	$p = 0.0069$*	$p = 0.0009$*	$p < 0.0001$*
	w. SM				$p = 0.0019$*	$p = 0.0457$*	$p = 0.0011$*
Mean Violation Distance	w.o. SM	$p < 0.0001$*	$p < 0.0001$*	$p < 0.0001$*	$p = 0.0187$*	$p < 0.0001$*	$p < 0.0001$*
	w. SM				$p = 0.0401$*	$p = 0.0046$*	$p = 0.0058$*
MDE	w.o. SM	$p < 0.0001$*	$p < 0.0001$*	$p < 0.0001$*	$p = 0.0019$*	$p = 0.1817$	$p = 0.0001$*
	w. SM				$p = 0.0830$	$p = 0.9335$	$p = 0.0829$
Mean Velocity	w.o. SM	$p = 0.0026$*	$p = 0.0092$*	$p = 0.0074$*	$p < 0.0001$*	$p < 0.0001$*	$p = 0.4926$
	w. SM				$p < 0.0001$*	$p < 0.0001$*	$p = 0.9314$

Note: w.o. ASC = without assistive sensory cues; w. ASC = with assistive sensory cues; w.o. SM = without sensory manipulation; w. SM = with sensory manipulation; * after the p-value indicates statistical significance

error, and a negative correlation was observed in the mean number of violations and time spent under violation.

2) PD-OFF Vs. PD-ON:

a) With and Without ASC: In tasks without ASC, PD-OFF reached more targets than PD-ON. The efficiency of PD-OFF was marginally better as their MDE was 2.7% lower than PD-ON. While the mean endpoint and mean direction error for PD-ON were 9.4% and 11% lower than for PD-OFF, respectively, the maximum endpoint and maximum direction error for PD-ON were 29% and 46% higher than for PD-OFF. Moving to tasks with ASC, PD-ON reached more targets than PD-OFF. PD-ON was also statistically significantly more efficient than PD-OFF. Moreover, the mean endpoint and mean direction errors for PD-ON were also 18% and 88% lower than PD-OFF. However, the maximum direction error committed by PD-ON was 93% higher than by PD-OFF.

b) With and Without Sensory Manipulation: For tasks without sensory manipulations, PD-ON reached more targets than PD-OFF in the third sub-task of RT. In error metrics, PD-OFF had 12% more mean endpoint error and 16% more mean direction error than PD-ON. Further, PD-ON also showed a statistically significant improvement in efficiency compared to PD-OFF. Moving to the TT without delay, PD-ON had fewer violations than PD-OFF. However, the mean violation distance and time spent under violation for PD-ON were 10% and 81% higher than PD-OFF, respectively.

The performance of PD-ON in tasks with sensory manipulations was compared with PD-OFF. In the fourth sub-task of RT, PD-OFF reached marginally more targets than PD-ON. However, this difference was not statistically significant. Additionally, the PD-OFF was more efficient than PD-ON. Mean direction error, a primary performance indicator for this sub-task, was 22% higher in PD-ON than in PD-OFF, and this difference was statistically significant. Finally, the endpoint error for PD-OFF was 15% higher than for PD-ON. Therefore, apart from the endpoint error, PD-ON performed worse than PD-OFF in all other features, including the direction error, which evaluates how the patients adapt to

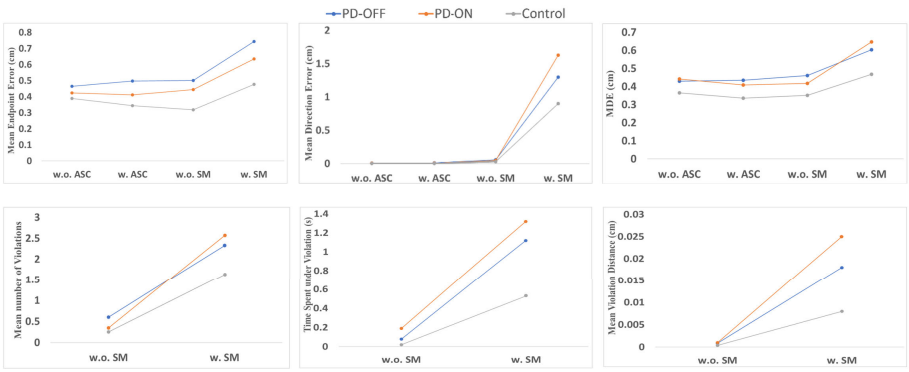

Fig. 4. Comparing the error metrics (mean endpoint error, mean direction error, MDE, mean number of violations, time spent under violation, mean violation distance) of the three groups. Note: w.o. ASC = without assistive sensory cues; w. ASC = with assistive sensory cues; w.o. SM = without sensory manipulation; w. SM = with sensory manipulation.

