NEURAL EFFECTS OF MULTISENSORY DANCE TRAINING IN PARKINSON'S DISEASE: A LONGITUDINAL NEUROIMAGING CASE STUDY

ROYZE SIMON

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ABSTRACT

Dance is associated with a range of motor and non-motor benefits in people with Parkinson's disease (PD) and recent evidence suggests that regular dance participation may delay progression of these symptoms. However, little is known about the neurobiological mechanisms of dance interventions in PD.

This thesis aimed to explore potential neuroplastic changes in a 69-year-old male with mild PD participating in regular dance classes over 29 weeks. Functional MRI was performed at four timepoints (pre-training, 11 weeks, 18 weeks, 29 weeks), in which the participant imagined a dance choreography while listening to music.

Neural activity was compared between dance-imagery and fixation blocks. Region of interest analysis revealed significant BOLD signal activation in the supplementary motor area, right and left superior temporal gyri and the right insula, with modulation observed over the training period. These results suggest the potential for dance to induce neuroplastic changes in people with PD.

DEDICATION

This dissertation is dedicated to my late grandma Merly.
I miss your laugh and your smile every day.

This work is also dedicated to my adorable three-year old niece, Willow Grace.
Your curiosity and kindness have been very inspiring. Thank you for the never- ending hugs and kisses and the "I love yous" — they kept me going.

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INTRODUCTION

Parkinson's disease (PD) is caused by degeneration of dopamine producing neurons in the substantia nigra pars compacta (Simon et al., 2020). Characteristic features of PD include motor symptoms such as bradykinesia, tremor, rigidity, and postural instability. People living with PD also experience a range of non-motor symptoms including depression, anxiety, and apathy (Poewe, 2008). Currently PD is incurable, but treatments are available to alleviate symptoms and improve quality of life. However, while medical and surgical treatments can be effective, they are associated with risks and side effects. For example, levodopa, the most common medication for PD, improves motor impairments but can lead to structural alterations in the brain causing complications such as dyskinesia (Ogawa et al., 2021). Additionally, deep brain stimulation (DBS) can be effective for some individuals, but costs of surgery are substantial and intensive post-surgery care is needed (Erdem et al., 2022; Lozano et al., 2019). The importance of non- invasive and non-pharmacologic approaches such as physiotherapy, exercise, and dance are increasingly recognized, particularly as the burden to healthcare systems continues to grow at an unsustainable rate with the increasing prevalence of PD (Dorsey et al., 2018).

Dance is a complex form of human movement which activates an intricate network of regions in the brain (Dhami et al., 2015). Engaging these areas of the brain through dance training facilitates structural and functional changes which leads to more efficient functioning in expert dancers (Bar & DeSouza, 2016; Burzynska, Finc, et al., 2017). In people with PD, numerous studies have associated dance with improvements in motor functioning as well as non-motor symptoms (for reviews see: Bek et al., 2020; Kshtriya et al., 2015). Although few studies have examined the effects of long-term dance training in PD, a recent 3-year

longitudinal study found evidence that regular dance participation may delay progression of motor symptoms in people with mild PD (Bearss & DeSouza, 2021).

Motor Networks and Aging

In healthy adults, motor control is managed by a complex network of cortical and subcortical regions, often referred to as "motor loops." These loops enable the precise planning, execution, and regulation of voluntary movements. The motor cortex, basal ganglia, supplementary motor area (SMA), premotor cortex, and cerebellum are particularly significant components within these motor networks (Leisman et al., 2016; Middleton & Strick, 2000). The basal ganglia, for example, play a pivotal role in modulating motor commands by controlling the flow of excitatory input from the cortex through both direct and indirect pathways, thereby refining movement selection and inhibition (Alexander & Crutcher, 1990; Obeso et al., 2000). Through these pathways, the basal ganglia assist in selecting and reinforcing the intended motor actions while inhibiting competing, unnecessary ones. The SMA, an essential cortical region within the motor loop, contributes to movement sequencing and timing, coordinating complex movements like dance that require precise, rhythmic synchronization (Nachev et al., 2008).

Research indicates that aging affects both the structure and function of these motor loops, leading to declines in motor control, coordination, and cognitive functions. Studies have documented age-related reductions in volume within subcortical structures, particularly the basal ganglia, which affects dopamine synthesis and disrupts movement control (Raz et al., 1998). Structural changes in motor regions such as the primary motor cortex and SMA, such as decreases in gray matter density and cortical thinning, contribute to age-related declines in motor responses and coordination (Fjell & Walhovd, 2010;Reuter-Lorenz & Park, 2014).

Functionally, older adults often display altered patterns of motor cortical activation,

with an increased reliance on bilateral cortical activation during motor tasks. This phenomenon, often called “dedifferentiation,” involves the recruitment of both hemispheres for tasks that younger adults perform unilaterally, potentially as a compensatory strategy to maintain performance (Cabeza, 2002; Mattay et al., 2002). Although this bilateral recruitment can sometimes help maintain motor performance, it is generally considered less efficient and may contribute to declines in motor accuracy and stability over time (Heuninckx et al., 2010).

The brain’s ability to reorganize itself and form new neural connections is a process that is crucial in cognitive health especially in the aging brain. Research indicates that this ability declines with age. However, certain interventions may help mitigate this process. Studies have highlighted the role of enriched environments and physical activities in enhancing neuroplasticity. For instance, aerobic exercises have been associated with increased hippocampal volume and improved memory performance in elderly individuals (Erickson et al., 2011). Similarly, cognitive training exercises can lead to structural and functional brain changes, fostering cognitive resilience (Lövdén et al., 2012).

Among various interventions, dance has emerged as a particularly effective activity for promoting neural flexibility. Dance integrates physical, cognitive, and social components, providing a comprehensive approach to enhancing brain health. It involves complex movements that require coordination, rhythm, and memory, stimulating various brain regions simultaneously . Additionally, the social interaction and emotional engagement involved in dance can further enhance its neuroplastic effects, making it a unique and multifaceted intervention (Rehfeld et al., 2017). Moreover, studies have also demonstrated that older adults who participate in dance classes exhibit improved balance, gait, and overall motor function (Coubard et al., 2011). Neuroimaging studies have also revealed increased connectivity in brain areas associated with motor and cognitive functions among elderly dancers (Burzynska, Jiao, et al., 2017). These findings underscore the potential of dance as an

intervention to maintain and even enhance cognitive health in aging populations.

Parkinson's Disease: Implications on Movement, Cognition, and Neuroplasticity

Parkinson's disease (PD) is characterized by a range of motor deficits, including bradykinesia (slowness of movement), rigidity, tremor, and postural instability, which result from disruptions in the basal ganglia circuitry, particularly the loss of dopamine- producing neurons. The basal ganglia, along with other cortical and subcortical motor regions, plays a critical role in the regulation of movement, including motor initiation, control, and coordination.

In PD, the pathological process of dopaminergic degeneration leads to both hypo- and hyper-activation of various motor regions, further complicating the motor dysfunctions observed in the disease (Jahanshahi et al., 1995). The basal ganglia-thalamo- cortical loops are disrupted, leading to maladaptive changes in the activation patterns of motor regions, particularly in areas such as the primary motor cortex (M1), the pre-motor cortex (PMC), and the supplementary motor area (SMA), among others (DeLong & Wichmann, 2007).

Parkinson's disease (PD) is driven by progressive degeneration of dopaminergic neurons in the substantia nigra pars compacta, a key component of the basal ganglia. This degeneration disrupts the basal ganglia-thalamo-cortical (BGTC) loops, which are integral for motor control, motor planning, and movement execution. These loops consist of several interconnected regions, including the basal ganglia (substantia nigra, striatum, globus pallidus, and subthalamic nucleus), the thalamus, and motor-related cortical areas, such as the primary motor cortex (M1), supplementary motor area (SMA), and premotor cortex (PMC) (DeLong & Wichmann, 2007).

In PD, the disruption of dopaminergic signaling leads to a shift in the balance between the direct and indirect pathways of the basal ganglia. The direct pathway, which facilitates movement, is underactive due to the depletion of dopamine, while the indirect pathway,

which inhibits movement, becomes hyperactive. This imbalance contributes to bradykinesia and other motor impairments, and this dysfunction is reflected in altered patterns of brain activation during motor tasks.

The BGTC loops function through two primary pathways: the direct pathway, which facilitates voluntary movement, and the indirect pathway, which inhibits competing or involuntary movements. In a healthy brain, the direct pathway is activated by dopaminergic input from the substantia nigra, resulting in excitatory output to the motor cortex. Conversely, the indirect pathway suppresses motor signals, preventing unwanted movements through inhibitory connections. The balance between these pathways ensures smooth and controlled motor execution (Albin et al., 1989; DeLong, 1990).

The degeneration of dopaminergic neurons diminishes activity in the direct pathway, reducing excitatory input to the motor cortex. Simultaneously, the indirect pathway becomes overactive due to the loss of dopaminergic modulation, leading to excessive inhibition of motor output. This imbalance results in hallmark motor symptoms such as bradykinesia (slowness of movement), rigidity, and tremor (DeLong & Wichmann, 2007). Studies suggest that bradykinesia is linked to reduced cortical excitability due to weakened direct pathway signals, while rigidity may stem from overactive indirect pathway circuits (Lewis & Barker, 2009).

Research using functional neuroimaging has shown that in PD, motor regions like the primary motor cortex (M1) and the premotor cortex (PMC) can exhibit both hypo- and hyper-activation depending on the type of movement task. For example, studies have demonstrated that during simple or automatic motor tasks, PD patients often show hypo-activation in M1 and other cortical motor regions, reflecting difficulties in movement initiation and reduced motor output (Jahanshahi et al., 1995). Conversely, in more complex or internally driven tasks, there is often compensatory hyper-activation of regions like the SMA, pre-SMA, and

PMC, which are recruited to compensate for the impaired basal ganglia function (Nambu, 2008). This compensatory hyper-activation is thought to be an attempt by the brain to overcome the motor deficits caused by dopaminergic loss, but it is often inefficient and can lead to motor dysfunctions like rigidity and difficulty with movement fluidity (Monchi et al., 2004).

Moreover, PD patients often exhibit abnormal connectivity between motor regions, particularly between M1 and other brain areas involved in motor control. These altered connectivity patterns can contribute to the motor deficits observed in PD, including difficulties in motor planning, coordination, and execution (Wu & Hallett, 2005). For instance, hypo-connectivity between the basal ganglia and motor cortical areas can impair the flow of motor commands, while hyper-connectivity between regions like the SMA and pre-SMA may disrupt the efficient execution of motor sequences.

Multisensory Dance Training in PD

While neuroplasticity naturally declines with age, interventions such as physical exercise, cognitive training, and especially dance can significantly mitigate this decline. Understanding the underlying mechanisms and effects of these activities on the aging brain is essential for developing effective strategies to support cognitive health in older adults.

Neuroimaging studies provide insight into the neural mechanisms by which dance may benefit multisensory integration in PD. Functional MRI (fMRI) and positron emission tomography (PET) scans have revealed increased activation in brain areas involved in sensorimotor integration, such as the basal ganglia, cerebellum, and parietal cortex, following dance interventions. These findings suggest that dance training can promote neural plasticity and strengthen the connections between sensory and motor regions, thereby improving motor control and reducing symptoms in PD patients (Teixeira- Machado et al., 2019).

The rhythmic and repetitive nature of dance movements can help reinforce motor patterns and improve timing and coordination. Rhythmic auditory stimulation (RAS), a technique often used in dance therapy, has been shown to enhance gait parameters and reduce freezing episodes in PD patients by providing a steady auditory cue that facilitates movement initiation and execution (M. Thaut, 2007). This multisensory approach highlights the importance of integrating auditory and motor training to optimize functional outcomes in PD. The brain can combine information from different sensory modalities, and this process of multisensory integration is a key process for motor and cognitive functions.

In Parkinson's disease however, this process is often impaired which leads to various difficulties in movement, coordination and balance. Motor planning and execution are essential for simple and complex movements and multisensory integration is an essential process of movement planning and execution. Healthy individuals can seamlessly combine visual, auditory, and proprioceptive inputs to create a coherent representation of the body's position and movements. However, in individuals with PD, this ability to integrate sensory inputs might be compromised. This compromised integration results in motor deficits as well as other complications. Additionally, PD patients often struggle with tasks that require integration of visual and proprioceptive information and impairs their ability to navigate their environment safely (Hackney & Earhart, 2009).