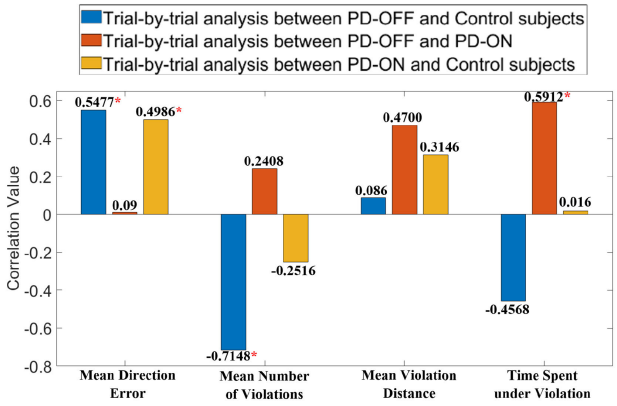

Fig. 5. Trial-by-Trial analysis. Note: ∗ indicates statistical significance.

sensory manipulation. Moving to TT with delay, PD-ON did considerably worse than PD-OFF across all features. PD-ON committed 9.7% more violations than PD-OFF when encountering a visual delay. Further, the mean violation distance and time spent under violation in PD-ON increased by 32% and 16%, respectively, compared to PD-OFF, with the difference being statistically significant. Lastly, PD-ON showed less efficiency than PD-OFF, as shown by their MDE in the TT. However, the medication improved the mean velocity in both RT and TT across all sensory conditions. In the trial-by-trial analysis between PD-OFF and PD-ON, there was a positive correlation seen in mean violation distance, time spent under violation, and the mean number of violations.

3) PD-ON Vs. Control Subjects:

a) With and Without ASC: In the task without ASC, the control subjects reached more targets than PD-ON and had 8% and 66% fewer endpoint and direction errors, respectively, than PD-ON. Furthermore, the efficiency of control subjects was also statistically significantly better than for PD-ON. When provided with ASC, the control subjects reached a marginally higher number of targets, committed lesser mean endpoint and mean direction errors, and were also more efficient than PD-ON.

b) With and Without Sensory Manipulation: For the RT without sensory manipulation, PD-ON reached statistically significantly fewer targets, committed fewer errors, and was less efficient than the control subjects. Looking at the TT without delay, features such as mean number of violations, mean violation distance, and time spent under violation were 33%, 85%, and 161% better in control subjects than PD-ON. In terms of efficiency, the MDE for PD-ON was 49% higher than that for control subjects.

In tasks with sensory manipulation, for the fourth sub-task of RT, the PD-ON reached lesser targets, had a 28% higher mean endpoint error, 57% higher mean direction error, and exhibited poorer efficiency than the control subjects. The difference in direction error between the two groups was statistically significant. For TT with delay, PD-ON exhibited 44% more violations, 103% higher mean violation distance, 85% higher time spent under violation, and poorer efficiency than control subjects. While medication improved the mean velocity, PD-ON was still much slower than the control subjects. In trial-by-trial analysis, a positive correlation was observed in the direction error and mean violation distance. Further, there was a negative correlation observed in mean number of violations.

IV. Discussion

The aim of this study was to quantify deficits in SMI by assessing the performance of 43 control participants and 100 PD patients in their OFF and ON states using a custom-designed robot-assisted assessment tool under varying sensory conditions (with/ without ASC and with/ without sensory manipulation). Research exploring sensory abnormalities in PD patients has gained pace in recent years. Studies have explored impairments in kinesthesia [6] and visual [7], haptic [8], and auditory [9] perception due to PD. However, these studies have only focused on perceptual deficits associated with a single modality. Even in studies [20] that report an altered SMI in PD patients, only haptic perception was tested. Therefore, in our study, we investigated the deficits in multi-sensory integration by examining the patient's performance when provided with multi-modal ASC. Muller et al. [18] studied the relationship between cholinergic terminal loss and dopaminergic denervation with postural sensory integration in PD. However, the SMI deficits related to voluntary movement or the effect of medication were