Dance-based interventions have shown promise in enhancing multisensory integration in PD patients. Dance requires the synchronization of movements with music, which involves the integration of auditory and proprioceptive feedback. Additionally, dance often includes social interaction and visual cues from instructors or partners, further engaging multiple sensory modalities. Research has indicated that dance can improve gait, balance, and overall mobility in PD patients, suggesting enhanced multisensory processing as a potential underlying mechanism (Bearss & DeSouza, 2021; Houston & McGill, 2013).

Dance training has been found to promote neural plasticity in professional dancers (Bar and DeSouza, 2016; Burzynska et al., 2017). For example, Bar and DeSouza (2016) found that learning a new dance choreography over 8 months was associated with a significant decrease in activation in the supplementary motor area (SMA) and the left and right auditory cortices. In older adults, behavioral changes resulting from dance training have been associated with structural and functional changes in the brain such as increased functional connectivity, increased white matter integrity, and increased volume in cognitive and motor regions (Balazova et al., 2021; Meulenberg et al., 2023; Rehfeld et al., 2018; Teixeira-Machado et al., 2019).

A recent study investigating the neuroplastic effects of dance for people with PD found changes in activation in areas of the motor cortex and cerebellum after 12 weeks of a Tango intervention (Kashyap et al., 2021). A previous single case study of an individual with PD also found an increase in functional connectivity between the basal ganglia and premotor cortex after 5 days of dance training (Batson et al., 2014). However, the neural mechanisms underlying motor improvement through long-term dance participation remain largely under-investigated in people living with PD (Meulenberg et al., 2023).

This dissertation reports a longitudinal investigation of an individual with PD participating in regular dance classes over a period of 29 weeks, as part of a larger study to identify potential indicators of neuroplastic changes associated with dance training (Bearss and DeSouza, 2021). Functional magnetic resonance imaging (fMRI) was performed at four timepoints across the training period, to examine modulation of cortical activity when the individual imagined dance while listening to the music associated with the learned choreography.

METHODS

Participant Characteristics

The participant was a 69-year-old male with mild idiopathic PD with disease duration of 4 years and a Unified Parkinson's Disease Rating Scale (MDS-UPDRS) (Goetz et al., 2007) motor score of 12, who was taking dopaminergic medication at the time of the study. The participant was left-handed according to the Edinburgh Handedness Inventory (Oldfield, 1971). A UPDRS motor score of 12 indicates mild motor impairment, meaning the individual experiences subtle Parkinsonian symptoms such as slight tremors, mild bradykinesia, or minimal rigidity. In comparison, a healthy individual would have a score of 0, as they exhibit no motor symptoms. Since the total motor score ranges from 0 to 132, a score of 12 is relatively low and suggests that while some motor difficulties are present, they are not severely impacting daily function. This places the individual well below the threshold for moderate or severe Parkinson's disease, where mobility and independence become more significantly affected.

In addition to participation in weekly dance classes, the participant also reported regularly walking 6 miles per week. The participant had no previous dance experience. The study was approved by the Office of Research Ethics committee at York University (REB#2013–211). All procedures were conducted in accordance with the requirements of the ethical approval and the Declaration of Helsinki. The participant provided written informed consent prior to the data collection.

Dance Training

The participant attended weekly specialist dance classes (75 minutes in duration) taught by a certified Dance for PD® instructor at Canada's National Ballet School (NBS) in Toronto, Ontario. Classes were attended by an average of 20 people with PD, with 15- 20 trained volunteers assisting as needed.

The dance classes included elements of jazz steps, ballet, Argentinian tango, dance theatre, freestyle and choreographed movements, accompanied by live music from a pianist. Each class included a warm-up, followed by seated, then standing and walking through space learning the choreography (see Table 1, for further details).

Sections of the choreography were based on a narrative, which the instructor would first describe before demonstrating the movements. A video illustrating the choreography is available at: https://bit.ly/42cMlth. In addition to the weekly dance classes, the participant reported practicing the dance at home for 4.5 hours per week as well as 0.5-1 hour per week imagining the dance with and without physical practice.

Table 1

Dance for PD® class routine

Part	Description
Opening	Participants introduced themselves by stating names accompanied by a dance movement. Additionally, the participants played simple games such as naming games.
Warm-up	Stretching arms and legs as well as knees and ankles to facilitate flexibility and mobility while also strengthening the core.
Exercise	While seated, participants slowly rise to practice safely rising in a seated position. Next part was to do the paired mirror dance, where the participants improvise movements and copy each other. After this exercise, they will practice their balance by lunging side to side while holding onto the back of a chair.
Dance Training	Participants dance to the triplet rhythm of waltz. The participants also built confidence by performing a seated shuffle dance of gradually increasing expression of dance movements. Finally, the participants perform the "Showdown Hoedown" dance done facing a partner, comprising of a 2 min choreography with multiple steps and movements sequences.

Note. The table outlines the dance session structure, starting with introductions and interactive games, followed by a warm-up to enhance flexibility. Exercises focus on functional movements, balance, and coordination. Dance training incorporates rhythmic patterns, expressive sequences, and partner-based choreography to build confidence and motor control.

Scanning procedure

The participant underwent a series of 4 fMRI scanning sessions over a period of 29 weeks. Prior to each scanning session, safety screening was completed and training for the dance-imagery task was provided.

A 3T Siemens Tim Trio MRI scanner was used to acquire functional and anatomical images using a 32-channel head coil. T2*-weighted echo planar imaging was performed using parallel imaging (GRAPPA) with an acceleration factor of 2X with the following parameters: 32-slices, 56 × 70 matrix, 210 mm × 168 mm FOV, 3 × 3 × 4 mm slice thick, TE = 30 ms, flip angle of 90°, volume acquisition time of 2,000 ms. Each scan consisted of 240 volumes. Echo-planar images were co-registered with the high-resolution (1 mm^3) anatomical scan of the participant's brain taken at the end of each session (spin echo, TR = 1,900 ms, TE = 2.52 ms, flip angle = 9°, 256 × 256 matrix). The participant's head was secured in place with cushions to minimize movements.

While in the scanner, the participant was instructed to imagine the choreography practiced during training in the dance studio, from a first-person perspective (including both visual and kinesthetic modalities), while the first minute of the music associated with the 2-min choreography was played through headphones. A block-design was employed where 60 s of the dance-imagery task (ON state) alternated with fixation blocks of 30 s (OFF state). These blocks were alternated and repeated five times for both blocks with a total scan time of 8 min (the first 15 volumes are not included in the analysis). The four timepoints were: pre-training (T1), where the participant had only attended one class with the music and choreography to be learned; after 11 weeks of training (T2); after 18 weeks of training (T3) and after 29 weeks of training (T4).

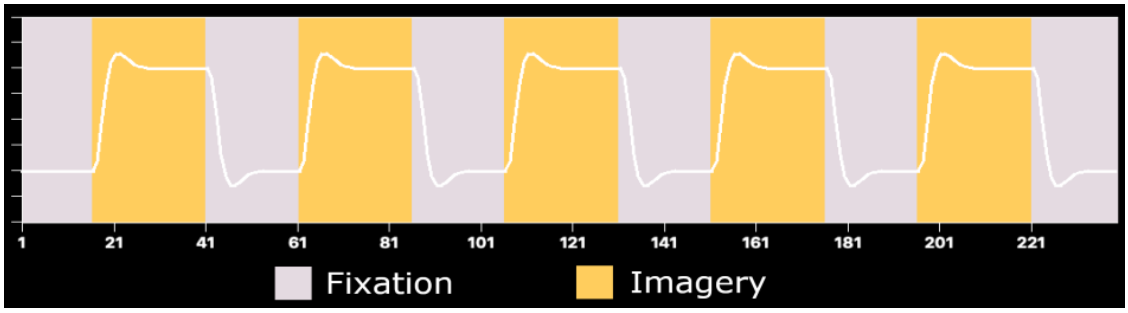

Figure 1. Scanning paradigm: five blocks of 60 s (=30 TRs) of the dance-imagery task were alternated with 30 s (=15 TRs) fixation blocks. The white waveform has the hemodynamic function convolved with the boxcar stimulus.

Data Processing and Analysis

Processing and analysis of the fMRI data was conducted using BrainVoyager QX (version 22.4.2, Brain Innovation, Maastricht, The Netherlands). Functional data were superimposed on an anatomical scan and transformed into Talairach space. Pre- processing steps (slice time correction, motion correction, and temporal high pass filtering) were applied to all runs. To account for periodic fluctuations in the fMRI signal, a General Linear Model (GLM) incorporating Fourier basis functions was applied, including two sine and two cosine functions to model low-frequency drifts and physiological noise. Across the four timepoints, the maximum motion correction did not exceed 1 mm for translation and 3 mm for rotation. None of the scans was excluded because of head movements. A fixed effects single-subject (FFX GLM) analysis was subsequently performed to compare activity during the dance-imagery blocks and the fixation blocks within each timepoint (T1, T2, T3, and T4).

Functionally defined regions were identified from the GLM of dance-imagery versus fixation across all four timepoints, according to a statistical threshold of $p < 0.0001$ (Bonferroni-corrected) with a cluster threshold of $k > 22$. The BOLD percent signal change was calculated relative to a baseline, defined as the average of the two volumes acquired prior to the start of the music.

Modulation of task-related BOLD signal change (dance-imagery vs. fixation) was compared between timepoints for each of the functionally defined regions, using linear mixed-effects models to examine the effect of Time on percentage BOLD signal change associated with the dance-imagery task. The statistical models included Time (T1/T2/T3/T4) as a fixed factor with T1 as the reference level, as well as random effects for individual samples.

An autoregressive correlation structure of order 1 [AR (1)] was included to account for correlations between consecutive samples. An adjusted significance threshold of $p < 0.0033$ was used to correct for multiple comparisons within and between models. Statistical analyses were conducted in R (R Core Team, 2023).

RESULTS

Functionally defined regions based on clusters of functional activation across all four timepoints were identified from the GLM. These regions were SMA, left and right superior temporal gyrus (STG), and left and right insula, which were significantly activated at a statistical threshold of $p < 0.0001$ (Bonferroni-corrected) with a cluster threshold of $k > 22$ (see Figure 2). Talairach coordinates for these regions are provided in Table 2.

Table 2

Functionally Defined Regions of Interest

ROI	TAL coordinates (x , y , z)	# of voxels	Max stat-value
SMA	(-3 , 6, 55)	4535	16.07
Right STG	(56, -19, 11)	8084	26.89
Right Insula	(22, 14, 11)	605	14.25
Left STG	(-50, -24, 13)	7895	25.75
Left Insula	(-32, 20, 5)	403	13.04

Note. The table presents the regions of interest (ROIs) along with their respective Talairach coordinates (x, y, z), voxel counts, and maximum statistical values. The supplementary motor area (SMA), superior temporal gyrus (STG), and insula are reported bilaterally. The number of voxels represents the spatial extent of each ROI, while the max stat-value indicates the peak statistical significance within the region.