TABLE V
SUMMARY OF RESULTS

	PD-OFF	PD-ON	Controls
Tasks with and without assistive sensory cues	**Within-group comparison:** Motor performance deteriorated with ASC compared to without ASC	**Within-group comparison:** Motor performance neither improved nor deteriorated with ASC	**Within-group comparison:** Motor performance improved when provided with ASC
	Between-group comparison: Mean velocity lowest among the three groups	**Between-group comparison:** Medication improved the movement speed	**Between-group comparison:** Movement speed highest among the three groups
	Between-group comparison: Performance of PD-OFF better than PD-ON in features such as maximum endpoint and direction error	**Between-group comparison:** PD-ON performed better than PD-OFF in most features except features such as maximum endpoint and direction error	**Between-group comparison:** Performance of control subjects was the best among the three groups across all features
	Inference: Exhibited deficits in integrating multi-modal inputs resulting in worsening of motor performance; ability to modulate motor outputs based on the perceptual estimate is still intact.	**Inference:** Sensory inputs had no significant effect on motor performance; unable to correct errors once committed, leading to increased maximum endpoint and direction error; implies a breakdown in the ability to modulate motor outputs based on sensory inputs.	**Inference:** Exhibited optimal sensorimotor integration, thereby benefitted from multi-modal assistive sensory cues
Tasks with and without sensory manipulation	**Between-group comparison:** PD-OFF was able to correct errors as indicated by their lower mean violation distance and time spent under violation than PD-ON	**Between-group comparison:** In line with earlier observation, PD-ON struggled to correct errors, as indicated by their higher mean violation distance and time spent under violation than PD-OFF	**Between-group comparison:** Compared to PD-OFF and PD-ON, the controls were better across all features in reaching and tracing task
	Between-group comparison: Performed better than PD-ON across most features when encountering sensory manipulation	**Between-group comparison:** Significant performance deterioration after medication indicating an inability to adapt to sensory manipulation	**Between-group comparison:** Controls performed the best compared to other groups.
	Trial-by-Trial analysis: Able to learn and improve their performance over time	**Trial-by-Trial analysis:** Unable to use sensory inputs to learn and improve motor performance	**Trial-by-Trial analysis:** Ability to learn and adapt to sensory conditions was much better than PD-OFF and PD-ON.
	Inference: Exhibited impairments in multi-sensory integration; retains the ability to modulate motor output based on the perceptual estimate; able to correct errors, learn and modify motor plan to adapt to various sensory conditions, although this learning and adaptation process takes longer than controls.	**Inference:** Medication affected the patient's ability to modulate motor outputs based on sensory inputs; unable to correct errors, learn or modify their motor plan based on sensory inputs to suit the demands of the environment.	**Inference:** Was the best performer among the three groups due to optimal functioning of SMI

not explored. Dubbioso et al. [19] reported abnormalities due to PD at the cortical level, where the sensory inputs are integrated. However, there was no conclusive evidence to understand the nature of SMI deficits and how they affect motor control. Other recent studies [21], [22], [23] that investigate SMI deficits also do not study the patients under dynamic sensory conditions or use objective metrics to evaluate the impairments. To address such limitations, in our study, an objective investigation of SMI deficits in PD patients under varying sensory conditions was conducted. Further, unlike the earlier studies, the effect of medication on SMI impairments was also explored. Table V gives a summary of the results.

Looking at the within-group comparison, PD-OFF performed worse in trials with ASC than in trials without ASC, indicating an impairment among PD-OFF in integrating multi-modal inputs. When no multi-modal ASC was provided, PD-OFF did not need to integrate multi-modal inputs. Their motor action was only guided by the visual input obtained through the VR display, resulting in better performance. However, when receiving multi-modal ASC, PD-OFF exhibited deficits in integrating multiple modalities resulting in an inaccurate perceptual estimate. Modulation of the motor output based on this inaccurate perceptual estimate led to the deterioration of performance when encountering ASC. In contrast, the control subjects performed better in trials with ASC compared to trials without ASC, implying that the control subjects could optimally integrate multiple modalities and therefore benefitted from the ASC. In PD-ON, no statistically significant improvement or deterioration was observed in any feature with or without the ASC. This may suggest that the multi-modal ASC had no significant effect on PD-ON's motor output.