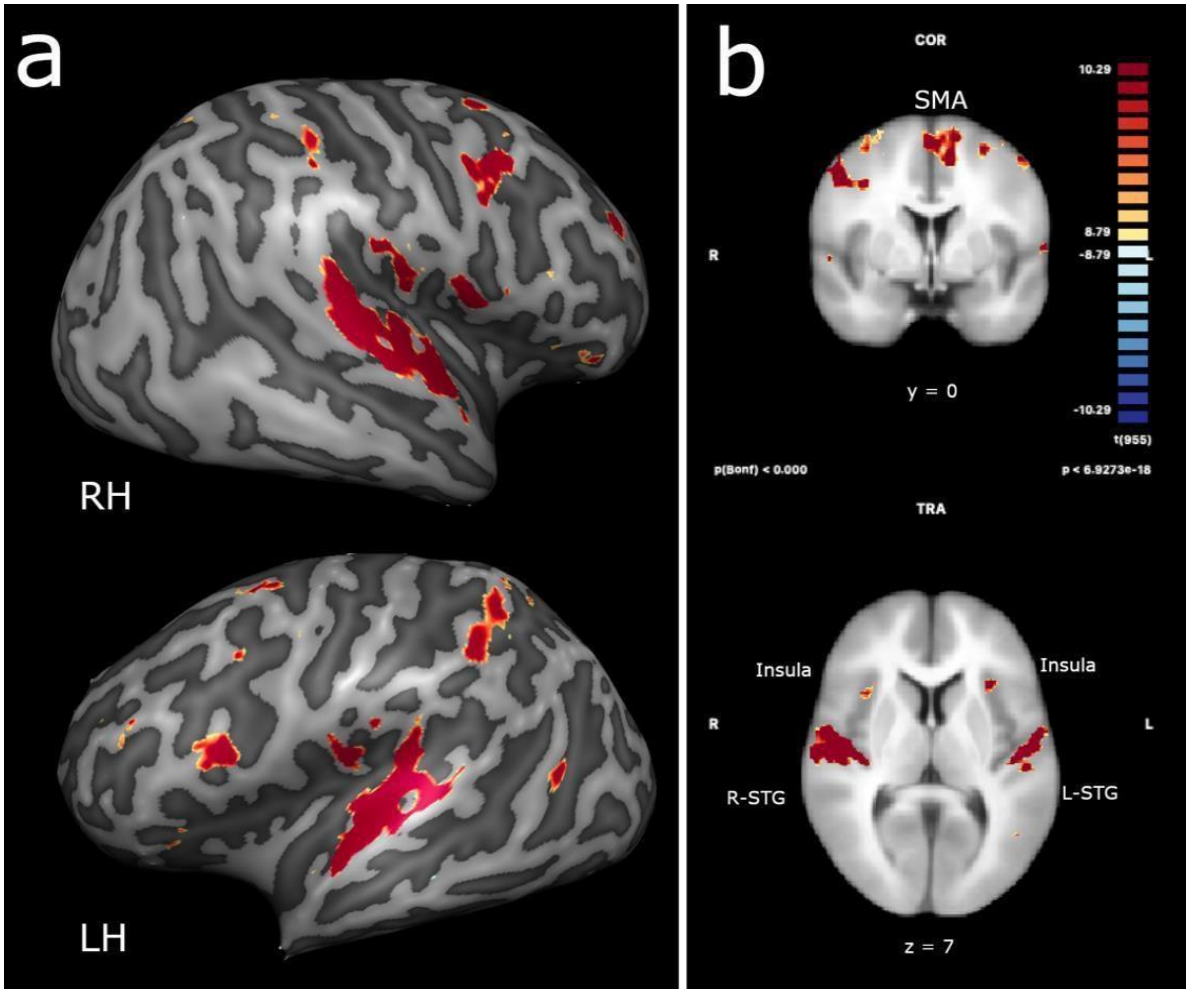

Figure 2. Regions of interest (ROIs): (a) activated regions are projected onto the inflated cortex of the right and left hemispheres, displayed at a statistical threshold of p<.0001, Bonferroni-corrected, cluster threshold k > 22; (b) locations of ROIs as labelled on BOLD activation map overlaid on the MNI brain. Legend: RH = right hemisphere; LH = left hemisphere; COR = Coronal; TRA = Transverse; SMA = Supplementary Motor Area; STG = Superior Temporal Gyrus.

Linear mixed-effect modelling revealed significant modulation of BOLD signal activation in the SMA (using the adjusted significance threshold) at T2 ($b = -0.35$, SE = 0.055, $t(413) = -6.32$, $p < 0.001$) and at T4 ($b = -0.23$, SE = 0.054, $t(413) = -4.19$, $p < 0.001$), but not at T3 ($b = -0.09$, SE = 0.054, $t(413) = -1.70$, $p = 0.09$), relative to T1. As illustrated in Figure 3, activation decreased from T1 (pre-training) to T2 (11 weeks of training), followed by an increase from T2 to T3 (18 weeks of training) and a subsequent decrease at T4 (29 weeks of training).

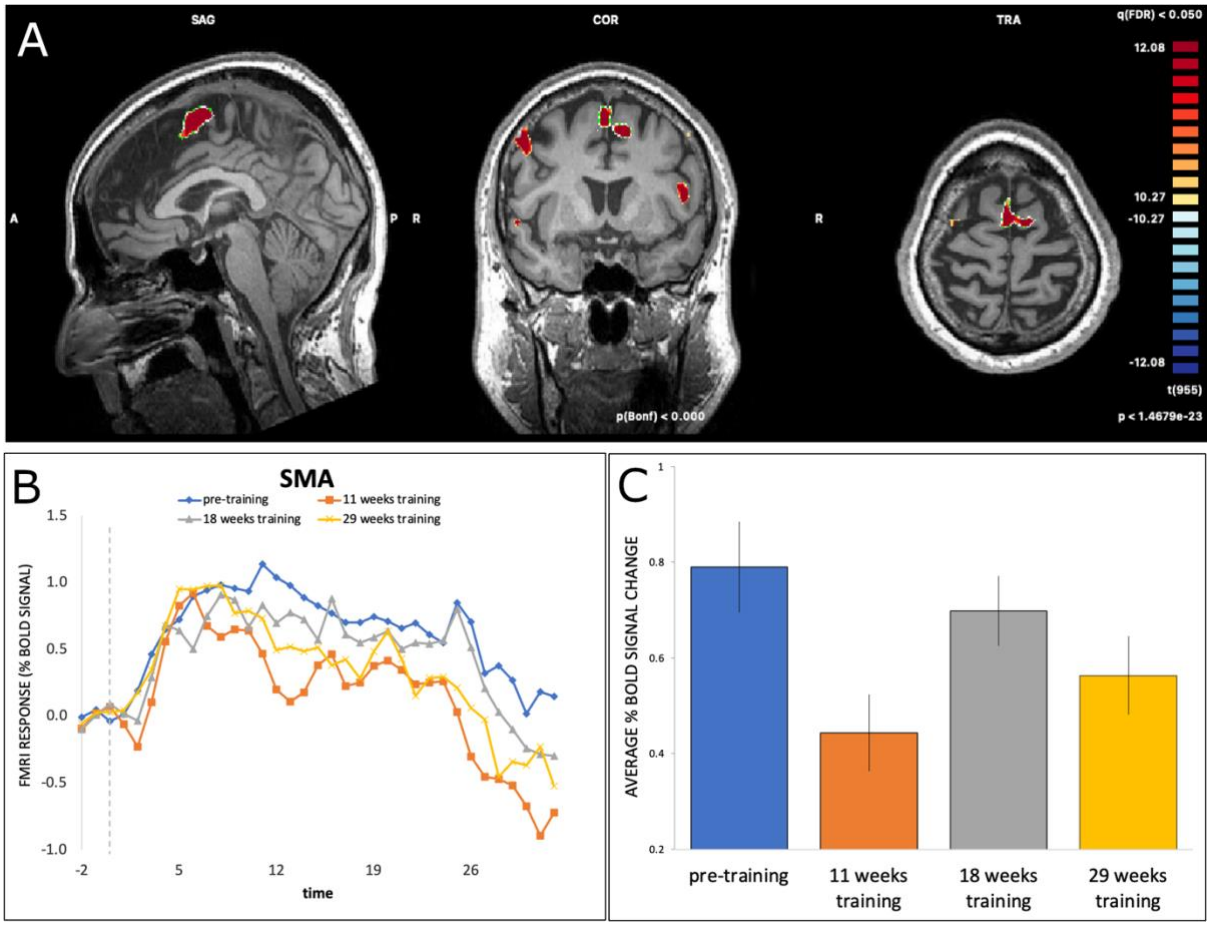

Figure 3. **(A)** BOLD activation of SMA during dance-imagery shown in sagittal, coronal, and transverse view in the 3D Talairach space, displayed at a statistical threshold of $p < 0.0001$, Bonferroni-corrected, with cluster threshold $k > 22$; **(B)** fMRI response (average percent BOLD signal change) of SMA during the dance-imagery blocks within each of the four timepoints (dashed line indicates the start of the music played in the scanner); **(C)** average percent BOLD signal change of SMA between the four timepoints. Error bars represent S.E.M.

Significant modulation of BOLD signal was also found for the right STG at T2 ($b = -1.0$, SE = 0.075, $t(412) = -13.21$, $p < 0.001$), T3 ($b = -0.41$, SE = 0.074, $t(412) = -5.49$, $p < 0.001$), and T4 ($b = -0.95$, SE = 0.074, $t(412) = -12.84$, $p < 0.001$), and the left STG at T2 ($b = -0.73$, SE = 0.074, $t(413) = -9.87$, $p < 0.001$) and T4 ($b = -0.48$, SE = 0.073, $t(413) = -6.51$, $p < 0.001$), but not T3 ($b = -0.10$, SE = 0.073, $t(413) = -1.35$, $p = 0.18$). As shown in Figure 4, the changes in activation between timepoints for both right and left STG followed a similar pattern to the SMA, with an initial decrease from T1 to T2 followed by an increase from T2 to T3 and then a decrease at T4.

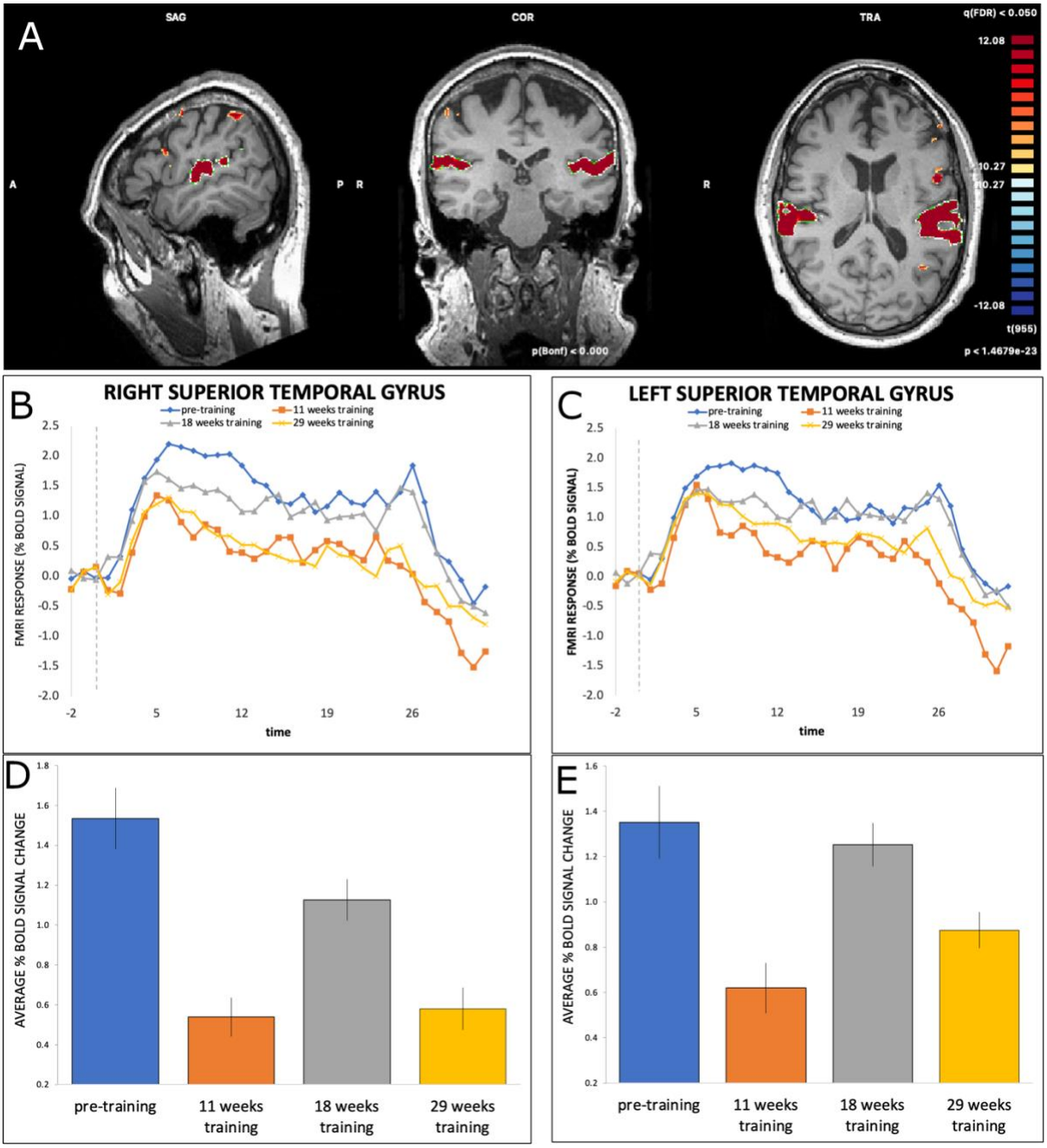

Figure 4. (A) BOLD activation of right and left STG during dance-imagery shown in sagittal, coronal, and transverse view in the 3D Talairach space, displayed at a statistical threshold of $p < 0.0001$, Bonferroni-corrected, cluster threshold $k > 22$; (B,C) average percent BOLD signal change of right and left STG during dance-imagery blocks within each of the four timepoints (dashed line indicates the start of the music played in the scanner); (D,E) average percent BOLD signal change of right and left STG between the four timepoints. Error bars represent S.E.M.

The right insula also showed a similar pattern, as shown in Figure 5, with a significant effect of Time at T2 ($b = -0.26$, SE = 0.075, $t(415) = -3.46$, $p = 0.0006$) and T4 ($b = -0.33$, SE = 0.074, $t(415) = -4.49$, $p < 0.001$), but not at T3 ($b = -0.17$, SE = 0.074, $t(415) = -2.28$, $p = 0.023$). Finally, the left insula did not show any significant effects of Time (all $p > 0.004$).

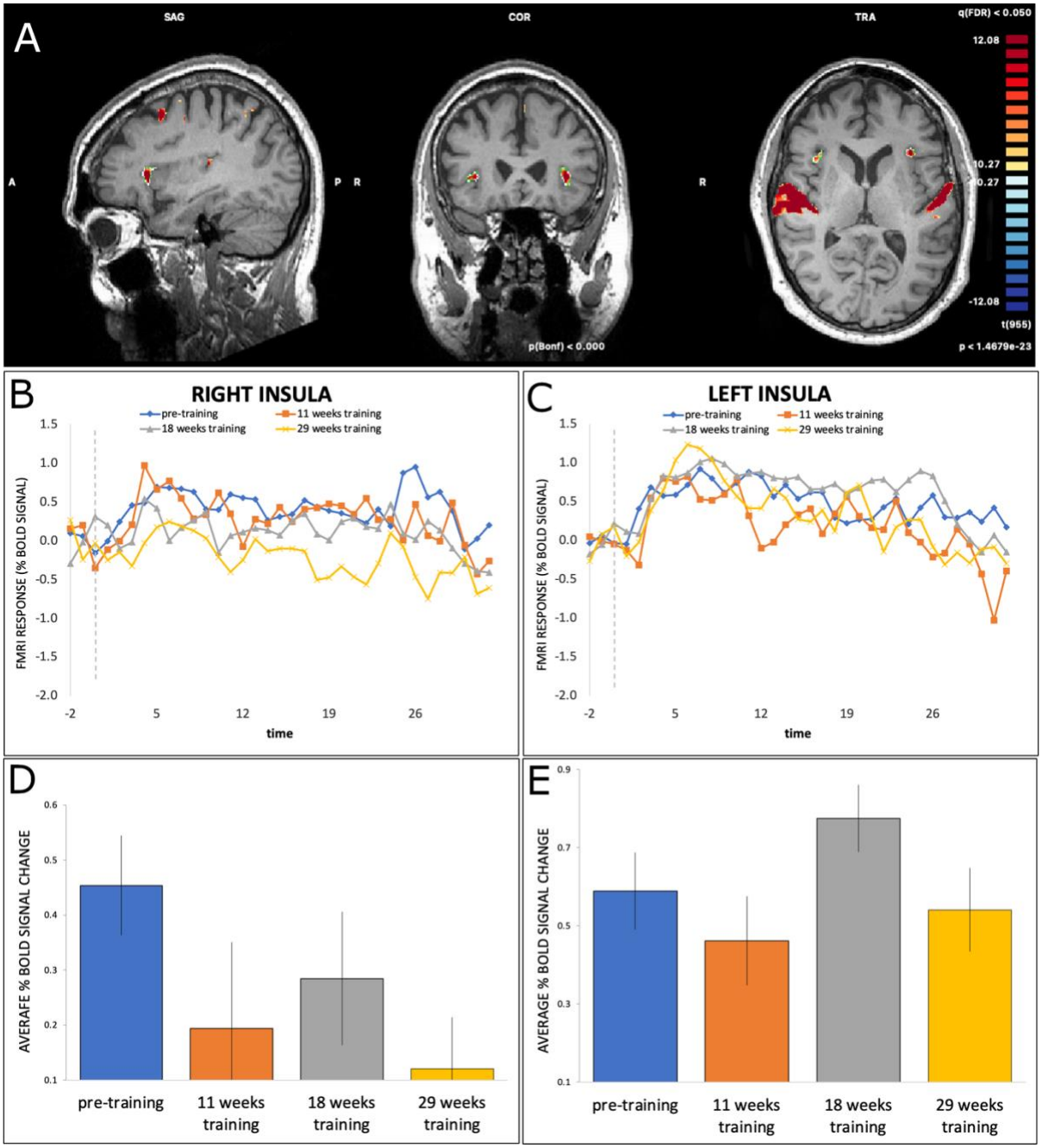

Figure 5. **(A)** BOLD activation of right and left insula during dance-imagery shown in in sagittal, coronal, and transverse view in the 3D Talairach space, displayed at a statistical threshold of $p < 0.0001$, Bonferroni-corrected, with cluster threshold $k > 22$; **(B,C)** average percent BOLD signal change of right and left insula during dance-imagery blocks within each of the four timepoints (dashed line indicates the start of the music played in the scanner); **(D,E)**average percent BOLD signal change of right and left insula between the four timepoints. Error bars represent S.E.M.

DISCUSSION

The findings of the present case study suggest that, in an individual with mild PD, long-term dance training promoted functional changes in cortical regions while imagining the dance learned during classes.

The SMA, which is implicated in processes of motor planning, preparation and imagery (Lotze & Halsband, 2006; Shima & Tanji, 1998, 2000), was significantly activated during all four timepoints. The SMA has been found to be activated in people with PD during motor imagery (Cunnington et al., 2001; Weiss et al., 2015), to a similar degree as in healthy controls (Cunnington et al., 2001).

In previous work applying the same paradigm as the present study to expert dancers, activations were found in SMA and primary motor cortex (M1) (Bar and DeSouza, 2016), further indicating the role of motor processes during imagined dance. The high initial level of activation in the SMA at T1, when the participant had minimal experience of the music and choreography, might reflect the novelty of the music and/or difficulty in generating motor imagery. Consistent with the latter point, neural activity in people with PD when performing an implicit test of motor imagery (hand laterality judgment) has previously been found to increase with task difficulty in areas including the SMA (Helmich et al., 2007). At T2, a decrease in SMA activity was observed, following 11 weeks of dance classes learning the choreography alongside additional imagery practice with the music at home. This decrease might indicate a reduction in the demands of generating imagery, since the dance choreography was now familiar but not fully learned.

The initial pattern of decreasing activation in SMA from T1 to T2 is also consistent with the findings of Olshansky et al. (2015), where decreased activation in this region was found during motor imagery with familiar music compared to unfamiliar music. The pattern of activation also suggested a subsequent increase in SMA activation at 18 weeks into training

(T3), which might reflect greater generation of imagery as learning progressed (e.g., more sustained or more detailed images), followed by a decrease at the final timepoint (T4). In expert dancers, a decrease in SMA activation was found after 34 weeks of learning a new choreography (Bar and DeSouza, 2016), indicating greater ease or efficiency of motor imagery over time. In previous investigations of music and familiarity, the SMA and auditory regions were found to be activated when music was familiar, together with other motor-related regions such as the basal ganglia, cerebellum, and dorsal premotor cortex, further suggesting a pattern of motor-related activations (Zatorre et al., 2007). Additionally, recent self-report data indicated that music could evoke motor imagery in people with PD (Poliakoff et al., 2023), and that the vividness of music-evoked motor imagery correlated with musical training and the urge to dance.

The present analysis did not examine functional activity in the pre-SMA, which is a subregion of the SMA located rostral to the SMA-proper. While both areas are involved in motor planning and sequencing (Shima and Tanji, 1998; Shima and Tanji, 2000), the pre-SMA may be more involved in learning new motor sequences, due to its connections with prefrontal areas that are involved in learning and performing movement sequences (Hikosaka et al., 1996; Shima & Tanji, 1998, 2000). The pre-SMA may also be more involved in inhibition of action (Obeso et al., 2013), compared to the SMA-proper which has more dorsal connections. The function of the pre-SMA may also be more impacted in PD than the SMA-proper (Cunnington et al., 2001). Future studies could thus attempt to differentiate the effects of dance training on activity of the SMA-proper and the pre-SMA in people with PD.

The bilateral STG, which have a key role in auditory processing (Rivier and Clarke, 1997) showed a similar pattern of activity to the SMA across the four timepoints, which was also similar to findings from expert dancers (Bar and DeSouza, 2016). In the present study, 29 weeks of training with the same music and choreography promoted an overall decrease in

the STG activation in both hemispheres. One possible explanation of this is that novel music strongly activates auditory regions, and this activation decreases with familiarity (Olshansky et al., 2015).

The right and left insula were activated across all timepoints in the present study, but only the right insula showed a significant change across time. In humans, the insula has connections with neural structures such as the frontal, parietal, and temporal lobes, the cingulate gyrus, amygdala, brainstem, thalamus, and basal ganglia (FLYNN, 1999). Multiple functions of the insula have been proposed, including sensorimotor processes such as body awareness, error awareness, attention to pain, and representing the physiological condition of the body (Craig, 2009). In addition, the insula has been proposed to provide an interface between body awareness and movement (Tinaz et al., 2018).

The present study found an asymmetry in activation between right and left insula, which may be due to the differences between ascending and descending connections that utilize different frequency bands depending on feedforward or feedback communication (Bastos et al., 2015) or anatomical connections (Rivier & Clarke, 1997). The right insula has been found to be more activated by visual and auditory perception of emotional music (Petrini et al., 2011) as well as processing of rhythm (Lappe et al., 2013) and melody (M. H. Thaut et al., 2014) compared to the left. Moreover, the right insula has been suggested to be important for multisensory integration (Chen et al., 2015) and in the present study may have been involved in integrating sensory aspects of the imagined movement with the music. The insula has also been suggested to act as a hub for connecting attentional control and memory related regions (Mayer et al., 2007); thus, it is also possible that the decrease in activation of the right insula in the present study reflects reduced demands on attentional processing, emotion processing and/or memory. Further evidence for a role of the insula in dance was found in a study of older adults (Rehfeld et al., 2018), in which dance training was associated with an

increase in grey matter in various brain regions including the left insula, when compared to an active control group who practiced repetitive movements.

These findings contrast somewhat with the present study, where a clearer change in activation was found for the right than left insula. However, the previous study emphasized continual learning of different movements and choreographies, which may differently recruit the insula; for example, the left insula appears to be more involved in speech and language processing (Oh et al., 2014), which may be important for following instructions for new dance routines. Moreover, we did not analyze structural changes, which may reveal different effects than functional data.

While previous studies of dance for PD have not examined neuroplastic effects in the same regions as investigated in the present study, some evidence of functional neural changes resulting from dance training has been reported in PD as noted above (Batson et al., 2014).

Neuroplastic effects of other forms of physical activity, such as aerobic exercise and treadmill training, have also been documented in people with PD (Duchesne et al., 2016; Johansson et al., 2020). In addition, evidence of functional changes in brain areas related to motor imagery, alongside improved motor imagery vividness, was found following training with action observation and motor imagery in participants with PD (Sarasso et al., 2023). Since dance involves observation and imagery of movement (Bek et al., 2020), the neural changes indicated by the present study may thus reflect both motor learning of the dance choreography and improved motor imagery ability.

Study Limitations

This dissertation has several limitations that should be addressed in future work to further understand the neural effects of dance for people with PD. Although the results of a single case study cannot be generalized, this study provides proof of concept of a dance learning paradigm that can be applied to larger numbers of participants to investigate neuroplastic effects of dance. Future studies should compare participants receiving dance training to participants in a control condition, such as an exercise program or no intervention. It would also be informative to collect longitudinal data on performance or recall of the dance choreography, as well as disease status (e.g., UPDRS) to examine in relation to changes in functional activation. In the present study, it cannot be ruled out that stress or anxiety contributed to the high levels of BOLD activity observed at the first timepoint, and this could be addressed in future studies by incorporating physiological measures such as skin conductance and heart rate.