Compared with control subjects, PD-OFF performed worse in tasks with and without ASC. Further, the difference between the two groups increased in most features when encountering ASC compared to the task without ASC. Features such as target reach, mean and maximum direction error were statistically significantly different between the groups in tasks with ASC. However, no statistical significance was found for these features in the tasks without ASC. This may be because, as mentioned in the within-group comparison, while the ASC improved the performance of control subjects, it deteriorated the performance of PD-OFF due to their SMI impairments, increasing the difference between the performance of the two groups. This finding aligns with our earlier inference that PD-OFF may struggle to integrate multi-modal inputs. Computational models such as a Maximum Likelihood Estimator (MLE) [34] hypothesizing the criterion used for multi-sensory integration show that the modalities are ranked based on the noise associated with it by assigning an optimal weight value and then integrated to obtain a perceptual estimate. Interpreting this result from the perspective of the MLE model, PD-OFF may be unable to rank each modality resulting in an impaired SMI process. This aligns with the study by Brown et al. [14] that hypothesizes a deficit among PD patients in organizing

and ranking modalities based on their accuracy. In tasks without sensory manipulation, the control subjects performed better in both reaching and tracing tasks than PD-OFF. Therefore, the SMI deficit affected a diverse range of voluntary movements, including tracing actions. Similarly, in tasks with sensory manipulation, the control subjects outperformed PD-OFF in all tasks. Across all sensory conditions, PD-OFF was significantly slower than controls in both reaching and tracing tasks. However, many features (direction error, mean number of violations, and MDE) that were statistically significantly different between the two groups in trials without sensory manipulation had no statistical significance when the groups encountered sensory manipulation. This may imply that PD-OFF could modulate their motor output, considering the sensory manipulation. As indicated earlier, SMI has two facets: (i) multi-sensory integration and (ii) adjusting motor output based on the perceptual estimates. The findings suggest that while PD-OFF showed deficits in the first facet of SMI (multi-sensory integration), they still retain the ability to modulate the motor output using the perceptual estimates obtained from the impaired multi-sensory integration process, thereby adapting to the sensory manipulation. However, this ability to adapt to sensory manipulations in PD-OFF was not as efficient as it was for control subjects, as the controls still performed better than PD-OFF. The negative correlation observed in the trial-by-trial analysis for the time spent under violation and the mean number of violations further validates this hypothesis that PD-OFF could learn to adapt to sensory manipulation. Therefore, as they completed more trials, PD-OFF could get their performance closer to that of the control subjects, reducing the difference between the two groups. Moreover, this implies that the ability to modulate motor outputs based on sensory inputs, which is vital for motor learning [35], remains intact in PD-OFF. However, a positive correlation was observed during trial-by-trial analysis for direction error. This may be because, in the tracing task, the participants were guided by ASC throughout the entire task, whereas, in the reaching task, these ASC were provided only when reaching a target, and they were not guided to the target using these ASC. This may have resulted in PD-OFF being unable to reduce the direction error in the reaching task with sensory manipulation as opposed to the tracing task with sensory manipulation, where PD-OFF were able to improve their performance. This is evidence that if PD-OFF is provided with motor training or rehabilitation therapies under optimal sensory conditions that guide them throughout their task, PD-OFF can improve their motor performance over time.