Additionally, although the present study provides initial evidence that regular dance participation could promote neuroplasticity in people with PD, it is important to note that the participant in this case study might not be representative of a typical person with PD, given his high level of physical activity including additional dance practice (both physical and via imagery) outside of classes. Moreover, given the heterogeneous nature of PD, the neural effects of dance may differ between participants at different disease stages or with different symptom profiles.

Future Directions

Future research with larger samples could investigate this by comparing groups of participants with different subtypes of PD. Alternatively, heterogeneity could be better controlled by focusing only on one subtype, as some previous fMRI studies have done (Sarasso et al., 2023). Finally, since difficulties with motor imagery are sometimes reported in PD (Readman et al., 2023; Scarpina et al., 2019), future studies could also screen participants to ensure an adequate level of imagery ability, as well as providing training on the use of motor imagery prior to undertaking the fMRI protocol.

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Appendix A: Supplementary Analysis

BOLD Activation Across ROIs Linear Mixed-Effects Model Results

A series of linear mixed-effects models were conducted to examine the effect of TIMEPOINT on BOLD signal changes for each Region of Interest (ROI) while accounting for repeated measures within BLOCK as a random effect.

The models were fitted using maximum likelihood estimation (ML) with the following formula:

$$BOLD \sim TIMEPOINT + (1 \mid BLOCK)$$

A Type III ANOVA revealed a significant effect of TIMEPOINT on BOLD activation across all regions ($p < .001$ for all models), indicating that neural activation varied across timepoints in each ROI.

Pairwise comparisons with Bonferroni correction revealed significant decreases in activation from T1 to T2, followed by partial recovery at T3 and subsequent decreases at T4 in most regions.

This supplementary analysis should be interpreted with caution, as it was conducted to provide additional insights into temporal modulation of BOLD activation rather than to serve as the primary statistical approach. Given the single-subject design, these results reflect within-subject variability and may not generalize to broader populations. However, they offer valuable information regarding potential neuroplastic adaptations across different timepoints.

Table S1

Model Fit Statistics for Each ROI

ROI	AIC	BIC	Log-Likelihood	Deviance	Residual df
Supplementary Motor Area	406.6	430.8	-197.3	394.6	411
Right Superior Temporal Gyrus	672.9	697.1	-330.4	660.9	410
Left Superior Temporal Gyrus	660.9	685.1	-324.5	648.9	411
Left Insula	557.6	581.7	-272.8	545.6	409
Right Insula	681.6	705.9	-334.8	669.6	413

A Type III ANOVA (Wald Chi-Square test) revealed a significant effect of TIMEPOINT on BOLD activation across all Regions of Interest (ROIs) ($p < .001$ for all models). The right STG exhibited the strongest effect ($\chi^2 = 245.07$), followed by the left STG ($\chi^2 = 128.26$) and SMA ($\chi^2 = 47.20$). The insula (left and right) showed comparatively smaller but still significant effects ($\chi^2 = 25.31$ and 22.64, respectively), indicating time-dependent changes in neural activity in all examined regions.

Table S2

ROI	Chi-Square (χ^2)	df	p-value
SMA	47.20	3	< .001 ***
Right STG	245.07	3	< .001 ***
Left STG	128.26	3	< .001 ***
Left Insula	25.31	3	< .001 ***
Right Insula	22.64	3	< .001 ***

Type III ANOVA Results (Wald Chi-Square Tests)

Note. Significant effects of TIMEPOINT indicate that BOLD activation changed significantly over time in each region.

Table S3 presents the estimated marginal means (EMMs) for BOLD activation across the four timepoints for each region of interest (ROI). These values represent the mean BOLD activation (emmean) at each timepoint, along with standard errors (SEs), degrees of freedom (df), and 95% confidence intervals (CIs).

Overall, the Right and Left Superior Temporal Gyrus (STG) showed the highest mean BOLD activation at T1, followed by reductions at T2, partial recovery at T3, and another decline at T4. The Supplementary Motor Area (SMA) exhibited a similar pattern, with an initial decrease at T2, a partial rebound at T3, and another drop at T4. The Left and Right Insula demonstrated more variable responses, with significant fluctuations over time, particularly between T2 and T3.

These findings indicate dynamic changes in BOLD activation across different brain regions over the training period, with STG and SMA showing the most pronounced fluctuations. The reported confidence intervals provide insight into the variability and precision of the estimates.

Table S3

Estimated Marginal Means for BOLD Activation by Timepoint

ROI	TIMEPOINT	Mean BOLD Activation (emmean)	SE	df	95% CI (Lower)	95% CI (Upper)
SMA	T1	0.79	0.0496	23.5	0.687	0.892
	T2	0.446	0.0503	25.1	0.342	0.55
	T3	0.699	0.0495	23.2	0.596	0.801
	T4	0.564	0.0495	23.2	0.462	0.666
Right STG	T1	1.534	0.0563	64.7	1.421	1.646
	T2	0.539	0.0574	68.5	0.425	0.654
	T3	1.126	0.0559	62.7	1.015	1.238
	T4	0.58	0.0559	62.7	0.469	0.692
Left STG	T1	1.351	0.0607	35.9	1.228	1.474
	T2	0.621	0.0618	38.6	0.496	0.746
	T3	1.253	0.0605	35.4	1.13	1.375
	T4	0.876	0.0605	35.4	0.753	0.999
Left Insula	T1	0.588	0.0512	46.4	0.485	0.691
	T2	0.462	0.0523	49.9	0.357	0.567
	T3	0.775	0.0512	46.4	0.672	0.878
	T4	0.542	0.0512	46.4	0.438	0.645
Right Insula	T1	0.454	0.0525	58.6	0.349	0.559
	T2	0.194	0.0539	62.7	0.086	0.301
	T3	0.285	0.0525	58.6	0.179	0.39
	T4	0.12	0.0525	58.6	0.015	0.225

Table S4 presents the pairwise comparisons of BOLD activation, highlighting significant differences between T1-T2, T1-T4, and T2-T3 for most ROIs. These findings suggest a nonlinear modulation pattern over time.

The right STG and SMA exhibited the largest effect sizes, supporting prior findings of their involvement in dance-imagery-induced neuroplasticity. To account for multiple comparisons, Bonferroni correction was applied to the reported p-values.

Table S4

Pairwise Comparisons of BOLD Activation Between Timepoints (Bonferroni-Corrected)

ROI	Contrast	Estimate	SE	df	t-ratio	p-value
SMA	T1 - T2	0.3439	0.0541	415	6.354	< .001 ***
	T1 - T3	0.0913	0.0533	415	1.713	0.5247
	T1 - T4	0.226	0.0533	415	4.239	< .001 ***
	T2 - T3	-0.2526	0.054	415	-4.678	< .001 ***
	T2 - T4	-0.118	0.054	415	-2.185	0.1768
	T3 - T4	0.1346	0.0532	415	2.532	0.0703
Right STS	T1 - T2	0.9945	0.0752	415	13.223	< .001 ***
	T1 - T3	0.4073	0.0741	414	5.499	< .001 ***
	T1 - T4	0.9531	0.0741	414	12.868	< .001 ***
	T2 - T3	-0.5872	0.0749	415	-7.844	< .001 ***
	T2 - T4	-0.0414	0.0749	415	-0.553	1
	T3 - T4	0.5458	0.0737	414	7.405	< .001 ***
Left STS	T1 - T2	0.7299	0.0736	416	9.916	< .001 ***
	T1 - T3	0.0983	0.0725	415	1.356	1
	T1 - T4	0.475	0.0725	415	6.553	< .001 ***
	T2 - T3	-0.6316	0.0734	416	-8.601	< .001 ***
	T2 - T4	-0.2549	0.0734	416	-3.471	0.0034
	T3 - T4	0.3768	0.0723	415	5.21	< .001 ***
Left Insula	T1 - T2	0.1265	0.0653	414	1.936	0.3211
	T1 - T3	-0.1869	0.0645	413	-2.898	0.0237
	T1 - T4	0.0467	0.0645	413	0.725	1
	T2 - T3	-0.3134	0.0653	414	-4.797	< .001 ***
	T2 - T4	-0.0798	0.0653	414	-1.221	1
	T3 - T4	0.2336	0.0645	413	3.623	0.002
Right Insula	T1 - T2	0.2601	0.0752	420	3.458	0.0036
	T1 - T3	0.1692	0.0743	419	2.279	0.1391
	T1 - T4	0.3335	0.0743	419	4.491	0.0001
	T2 - T3	-0.0909	0.0752	420	-1.208	1
	T2 - T4	0.0734	0.0752	420	0.976	1
	T3 - T4	0.1643	0.0743	419	2.213	0.1648

Note. T1, T2, T3, and T4 represent different timepoints in the study. Values indicate mean differences (change in BOLD activation) between timepoints for each Region of Interest (ROI). p-values have been Bonferroni-corrected to control for multiple comparisons.

Significance levels are as follows: $p < .001$* (highly significant), $p < .01$ (moderately significant), and $p < .05$ (significant)

Appendix B: MDS – UPDRS

MDS-UPDRS

The *Movement* Disorder Society (MDS)-sponsored new version of the UPDRS is founded on the critique that was formulated by the Task Force for Rating Scales in Parkinson's disease (*Mov Disord* 2003;18:738-750). Thereafter, the MDS recruited a Chairperson to organize a program to provide the Movement Disorder community with a new version of the UPDRS that would maintain the overall format of the original UPDRS, but address issues identified in the critique as weaknesses and ambiguities. The Chairperson identified subcommittees with chairs and members. Each part was written by the appropriate subcommittee members and then reviewed and ratified by the entire group. These members are listed below.

The MDS-UPDRS has four parts: Part I (non-motor experiences of daily living), Part II (motor experiences of daily living, Part III (motor examination) and Part IV (motor complications). Part I has two components: IA concerns a number of behaviors that are assessed by the investigator with all pertinent information from patients and caregivers, and IB is completed by the patient with or without the aid of the caregiver, but independently of the investigator. These sections can, however, be reviewed by the rater to ensure that all questions are answered clearly and the rater can help explain any perceived ambiguities. Part II is designed to be a self-administered questionnaire like Part IB, but can be reviewed by the investigator to ensure completeness and clarity. Of note, the official versions of Part IA, Part IB and Part II of the MDS-UPDRS do not have separate on or off ratings. However, for individual programs or protocols the same questions can be used separately for on and off. Part III has instructions for the rater to give or demonstrate to the patient; it is completed by the rater. Part IV has instructions for the rater and also instructions to be read to the patient. This part integrates patient-derived information with the rater's clinical observations and judgments and is completed by the rater.

The authors of this new version are: Chairperson: Christopher G. Goetz

Part I: Werner Poewe (chair), Bruno Dubois, Anette Schrag
Part II: Matthew B. Stern (chair), Anthony E. Lang,
Peter A. LeWitt Part III: Stanley Fahn (chair), Joseph
Jankovic, C. Warren Olanow
Part IV: Pablo Martinez-Martin (chair), Andrew Lees, Olivier Rascol, Bob van Hilten
Development Standards: Glenn T. Stebbins (chair), Robert Holloway, David Nyenhuis
Appendices: Cristina Sampaio (chair), Richard Dodel, Jaime Kulisevsky
Statistical Testing: Barbara Tilley (chair), Sue Leurgans, Jean Teresi,
Consultant: Stephanie Shaftman, Nancy LaPelle Contact person: Christopher G. Goetz, MD
Rush University Medical Center 1725 W. Harrison Street, Suite 755 Chicago, IL USA 60612
Telephone 312-942-8016 Email: cgoetz@rush.edu July 1, 2008

Overview: This portion of the scale assesses the non-motor impact of Parkinson's disease (PD) on patients' experiences of daily living. There are 13 questions. Part 1A is administered by the rater (six questions) and focuses on complex behaviors. Part 1B is a component of the self-administered Patient Questionnaire that covers seven questions on non-motor experiences of daily living.

Part 1A:

In administering Part IA, the examiner should use the following guidelines:

1. Mark at the top of the form the primary data source as patient, caregiver, or patient and caregiver in equal proportion.
2. The response to each item should refer to a period encompassing the prior week including the day on which the information is collected.
3. All items must have an integer rating (no half points, no missing scores). In the event that an item does not apply or cannot be rated (e.g., amputee who cannot walk), the item is marked UR for Unable to Rate.
4. The answers should reflect the usual level of function and words such as "usually", "generally", "most of the time" can be used with patients.
5. Each question has a text for you to read (Instructions to patients/caregiver). After that statement, you can elaborate and probe based on the target symptoms outlined in the Instructions to examiner. You should NOT READ the RATING OPTIONS to the patient/caregiver, because these are written in medical terminology. From the interview and probing, you will use your medical judgment to arrive at the best response.
6. Patients may have co-morbidities and other medical conditions that can affect their function. You and the patient must rate the problem as it exists and do not attempt to separate elements due to Parkinson's disease from other conditions.

EXAMPLE OF NAVIGATING THROUGH THE RESPONSE OPTIONS FOR PART 1A

Suggested strategies for obtaining the most accurate answer:

After reading the instructions to the patient, you will need to probe the entire domain under discussion to determine Normal vs. problematic: If your questions do not identify any problem in this domain, record 0 and move on to the next question.

If your questions identify a problem in this domain, you should work next with a reference anchor at the mid-range (option 2 or Mild) to find out if the patient functions at this level, better or worse. You will not be reading the choices of responses to the patient as the responses use clinical terminology. You will be asking enough probing questions to determine the response that should be coded.

Work up and down the options with the patient to identify the most accurate response, giving a final check by excluding the options above and below the selected response.

Is this item normal for you? 'Yes'. Mark (0) Normal.

'No, I have problems.'

Consider mild (2) as a reference point 'Yes, slight is closest'. Confirm and mark (1) Slight.

If mild is closer thanand then slight.compare with slight (1).

Consider moderate (3) to see if this 'No, moderate is too severe'. Confirm and mark (2) Mild. answer fits better.

If moderate is closer thanConsider severe mild. (4) to see if this 'No, severe is too severe'.

Confirm and mark (3) Moderate. answer fits better.

'Yes, severe is closest.' Confirm and mark (4) Severe.

Patient Name or Subject ID	Site ID	(mm-dd-yyyy) Assessment Date	Investigator's Initials

MDS UPDRS

Part I: Non-Motor Aspects of Experiences of Daily Living (nM-EDL)

Part 1A: Complex behaviors: [completed by rater]

Primary source of information:

☐ Patient ☐ Caregiver ☐ Patient and Caregiver in Equal Proportion

To be read to the patient: I am going to ask you six questions about behaviors that you may or may not experience. Some questions concern common problems and some concern uncommon ones. If you have a problem in one of the areas, please choose the best response that describes how you have felt MOST OF THE TIME during the PAST WEEK. If you are not bothered by a problem, you can simply respond NO. I am trying to be thorough, so I may ask questions that have nothing to do with you.

SCORE

1.1 COGNITIVE IMPAIRMENT

Instructions to examiner: Consider all types of altered level of cognitive function including cognitive slowing, impaired reasoning, memory loss, deficits in attention and orientation. Rate their impact on activities of daily living as perceived by the patient and/or caregiver.

Instructions to patients [and caregiver]: Over the past week have you had problems remembering things, following conversations, paying attention, thinking clearly, or finding your way around the house or in town? [If yes, examiner asks patient or caregiver to elaborate and probes for information]

0: Normal:	No cognitive impairment.	
1: Slight:	Impairment appreciated by patient or caregiver with no concrete interference with the patient's ability to carry out normal activities and social interactions.	☐
2: Mild:	Clinically evident cognitive dysfunction, but only minimal interference with the patient's ability to carry out normal activities and social interactions.	
3: Moderate:	Cognitive deficits interfere with but do not preclude the patient's ability to carry out normal activities and social interactions.	

4: Severe: Cognitive dysfunction precludes the patient's ability to carry out normal activities and social interactions.	

1.2 HALLUCINATIONS AND PSYCHOSIS	**SCORE**
Instructions to examiner: Consider both illusions (misinterpretations of real stimuli) and hallucinations (spontaneous false sensations). Consider all major sensory domains (visual, auditory, tactile, olfactory and gustatory). Determine presence of unformed (for example sense of presence or fleeting false impressions) as well as formed (fully developed and detailed) sensations. Rate the patients insight into hallucinations and identify delusions and psychotic thinking. *Instructions to patients [and caregiver]: Over the past week have you seen, heard, smelled or felt things that were not really there?* [If yes, examiner asks patient or caregiver to elaborate and probes for information] 0: Normal: No hallucinations or psychotic behaviour. 1: Slight: Illusions or non-formed hallucinations, but patient recognizes them without loss of insight. 2: Mild: Formed hallucinations independent of environmental stimuli. No loss of insight. 3: Moderate: Formed hallucinations with loss of insight. 4: Severe: Patient has delusions or paranoia.	☐

1.3 DEPRESSED MOOD

Instructions to examiner: Consider low mood, sadness, hopelessness, feelings of emptiness or loss of enjoyment. Determine their presence and duration over the past week and rate their interference with the patient's ability to carry out daily routines and engage in social interactions.

Instruction to the patient (and caregiver): Over the past week have you felt low, sad, hopeless or unable to enjoy things? If yes, was this feeling for longer than one day at a time? Did it make it difficult for you carry out your usual activities or to be with people? If yes, examiner asks patient or caregiver to elaborate and probes for information]

0: Normal: No depressed mood.

1: Slight: Episodes of depressed mood that are not sustained for more than one day at a time. No interference with patient's ability to carry out normal activities and social interactions.

2: Mild: Depressed mood that is sustained over days, but without interference with normal activities and social interactions.

3: Moderate: Depressed mood that interferes with, but does not preclude, the patient's ability to carry out normal activities and social interactions.

4: Severe: Depressed mood precludes patient's ability to carry out normal activities and social interactions.

☐

1.4 ANXIOUS MOOD	SCORE
Instructions to examiner: Determine nervous, tense, worried or anxious feelings (including panic attacks) over the past week and rate their duration and interference with the patient's ability to carry out daily routines and engage in social interactions. *Instructions to patients [and caregiver]: Over the past week have you felt nervous, worried or tense? If yes, was this feeling for longer than one day at a time? Did it make it difficult for you to follow your usual activities or to be with other people*? [If yes, examiner asks patient or caregiver to elaborate and probes for information.] 0: Normal: No anxious feelings. 1: Slight: Anxious feelings present but not sustained for more than one day at a time. No interference with patient's ability to carry out normal activities and social interactions. 2: Mild: Anxious feelings are sustained over more than one day at a time, but without interference with patient's ability to carry out normal activities and social interactions. 3: Moderate: Anxious feelings interfere with, but do not preclude, the patient's ability to carry out normal activities and social interactions. 4: Severe: Anxious feelings preclude patient's ability to carry out normal activities and social interactions.	☐

1.5 APATHY

Instructions to examiner: Consider level of spontaneous activity, assertiveness, motivation and initiative and rate the impact of reduced levels on performance of daily routines and social interactions. Here the examiner should attempt to distinguish between apathy and similar symptoms that are best explained by depression.

Instructions to patients (and caregiver): Over the past week, have you felt indifferent to doing activities or being with people? If yes, examiner asks patient or caregiver to elaborate and probes for information.]

0: Normal: No apathy.

1: Slight: Apathy appreciated by patient and/or caregiver, but no interference with daily activities and social interactions. ☐

2: Mild: Apathy interferes with isolated activities and social interactions.

3: Moderate: Apathy interferes with most activities and social interactions.

4: Severe: Passive and withdrawn, complete loss of initiative.

1.6 FEATURES OF DOPAMINE DYSREGULATION SYNDROME

Instructions to examiner: Consider involvement in a variety of activities including atypical or excessive gambling (e.g. casinos or lottery tickets), atypical or excessive sexual drive or interests (e.g., unusual interest in pornography, masturbation, sexual demands on partner), other repetitive activities (e.g. hobbies, dismantling objects, sorting or organizing), or taking extra non-prescribed medication for non-physical reasons (i.e., addictive behavior). Rate the impact of such abnormal activities/behaviors on the patient's personal life and on his family and social relations (including need to borrow money or other financial difficulties like withdrawal of credit cards, major family conflicts, lost time from work, or missed meals or sleep because of the activity).

Instructions to patients [and caregiver]: Over the past week, have you had unusually strong urges that are hard to control? Do you feel driven to do or think about something and find it hard to stop? [Give patient examples such as gambling, cleaning, using the computer, taking extra medicine, obsessing about food or sex, all depending on the patients.

0: Normal: No problems present.

1: Slight: Problems are present but usually do not cause any difficulties for the patient or family/caregiver.

2: Mild: Problems are present and usually cause a few difficulties in the patient's personal and family life.

3: Moderate: Problems are present and usually cause a lot of difficulties in the patient's personal and family life.

4: Severe: Problems are present and preclude the patient's ability to carry out normal activities or social interactions or to maintain previous standards in personal and family life.

☐

Patient Questionnaire:

Instructions:

This questionnaire will ask you about your experiences of daily living.

There are 20 questions. We are trying to be thorough, and some of these questions may therefore not apply to you now or ever. If you do not have the problem, simply mark 0 for NO.

Please read each one carefully and read all answers before selecting the one that best applies to you.

We are interested in your average or usual function over the past week including today. Some patients can do things better at one time of the day than at others. However, only one answer is allowed for each question, so please mark the answer that best describes what you can do most of the time.

You may have other medical conditions besides Parkinson's disease. Do not worry about separating Parkinson's disease from other conditions. Just answer the question with your best response.

Use only 0, 1, 2, 3, 4 for answers, nothing else. Do not leave any blanks.

Your doctor or nurse can review the questions with you, but this questionnaire is for patients to complete, either alone or with their caregivers.

Who is filling out this questionnaire (check the best answer):

☐ Patient ☐ Caregiver ☐ Patient and Caregiver in Equal Proportion

Part I: Non-Motor Aspects of Experiences of Daily Living (nM-EDL)		
		SCORE
1.7 SLEEP PROBLEMS	ıave you had trouble going to sleep at night or staying sleep Consider how rested you felt after waking up in the ıorning. Over through the nnight?	
0: Normal:	No problems.	
1: Slight:	Sleep problems are present but usually do not cause trouble getting a full night of sleep.	
2: Mild:	Sleep problems usually cause some difficulties getting a full night of sleep.	
3: Moderate:	Sleep problems cause a lot of difficulties getting a full night of sleep, but I still usually sleep for more than half the night.	☐
4: Severe:	I usually do not sleep for most of the night.	
1.8 DAYTIME SLEEPINESS		
	Over the past week, have you had trouble staying awake during the daytime?	
0: Normal:	No daytime sleepiness.	
1: Slight:	Daytime sleepiness occurs but I can resist and I stay awake.	

2: Mild:	Sometimes I fall asleep when alone and relaxing. For example, while reading or watching TV.	
3: Moderate:	I sometimes fall asleep when I should not. For example, while eating or talking with other people.	☐
4: Severe:	I often fall asleep when I should not. For example, while eating or talking with other people.	

SENSATIONS		SCORE
1.9 PAIN AN	ek, have you had uncomfortable feelings in your body like pain, aches	
OTHER S		
Over tingling or cramps?		
0: Normal:		
1: Slight:	No uncomfortable feelings.	
2: Mild:	I have these feelings. However, I can do things and be with other people without difficulty.	
3: Moderate:	These feelings cause some problems when I do things or am with other people.	
	These feelings cause a lot of problems, but they do not stop me from doing things or being with other people.	
4: Severe:	These feelings stop me from doing things or being with other people.	☐

1.10 URINARY PROBLEMS

Over the past week, have you had trouble with urine control? For example, an urgent need to urinate, a need to urinate too often, or urine accidents?

0: Normal:	No urine control problems.	
1: Slight:	I need to urinate often or urgently. However, these problems do not cause difficulties with my daily activities.	
2: Mild:	Urine problems cause some difficulties with my daily activities. However, I do not have urine accidents.	
3: Moderate:	Urine problems cause a lot of difficulties with my daily activities, including urine accidents.	☐
4: Severe:	I cannot control my urine and use a protective garment or have a bladder tube.	

1.11	CONSTIPATION PROBLEMS	SCORE
	Over the past week have you had constipation troubles that cause you difficulty moving your bowels?	
0: Normal:	No constipation.	
1: Slight:	I have been constipated. I use extra effort to move my bowels. However, this problem does not disturb my activities or my being comfortable.	
2: Mild:	Constipation causes me to have some troubles doing things or being comfortable.	
3: Moderate:	Constipation causes me to have a lot of trouble doing things or being comfortable. However, it does not stop me from doing anything.	
4: Severe:	I usually need physical help from someone else to empty my bowels.	