A comparison between PD-OFF and PD-ON was done to understand the effects of dopaminergic medication on SMI deficits. In tasks with and without ASC, PD-ON performed better than PD-OFF in most features. However, the maximum endpoint and maximum direction error committed by PD-ON in tasks with/without ASC were higher than PD-OFF. These findings may imply that while PD-ON commit fewer errors than PD-OFF, when PD-ON do commit an error, they struggle to correct it, resulting in a much higher maximum error than PD-OFF. In reaching tasks without sensory manipulation, PD-ON performed better than PD-OFF. However, in the tracing task without sensory manipulation, while PD-ON committed fewer violations than PD-OFF, the mean violation distance and time spent under violation for PD-ON were statistically significantly higher than for PD-OFF. This aligns with our earlier inference that while PD-ON committed fewer violations than PD-OFF, when PD-ON did commit a violation, they were much worse than PD-OFF in correcting it. The findings suggest impaired online motor control (adjusting motor control strategies based on the perceptual estimates) in PD-ON, which is vital for performing any task-specific movements [3]. It further implies that PD-ON may have followed a pre-defined movement pattern and were unable to use the perceptual estimates to modulate the motor output when they committed an error. In contrast, while PD-OFF committed more errors due to impairments in multi-sensory integration, they could still use the perceptual estimates and correct the errors as they performed the task. Another result consistent with this conclusion was the within-group comparison, where the ASC did not yield any significant motor improvements for PD-ON. Finally, for tasks with sensory manipulation, apart from the endpoint error in the reaching task and mean velocity, PD-ON performed worse than PD-OFF across all other features. There was a statistically significant deterioration in performance experienced after medication for several features, such as direction error in reaching tasks, mean violation distance, and time spent under violation in tracing tasks. Congruent to our conclusion, PD-ON struggled to update their motor plan based on the perceptual estimates when encountering the manipulation of the testing environment. For the trial-by-trial analysis, there was a positive correlation between the two groups for mean violation distance, time spent under violation, and the mean number of violations in tracing tasks with sensory manipulation. This indicates that the difference in performance increased as the groups performed more trials. Therefore, in addition to PD-ON performing worse in these features than PD-OFF, PD-ON also failed to improve as they performed more trials. This further validates our claim that PD-OFF used the sensory inputs to improve while PD-ON was unable to do so. Although the movement speed in PD-OFF was slower, they retained the ability to modulate, update, and learn motor tasks using multi-modal sensory feedback. In contrast, while the movement speed increased after medication, the patients struggled to update or learn motor tasks using sensory feedback. Therefore, an increase in movement speed after medication did not translate to improved task performance. This is because task-specific movements can be optimally performed only by constantly updating motor commands based on sensory feedback that highlights the demands of the environment and the task at hand. These findings imply on a cautionary note that treatment with levodopa may impair the ability of PD patients to utilize sensory information and learn.

Comparing the PD-ON and the control subjects, the latter performed better than PD-ON in all tasks with/without ASC and sensory manipulation. While no statistical significance was found in error metrics for tasks without ASC, there was a statistically significant difference between the groups in error metrics when encountering ASC. In trial-by-trial analysis, for tasks with sensory manipulation, the difference between the

two groups increased in mean violation distance as more trials were performed. These findings suggest that the control subjects used the ASC to improve their motor performance and took into account sensory manipulation. In contrast, PD-ON exhibited deficits in using ASC to enhance their performance and adapt to sensory manipulation resulting in a significant difference between the performance of PD-ON and control subjects.

In summary, evidence from this study points to an apparent deficit in multi-sensory integration among PD-OFF, which, in turn, affects their voluntary movements. However, PD-OFF could still use the perceptual estimates obtained from an impaired multi-sensory integration process to modulate their motor output and improve their performance. Therefore, while PD-OFF exhibited impairment in the first facet of SMI (multi-sensory integration), the functioning associated with the second facet of SMI (ability to modulate motor output based on the perceptual estimates) is still intact. Furthermore, PD-OFF may be able to improve the multi-sensory integration over time, which contributes to the improvement in motor performance, as shown by the trial-by-trial analysis. Therefore, if provided with appropriate sensory feedback that guides them throughout the task, PD-OFF may improve their motor performance. For the PD-ON group, the administration of dopamine improved the movement speed while adversely affecting the SMI circuit leading to deterioration in overall task performance. The findings suggest that PD-ON struggled to modulate motor outputs based on their perceptual estimates and, therefore, could not adapt to the sensory manipulation. Additionally, while PD-OFF retained the motor learning ability, the medication disrupted the motor learning process as it heavily depends on the optimal integration between the sensory and motor systems, resulting in an inability to improve motor performance based on sensory feedback. Daily activities require learning new motor tasks and constant modification of the learned motor tasks based on sensory feedback to suit the demands of the environment. While the medication increased the movement speed, it deteriorated the movement accuracy, efficiency, and learning ability due to the worsening of SMI deficits. Improvement in the movement speed due to medication might help patients perform tasks faster. However, it may be at the cost of deterioration in their task performance owing to worsening accuracy, efficiency, and learning ability. Studies [15] have shown that providing appropriate sensory cues is vital to the efficacy of the rehabilitation program. Taking these results together, rehabilitation therapies may be more effective in PD-OFF as they retain the ability to utilize the sensory inputs to adjust their motor outputs and improve their performance. The therapies may not be effective in the ON state due to the deterioration in the ability to modulate motor outputs based on perceptual estimates. Therefore, rehabilitation programs with an enriched sensory environment may be effective in PD patients before medication, and such a sensory environment should involve inputs from multiple modalities. It must be noted that the sensory input provided should be consistent with the desired motor performance. Further, as discussed earlier, there is a lack of objective assessment methods to evaluate SMI performance in PD patients. Consequently, to objectively examine SMI, this study developed two assessment tasks that can be performed under dynamic sensory conditions. While assessments such as reaching tasks have been proposed in earlier studies [27], [36], the tasks used in these studies do not include a dynamic sensory environment, which is essential for assessing SMI. Therefore, this study also provides new insights into using objective methodologies to quantify SMI impairments effectively.