1.12 LIGHT HEADEDNESS ON STANDING

Over the past week, have you felt faint, dizzy or foggy when you stand up after sitting or lying down?

0: Normal:	No dizzy or foggy feelings.
1: Slight:	Dizzy or foggy feelings occur. However, they do not cause me troubles doing things.
2: Mild:	Dizzy or foggy feelings cause me to hold on to something, but I do not need to sit or lie back down.
3: Moderate:	Dizzy or foggy feelings cause me to sit or lie down to avoid fainting or falling.
4: Severe:	Dizzy or foggy feelings cause me to fall or faint.

☐

		SCORE
1.13 FATIGUE	Over the past week, have you usually felt fatigued? This feeling is not part of being sleepy or sad	
0: Normal:	No fatigue.	
1: Slight:	Fatigue occurs. However it does not cause me troubles doing things or being with people.	
2: Mild:	Fatigue causes me some troubles doing things or being with people.	
3: Moderate:		
4: Severe:	Fatigue causes me a lot of troubles doing things or being with people. However, it does not stop me from doing anything.	
	Fatigue stops me from doing things or being with people.	
Part II:	**Motor Aspects of Experiences of Daily Living (M-DL)**	
2.1 SPEECH		
Over the past week, have you had problems with your speech?		
0: Normal:	Not at all (no problems).	
1: Slight:	My speech is soft, slurred or uneven, but it does not cause others to ask me to repeat myself.	
2: Mild:	My speech causes people to ask me to occasionally repeat myself, but not everyday.	
3: Moderate:		

	My speech is unclear enough that others ask me to repeat myself every day even though most of my speech is understood.	
4: Severe:	Most or all of my speech cannot be understood.	

2.2 SALIVA & DROOLING	Over the past week, have you usually had too much saliva during when you are awake or when you sleep?	**SCORE**
0: Normal:	Not at all (no problems).	
1: Slight:	I have too much saliva, but do not drool.	
2: Mild:	I have some drooling during sleep, but none when I am awake.	
3: Moderate:	I have some drooling when I am awake, but I usually do not need tissues or a handkerchief.	
4: Severe:	I have so much drooling that I regularly need to use tissues or a handkerchief to protect my clothes.	☐

2.3 CHEWING AND SWALLOWING

Over the past week, have you usually had problems swallowing pills or eating meals? Do you need your pills cut or crushed or your meals to be made soft, chopped or blended to avoid choking?

0: Normal:	No problems.
1: Slight:	I am aware of slowness in my chewing or increased effort at swallowing, but I do not choke or need to have my food specially prepared.
2: Mild:	I need to have my pills cut or my food specially prepared because of chewing or swallowing problems, but I have not choked over the past week.
3: Moderate.	I choked at least once in the past week.
4: Severe:	Because of chewing and swallowing problems, I need a feeding tube.

		SCORE
2.4 EATING TASKS	Over the past week, have you usually had troubles handling your food and using eating utensils? For example, do you have trouble handling finger foods or using forks, knifes, spoons, chopsticks?	
0: Normal:	Not at all (No problems).	
1: Slight:	I am slow, but I do not need any help handling my food and have not had food spills while eating.	
2: Mild:	I am slow with my eating and have occasional food spills. I may need help with a few tasks such as cutting meat.	☐
3: Moderate:	I need help with many eating tasks but can manage some alone.	
4: Severe:	I need help for most or all eating tasks.	
2.5 DRESSING	Over the past week, have you usually had problems dressing? For example, are you slow or do you need help with buttoning, using zippers, putting on or taking off your clothes or jewelry?	
0: Normal:	Not at all (no problems).	
1: Slight:	I am slow but I do not need help.	
2: Mild:	I am slow and need help for a few dressing tasks (buttons, bracelets).	☐
3: Moderate:	I need help for many dressing tasks.	

4: Severe:	I need help for most or all dressing tasks.	

		SCORE
2.6 HYGIENE		
	Over the past week, have you usually been slow or do you need help with washing, bathing, shaving, brushing teeth, combing your hair or with other personal hygiene?	
0: Normal:	Not at all (no problems).	
1: Slight:	I am slow but I do not need any help.	
2: Mild:	I need someone else to help me with some hygiene tasks.	
3: Moderate:	I need help for many hygiene tasks.	
4: Severe:	I need help for most or all of my hygiene tasks.	☐
2.7 HANDWRITING		
	Over the past week, have people usually had trouble reading your handwriting?	
0: Normal:	Not at all (no problems).	

1: Slight: 2: Mild: 3: Moderate: 4: Severe:	My writing is slow, clumsy or uneven, but all words are clear. Some words are unclear and difficult to read. Many words are unclear and difficult to read. Most or all words cannot be read.	☐
2.8 DOING HOBBIES AND OTHER ACTIVITIES Over the past week, have you usually had trouble doing your hobbies or other things that you like to do? 0: Normal: 1: Slight: 2: Mild: 3: Moderate: 4: Severe:	Not at all (no problems). I am a bit slow but do these activities easily. I have some difficulty doing these activities. I have major problems doing these activities, but still do most. I am unable to do most or all of these activities.	☐

		SCORE
2.9 TURNING IN BED	Over the past week, do you usually have trouble turning over in bed?	
0: Normal:	Not at all (no problems).	
1: Slight:	I have a bit of trouble turning, but I do not need any help.	
2: Mild	I have a lot of trouble turning and need occasional help from someone else.	
3: Moderate:	To turn over I often need help from someone else.	
4: Severe:	I am unable to turn over without help from someone else.	
2.10 TREMOR	Over the past week, have you usually had shaking or tremor?	
0: Normal:	Not at all. I have no shaking or tremor.	
1: Slight:	Shaking or tremor occurs but does not cause problems with any activities.	
2: Mild:	Shaking or tremor causes problems with only a few activities.	
3: Moderate:	Shaking or tremor causes problems with many of my daily activities.	
4: Severe:	Shaking or tremor causes problems with most or all activities.	

2.11 GETTING OUT OF BED, A CAR, OR A DEEP CHAIR	Over the past week, have you usually had trouble getting out of bed, a car seat, or a deep chair?	
0: Normal:	Not at all (no problems).	
1: Slight:		
2: Mild:	I am slow or awkward, but I usually can do it on my first try. I need more than one try to get up or need occasional help.	☐
3: Moderate:	I sometimes need help to get up, but most times I can still do it on my own.	
4: Severe:	I need help most or all of the time.	

		SCORE
2.12 WALKING AND BALANCE		
0: Normal:	Over the past week, have you usually had problems with balance and walking?	
1: Slight:	Not at all (no problems).	
2: Mild:	I am slightly slow or may drag a leg. I never use a walking aid.	
3: Moderate:	I occasionally use a walking aid, but I do not need any help from another person.	
4: Severe:		

	I usually use a walking aid (cane, walker) to walk safely without falling. However, I do not usually need the support of another person. I usually use the support of another persons to walk safely without falling.	☐
2.13 FREEZING		
	Over the past week, on your usual day when walking, do you suddenly stop or freeze as if your feet are stuck to the floor.	
0: Normal:	Not at all (no problems).	
1: Slight:	I briefly freeze but I can easily start walking again. I do not need help from someone else or a walking aid (cane or walker) because of freezing.	
2: Mild:	I freeze and have trouble starting to walk again, but I do not need someone's help or a walking aid (cane or walker) because of freezing.	☐

3: Moderate:	When I freeze I have a lot of trouble starting to walk again and, because of freezing, I sometimes need to use a walking aid or need someone else's help.	
4: Severe:	Because of freezing, most or all of the time, I need to use a walking aid or someone's help.	

This completes the questionnaire. We may have asked about problems you do not even have, and may have mentioned problems that you may never develop at all. Not all patients develop all these problems, but because they can occur, it is important to ask all the questions to every patient. Thank you for your time and attention in completing this questionnaire.

Part III: Motor Examination

Overview: This portion of the scale assesses the motor signs of PD. In administering Part III of the MDS-UPDRS the examiner should comply with the following guidelines:

At the top of the form, mark whether the patient is on medication for treating the symptoms of Parkinson's disease and, if on levodopa, the time since the last dose.

Also, if the patient is receiving medication for treating the symptoms of Parkinson's Disease, mark the patient's clinical state using the following definitions:

ON is the typical functional state when patients are receiving medication and have a good response.

OFF is the typical functional state when patients have a poor response in spite of taking medications.

The investigator should "rate what you see". Admittedly, concurrent medical problems such as stroke, paralysis, arthritis, contracture, and orthopedic problems such as hip or knee replacement and scoliosis may interfere with individual items in the motor examination. In situations where it is absolutely impossible to test (e.g., amputations, plegia, limb in a cast), use the notation "**UR**" for Unable to Rate. Otherwise, rate the performance of each task as the patient performs in the context of co-morbidities.

All items must have an integer rating (no half points, no missing ratings).

Specific instructions are provided for the testing of each item. These should be followed in all instances. The investigator demonstrates while describing tasks the patient is to perform and rates function immediately thereafter. For Global Spontaneous Movement and Rest Tremor items (3.14 and 3.17), these items have been placed purposefully at the end of the scale because clinical information pertinent to the score will be obtained throughout the entire examination.

At the end of the rating, indicate if dyskinesia (chorea or dystonia) was present at the time of the examination, and if so, whether these movements interfered with the motor examination.

3a Is the patient on medication for treating the symptoms of Parkinson's Disease? ☐ No ☐ Yes

3b If the patient is receiving medication for treating the symptoms of Parkinson's Disease, mark the patient's clinical state using the following definitions:

☐ ON: On is the typical functional state when patients are receiving medication and have a good response.

☐ OFF: Off is the typical functional state when patients have a poor response in spite of taking medications.

3c Is the patient on Levodopa ? ☐ No ☐ Yes

3.C1 If yes, minutes since last levodopa dose: _____

3.1 SPEECH	SCORE
Instructions to examiner: Listen to the patient's free-flowing speech and engage in conversation if necessary. Suggested topics: ask about the patient's work, hobbies, exercise, or how he got to the doctor's office. Evaluate volume, modulation (prosody) and clarity, including slurring, palilalia (repetition of syllables) and tachyphemia (rapid speech, running syllables together). 0: Normal: No speech problems. 1: Slight: Loss of modulation, diction or volume, but still all words easy to understand. 2: Mild: Loss of modulation, diction, or volume, with a few words unclear, but the overall sentences easy to follow. 3: Moderate: Speech is difficult to understand to the point that some, but not most, sentences are poorly understood. 4: Severe: Most speech is difficult to understand or unintelligible.	☐

3.2 FACIAL EXPRESSION

Instructions to examiner: Observe the patient sitting at rest for 10 seconds, without talking and also while talking. Observe eye-blink frequency, masked facies or loss of facial expression, spontaneous smiling and parting of lips.

0: Normal: Normal facial expression.

1: Slight: Minimal masked facies manifested only by decreased frequency of blinking.

2: Mild: In addition to decreased eye-blink frequency, Masked facies present in the lower face as well, namely fewer movements around the mouth, such as less spontaneous smiling, but lips not parted.

3: Moderate: Masked facies with lips parted some of the time when the mouth is at rest.

4: Severe: Masked facies with lips parted most of the time when the mouth is at rest.

☐

	SCORE
3.3 RIGIDITY Instructions to examiner: Rigidity is judged on slow passive movement of major joints with the patient in a relaxed position and the examiner manipulating the limbs and neck. First, test without an activation maneuver. Test and rate neck and each limb separately. For arms, test the wrist and elbow joints simultaneously. For legs, test the hip and knee joints simultaneously. If no rigidity is detected, use an activation maneuver such as tapping fingers, fist opening/closing, or heel tapping in a limb not being tested. Explain to the patient to go as limp as possible as you test for rigidity. 0: Normal: No rigidity. 1: Slight: Rigidity only detected with activation maneuver. 2: Mild: Rigidity detected without the activation maneuver, but full range of motion is easily achieved. 3: Moderate: Rigidity detected without the activation maneuver; full range of motion is achieved with effort. 4: Severe: Rigidity detected without the activation maneuver and full range of motion not achieved.	Neck RUE LUE RLE LLE
3.4 FINGER TAPPING Instructions to examiner: Each hand is tested separately. Demonstrate the task, but do not continue to perform the task while the patient is being tested. Instruct the patient to tap the index finger on the thumb 10 times as quickly AND as big as possible. Rate each side separately, evaluating speed, amplitude, hesitations, halts and decrementing amplitude. 0: Normal: No problems. 1: Slight: Any of the following: a) the regular rhythm is broken with one or two interruptions or hesitations of the tapping movement; b) slight slowing; c) the amplitude decrements	

	near the end of the 10 taps.	R ☐ L
2: Mild:	Any of the following: a) 3 to 5 interruptions during tapping; b) mild slowing; c) the amplitude decrements midway in the 10-tap sequence.	
3: Moderate:	Any of the following: a) more than 5 interruptions during tapping or at least one longer arrest (freeze) in ongoing movement; b) moderate slowing; c) the amplitude decrements starting after the 1st tap.	
4: Severe:	Cannot or can only barely perform the task because of slowing, interruptions or decrements.	