This study has a few limitations that will be addressed in future work. While the study explored SMI deficits, other sensory deficits related to the scaling of sensory inputs and sensory overload must be explored. Understanding these deficits could assist in optimizing the treatments for PD. Although the participants were exposed to multi-modal sensory cues, the nature and intensity of these sensory cues remained unchanged. It would be worth investigating if the motor performance varies with changes in the amplitude of vibrotactile inputs, the brightness of visual inputs, or the loudness of the auditory cues. This could help determine the nature, type, and intensity of sensory cues that could be most effective in rehabilitation. It is also important to note that the assessment tool used in this study will not quantify all aspects of PD-related impairments and thus needs to be used in conjunction with other clinical evaluations. Additionally, while the study developed objective methodologies to evaluate SMI, the assessment tasks and the extracted features must be validated by clinical experts before they can be used in a clinical setting.

V. Conclusion

The subjects in this study performed a series of reaching and tracing tasks under different sensory conditions using a robotic manipulandum. Various features were extracted to evaluate the performance of the three groups. The results provided evidence of abnormalities in multi-sensory integration among PD-OFF and their adverse effect on voluntary movements. Further, the medication adversely affected the ability to modulate motor output based on perceptual estimates. While the performance of the PD-OFF group improved over time, an improvement was not seen in the performance of the PD-ON group. It can be concluded that while PD-OFF and PD-ON showed deficits in SMI, the impairments worsened after medication due to the disruption of online motor control. Therefore, rehabilitation therapy before medication may be more efficacious than after medication and may improve motor performance. Further, rehabilitation therapy that includes enriched sensory cues that are compatible with the desired motor performance could lead to motor improvement and delay the use of dopaminergic medication in early PD. This could therefore help to provide effective motor performance while avoiding the side effects of the medication, including the worsening of SMI mentioned in the paper. Our future work will focus on investigating other aspects of sensory deficits and how a change in the intensity of sensory cues may affect motor performance in PD patients.

References

[1] M. O. Ernst and H. H. Bülthoff, "Merging the senses into a robust percept," *Trends Cognit. Sci.*, vol. 8, no. 4, pp. 162–169, Apr. 2004, doi: 10.1016/j.tics.2004.02.002.

[2] B. E. Stein and M. A. Meredith, *The Merging of the Senses*. Cambridge, MA, USA: MIT Press, 1993.

[3] R. Shadmehr, M. A. Smith, and J. W. Krakauer, "Error correction, sensory prediction, and adaptation in motor control," *Annu. Rev. Neurosci.*, vol. 33, no. 1, pp. 89–108, Jun. 2010, doi: 10.1146/annurev-neuro-060909-153135.

[4] S. Sangani, A. Lamontagne, and J. Fung, "Cortical mechanisms underlying sensorimotor enhancement promoted by walking with haptic inputs in a virtual environment," *Prog. Brain Res.*, vol. 218, pp. 313–330, Jan. 2015, doi: 10.1016/bs.pbr.2014.12.003.

[5] G. Abbruzzese and A. Berardelli, "Sensorimotor integration in movement disorders," *Movement Disorders*, vol. 18, no. 3, pp. 231–240, Mar. 2003, doi: 10.1002/mds.10327.

[6] T. Klockgether, M. Borutta, H. Rapp, S. Spieker, and J. Dichgans, "A defect of kinesthesia in Parkinson's disease," *Movement Disorders*, vol. 10, no. 4, pp. 460–465, Jul. 1995, doi: 10.1002/mds.870100410.

[7] R. S. Weil, A. E. Schrag, J. D. Warren, S. J. Crutch, A. J. Lees, and H. R. Morris, "Visual dysfunction in Parkinson's disease," *Brain*, vol. 139, no. 11, pp. 2827–2843, Nov. 2016, doi: 10.1093/brain/aww175.

[8] J. Konczak, K.-Y. Li, P. J. Tuite, and H. Poizner, "Haptic perception of object curvature in Parkinson's disease," *PLoS ONE*, vol. 3, no. 7, p. e2625, Jul. 2008, doi: 10.1371/journal.pone.0002625.

[9] Z. Jafari, B. E. Kolb, and M. H. Mohajerani, "Auditory dysfunction in Parkinson's disease," *Movement Disorders*, vol. 35, no. 4, pp. 537–550, Apr. 2020, doi: 10.1002/mds.28000.

[10] M. Bernardinis, S. F. Atashzar, M. S. Jog, and R. V. Patel, "Differential temporal perception abilities in Parkinson's disease patients based on timing magnitude," *Sci. Rep.*, vol. 9, no. 1, p. 19638, Dec. 2019, doi: 10.1038/s41598-019-55827-y.

[11] N. Patel, J. Jankovic, and M. Hallett, "Sensory aspects of movement disorders," *Lancet Neurol.*, vol. 13, no. 1, pp. 100–112, 2014, doi: 10.1016/S1474-4422(13)70213-8.

[12] O. Halperin, S. Israeli-Korn, S. Yakubovich, S. Hassin-Baer, and A. Zaidel, "Self-motion perception in Parkinson's disease," *Eur. J. Neurosci.*, vol. 53, no. 7, pp. 2376–2387, Apr. 2021, doi: 10.1111/ejn.14716.

[13] J. P. Azulay, S. Mesure, B. Amblard, and J. Pouget, "Increased visual dependence in Parkinson's disease," *Perceptual Motor Skills*, vol. 95, no. 3, pp. 1106–1114, Dec. 2002, doi: 10.2466/pms.2002.95.3f.1106.

[14] L. A. Brown et al., "Parkinsonian deficits in sensory integration for postural control: Temporal response to changes in visual input," *Parkinsonism Rel. Disorders*, vol. 12, no. 6, pp. 376–381, Sep. 2006, doi: 10.1016/j.parkreldis.2006.03.004.

[15] R. Marchese, M. Diverio, F. Zucchi, C. Lentino, and G. Abbruzzese, "The role of sensory cues in the rehabilitation of Parkinsonian patients: A comparison of two physical therapy protocols," *Movement Disorders*, vol. 15, no. 5, pp. 879–883, 2000, doi: 10.1002/1531-8257(200009)15:5<879::AID-MDS1018>3.0.CO;2-9.

[16] P. O'Suilleabhain, "Proprioception in Parkinson's disease is acutely depressed by dopaminergic medications," *J. Neurol., Neurosurgery Psychiatry*, vol. 71, no. 5, pp. 607–610, Nov. 2001, doi: 10.1136/jnnp.71.5.607.

[17] D. Mongeon, P. Blanchet, and J. Messier, "Impact of Parkinson's disease and dopaminergic medication on proprioceptive processing," *Neuroscience*, vol. 158, no. 2, pp. 426–440, Jan. 2009, doi: 10.1016/j.neuroscience.2008.10.013.

[18] M. L. T. M. Müller et al., "Thalamic cholinergic innervation and postural sensory integration function in Parkinson's disease," *Brain*, vol. 136, no. 11, pp. 3282–3289, Nov. 2013, doi: 10.1093/brain/awt247.

[19] R. Dubbioso, F. Manganelli, H. R. Siebner, and V. Di Lazzaro, "Fast intracortical sensory-motor integration: A window into the pathophysiology of Parkinson's disease," *Frontiers Hum. Neurosci.*, vol. 13, p. 111, Apr. 2019, doi: 10.3389/fnhum.2019.00111.

[20] J. Konczak et al., "Parkinson's disease accelerates age-related decline in haptic perception by altering somatosensory integration," *Brain*, vol. 135, no. 11, pp. 3371–3379, Nov. 2012, doi: 10.1093/brain/aws265.

[21] D. Belvisi et al., "The pathophysiological correlates of Parkinson's disease clinical subtypes," *Movement Disorders*, vol. 36, no. 2, pp. 370–379, Feb. 2021, doi: 10.1002/mds.28321.

[22] G. Goelman, R. Dan, F. Růžička, O. Bezdicek, and R. Jech, "Asymmetry of the insula-sensorimotor circuit in Parkinson's disease," *Eur. J. Neurosci.*, vol. 54, no. 6, pp. 6267–6280, Sep. 2021, doi: 10.1111/ejn.15432.

[23] J. Caspers et al., "Within- and across-network alterations of the sensorimotor network in Parkinson's disease," *Neuroradiology*, vol. 63, no. 12, pp. 2073–2085, Dec. 2021, doi: 10.1007/s00234-021-02731-w.

[24] J. Koerts, L. Tucha, K. L. Leenders, M. van Beilen, W. H. Brouwer, and O. Tucha, "Subjective and objective assessment of executive functions in Parkinson's disease," *J. Neurol. Sci.*, vol. 310, nos. 1–2, pp. 172–175, Nov. 2011, doi: 10.1016/j.jns.2011.07.009.

[25] M. Delrobaei, N. Baktash, G. Gilmore, K. McIsaac, and M. Jog, "Using wearable technology to generate objective Parkinson's disease dyskinesia severity score: Possibilities for home monitoring," *IEEE Trans. Neural Syst. Rehabil. Eng.*, vol. 25, no. 10, pp. 1853–1863, Oct. 2017, doi: 10.1109/TNSRE.2017.2690578.

[26] R. Gentili, C. E. Han, N. Schweighofer, and C. Papaxanthis, "Motor learning without doing: Trial-by-trial improvement in motor performance during mental training," *J. Neurophysiol.*, vol. 104, no. 2, pp. 774–783, Aug. 2010, doi: 10.1152/jn.00257.2010.

[27] C. S. Mang et al., "Test-retest reliability of the KINARM end-point robot for assessment of sensory, motor and neurocognitive function in young adult athletes," *PLoS ONE*, vol. 13, no. 4, Apr. 2018, Art. no. e0196205, doi: 10.1371/journal.pone.0196205.

[28] L. A. Stirling, L. A. Lipsitz, M. Qureshi, D. G. Kelty-Stephen, A. L. Goldberger, and M. D. Costa, "Use of a tracing task to assess visuomotor performance: Effects of age, sex, and handedness," *J. Gerontol. A, Biol. Sci. Med. Sci.*, vol. 68, no. 8, pp. 938–945, Aug. 2013, doi: 10.1093/gerona/glt003.

[29] D. P. Sadaphal, A. Kumar, and P. K. Mutha, "Sensorimotor learning in response to errors in task performance," *eNeuro*, vol. 9, no. 2, pp. 1–14, Mar. 2022, doi: 10.1523/ENEURO.0371-21.2022.

[30] S. M. Mostafavi, S. Scott, S. Dukelow, and P. Mousavi, "Reduction of assessment time for stroke-related impairments using robotic evaluation," *IEEE Trans. Neural Syst. Rehabil. Eng.*, vol. 25, no. 7, pp. 945–955, Jul. 2017, doi: 10.1109/TNSRE.2017.2669986.

[31] P. Gaprielian, S. H. Scott, C. Lowrey, S. Reid, G. Pari, and R. Levy, "Integrated robotics platform with haptic control differentiates subjects with Parkinson's disease from controls and quantifies the motor effects of levodopa," *J. Neuroeng. Rehabil.*, vol. 16, no. 1, pp. 1–14, Dec. 2019, doi: 10.1186/s12984-019-0598-5.

[32] J. W. Krakauer, A. M. Hadjiosif, J. Xu, A. L. Wong, and A. M. Haith, "Motor learning," in *Comprehensive Physiology*. Hoboken, NJ, USA: Wiley, 2019, pp. 613–663, doi: 10.1002/cphy.c170043.

[33] K. F. Weaver, V. Morales, S. L. Dunn, K. Godde, and P. F. Weaver, "Mann–Whitney U and Wilcoxon signed-rank," in *An Introduction to Statistical Analysis in Research*. Hoboken, NJ, USA: Wiley, 2017, doi: 10.1002/9781119454205.ch7.

[34] M. O. Ernst and M. S. Banks, "Humans integrate visual and haptic information in a statistically optimal fashion," *Nature*, vol. 415, no. 6870, pp. 429–433, Jan. 2002, doi: 10.1038/415429a.

[35] Z. Matur and A. E. Oge, "Sensorimotor integration during motor learning: Transcranial magnetic stimulation studies," *Nöro Psikiyatri Arşivi*, vol. 54, no. 4, pp. 358–363, Dec. 2017, doi: 10.5152/npa.2016.18056.

[36] G. Cesarelli et al., "Using features extracted from upper limb reaching tasks to detect Parkinson's disease by means of machine learning models," *IEEE Trans. Neural Syst. Rehabil. Eng.*, vol. 31, pp. 1056–1063, 2023, doi: 10.1109/TNSRE.2023.3236834.