3.5 HAND MOVEMENTS Instructions to examiner: Test each hand separately. Demonstrate the task, but do not continue to perform the task while the patient is being tested. Instruct the patient to make a tight fist with the arm bent at the elbow so that the palm faces the examiner. Have the patient open the hand 10 times as fully AND as quickly as possible. If the patient fails to make a tight fist or to open the hand fully, remind him/ her to do so. Rate each side separately, evaluating speed, amplitude, hesitations, halts and decrementing amplitude.	**SCORE** ☐
0: Normal: No problem.	R ☐ L
1: Slight: Any of the following: a) the regular rhythm is broken with one or two interruptions or hesitations of the movement; b) slight slowing; c) the amplitude decrements near the end of the task.	
2: Mild: Any of the following: a) 3 to 5 interruptions during the movements; b) mild slowing; c) the amplitude decrements midway in the task.	
3: Moderate: Any of the following: a) more than 5 interruptions during the movement or at least one longer arrest (freeze) in ongoing movement; b) moderate slowing; c) the amplitude decrements starting after the 1st open-and-close sequence.	
4: Severe: Cannot or can only barely perform the task because of slowing, interruptions or decrements.	

3.6 PRONATION-SUPINATION MOVEMENTS OF HANDS

Instructions to examiner: Test each hand separately. Demonstrate the task, but do not continue to perform the task while the patient is being tested. Instruct the patient to extend the arm out in front of his/her body with the palms down; then to turn the palm up and down alternately 10 times as fast and as fully as possible. Rate each side separately, evaluating speed, amplitude, hesitations, halts and decrementing amplitude.

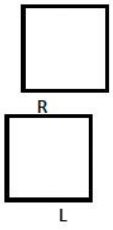
0: Normal: No problems.

1: Slight: Any of the following: a) the regular rhythm is broken with one or two interruptions or hesitations of the movement; b) slight slowing; c) the amplitude decrements near the end of the sequence.

2: Mild: Any of the following: a) 3 to 5 interruptions during the movements; b) mild slowing;
c) the amplitude decrements midway in the sequence.

3: Moderate: Any of the following: a) more than 5 interruptions during the movement or at least one longer arrest (freeze) in ongoing movement; b) moderate slowing c) the amplitude decrements starting after the 1st supination-pronation sequence.

4: Severe: Cannot or can only barely perform the task because of slowing, interruptions or decrements.



3.TOE TAPPING Instructions to examine Test each foot patient is bei then tap the toes 10 amplitude, hesitation	r: Have the patient sit in a straight-backed chair with arms, both feet on the floor. ately. Demonstrate the task, but do not continue to perform the task while the d. Instruct the patient to place the heel on the ground in a comfortable position and times as big and as fast as possible. Rate each side separately, evaluating speed, s, halts and decrementing amplitude.	**SCORE**
0: Normal:	No problem.	R L
1: Slight:	Any of the following: a) the regular rhythm is broken with one or two interruptions or hesitations of the tapping movement; b) slight slowing; c) amplitude decrements near the end of the ten taps. Any of the following: a) 3 to 5 interruptions during the tapping movements; b) mild slowing; c) amplitude decrements midway in the task.	
2: Mild:	Any of the following: a) more than 5 interruptions during the tapping movements or at least one longer arrest (freeze) in ongoing movement; b) moderate slowing; c) amplitude decrements after the first tap.	
3: Moderate:	Cannot or can only barely perform the task because of slowing, interruptions or decrements.	
4: Severe:		

3.8 LEG AGILITY

Instructions to examiner: Have the patient sit in a straight-backed chair with arms. The patient should have both feet comfortably on the floor. Test each leg separately. Demonstrate the task, but do not continue to perform the task while the patient is being tested. Instruct the patient to place the foot on the ground in a comfortable position and then raise and stomp the foot on the ground 10 times as high and as fast as possible. Rate each side separately, evaluating speed, amplitude, hesitations, halts and decrementing amplitude.

0: Normal:	No problems.
1: Slight:	Any of the following: a) the regular rhythm is broken with one or two interruptions or hesitations of the movement; b) slight slowing; c) amplitude decrements near the end of the task.

2: Mild:	Any of the following: a) 3 to 5 interruptions during the movements; b) mild slowness; c) amplitude decrements midway in the task.	R ☐ L
3: Moderate:	Any of the following: a) more than 5 interruptions during the movement or at least one longer arrest (freeze) in ongoing movement; b) moderate slowing in speed; c) amplitude decrements after the first tap.	
4: Severe:	Cannot or can only barely perform the task because of slowing, interruptions or decrements.	

		SCORE
3.9 ARISING FROM CHAIR	Have the patient sit in a straight-backed chair with arms, with	
Instructions to examiner: floor and sitting back in t across the chest and the u to two more times. If arms folded across th ch to push off using his/her If still not successful, ass 3.13	both feet on the he chair (if the patient is not too short). Ask the patient to cross his/her arms n to stand up. If the patient is not successful, repeat this attempt a maximum still unsuccessful, allow the patient to move forward in the chair to arise with est. Allow only one attempt in this situation. If unsuccessful, allow the patient hands on the arms of the chair. Allow a maximum of three trials of pushing off. ist the patient to arise. After the patient stands up, observe the posture for item	
0: Normal:	No problems. Able to arise quickly without hesitation.	
1: Slight:	Arising is slower than normal; or may need more than one attempt; or may need to move forward in the chair to arise. No need to use the arms of the chair.	
2: Mild:	Pushes self up from arms of chair without difficulty.	☐
3: Moderate:	Needs to push off, but tends to fall back; or may have to try more than one time using arms of chair, but can get up without help.	
4: Severe:	Unable to arise without help.	

3.10 GAIT

Instructions to examiner: Testing gait is best performed by having the patient walking away from and ~~towards the examiner so~~ that both right and left sides of the body can be easily observed simultaneously. The patient should walk at least 10 meters (30 feet), then turn around and return to the examiner. This item measures multiple behaviors: stride amplitude, stride speed, height of foot lift, heel strike during walking, turning, and arm swing, but not freezing. Assess also for "freezing of gait" (next item 3.11) while patient is walking. Observe posture for item 3.13

0: Normal:	No problems.
1: Slight:	Independent walking with minor gait impairment.
2: Mild:	Independent walking but with substantial gait impairment.
3: Moderate:	Requires an assistance device for safe walking (walking stick, walker) but not a person.
4: Severe:	Cannot walk at all or only with another person's assistance.

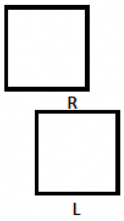
	SCORE
3.11 FREEZIN OF GAIT Instructions to examiner: episodes. Observe for st the end of the task. assessment. 0: Normal: 1: Slight: 2: Mild: 3: Moderate : 4: Severe:	While assessing gait, also assess for the presence of any gait freezing hesitation and stuttering movements especially when turning and ıching To the extent that safety permits, patients may NOT use sensory :ks during the No freezing. Freezes on starting, turning or walking through doorway with a single halt during any of these events, but then continues smoothly without freezing during straight walking. Freezes on starting, turning or walking through doorway with more than one halt during any of these activities, but continues smoothly without freezing during straight walking. Freezes once during straight walking. Freezes multiple times during straight walking.	☐
3.12 POSTURAL STABILITY Instructions to examiner: The test examines the response to sudden body displacement produced by a quick, forceful pull on the shoulders while the patient is standing erect with eyes open and feet comfortably apart and parallel to each other. Test retropulsion. Stand behind the patient and instruct the patient on what is about to happen. Explain that s/he is allowed to take a step backwards to avoid falling. There should be a solid wall behind the examiner, at least 1-2 meters away to allow for the observation of the number of retropulsive steps. The first pull is an instructional demonstration and is purposely milder and not rated. The second time the shoulders are pulled briskly and forcefully towards the examiner with enough force to displace the center of gravity so that patient MUST take a step backwards. The examiner needs to be ready to catch the patient, but must stand sufficiently back so as to allow enough room for the patient to take several steps to recover independently. Do not allow the patient to flex the body abnormally forward in anticipation of the pull. Observe for the number of steps backwards or falling. Up to and including two steps for recovery is considered normal, so abnormal ratings begin with three steps. If the patient fails to understand the test, the examiner can repeat the test so that the rating is based on an assessment that the	

examiner feels reflects the patient's limitations rather than misunderstanding or lack of preparedness. Observe standing posture for item 3.13

0: Normal:	No problems: Recovers with one or two steps.	
1: Slight:	3-5 steps, but subject recovers unaided.	☐
2: Mild:	More than 5 steps, but subject recovers unaided.	
3: Moderate:	Stands safely, but with absence of postural response; falls if not caught by examiner.	
4: Severe:	Very unstable, tends to lose balance spontaneously or with just a gentle pull on the shoulders.	

	SCORE
3.13 **POSTURE** Instructions examine dur walking, and wl to stand r: Posture is assessed with the patient standing erect after arising from a straight an in th chair, being tested for postural reflexes. If you notice poor posture, tell the three observa patient d see if the posture improves (see option 2 below). Rate the worst posture seen 0: Normal: tion points. Observe for flexion and side-to-side leaning. 1: Slight: No problems. 2: Mild: Not quite erect, but posture could be normal for older person. 3: Moderate: Definite flexion, scoliosis or leaning to one side, but patient can correct posture to normal posture when asked to do so. Stooped posture, scoliosis or leaning to one side that cannot be corrected volitionally to a normal posture by the patient. 4: Severe: Flexion, scoliosis or leaning with extreme abnormality of posture.	☐
3.14 GLOBAL SPONTANEITY OF MOVEMENT (BODY BRADYKINESIA) Instructions to examiner: This global rating combines all observations on slowness, hesitancy, and small amplitude and poverty of movement in general, including a reduction of gesturing and of crossing the legs. This assessment is based on the examiner's global impression after observing for spontaneous gestures while sitting, and the nature of arising and walking. 0: Normal: No problems. 1: Slight: Slight global slowness and poverty of spontaneous movements. 2: Mild: Mild global slowness and poverty of spontaneous movements. 3: Moderate: Moderate global slowness and poverty of spontaneous movements.	☐

4: Severe:	Severe global slowness and poverty of spontaneous movements.	
3.15 POSTURAL TRE _Instructions to examine to be included in this ra patient to stretch the ar the fingers comfortably seconds. 0: Normal: 1: Slight: 2: Mild: 3: Moderate: 4: Severe:	**MOR OF THE HANDS** r: All tremor, including re-emergent rest tremor, that is present in this posture is ting. Rate each hand separately. Rate the highest amplitude seen. Instruct the ms out in front of the body with palms down. The wrist should be straight and separated so that they do not touch each other. Observe this posture for 10 No tremor. Tremor is present but less than 1 cm in amplitude. Tremor is at least 1 but less than 3 cm in amplitude. Tremor is at least 3 but less than 10 cm in amplitude. Tremor is at least 10 cm in amplitude.	R L

		SCORE
3.16KINETIC TREMOR OF THE HANDS Instructions to examiner outstretched positio reaching as far as possib performed slowly enough with the other hand, ratin or as the tremor reache 0: Normal: 1: Slight: 2: Mild: 3: Moderate: 4: Severe:	: This is tested by the finger-to-nose maneuver. With the arm ing from the n, have the patient perform at least three finger-to- maneuvers with each hand le to touch the examiner's finger. The r-to-nose maneuver should be not to hide any tremor that could occur with very fast arm movements. Repeat each hand separately. The tremor can be present throughout the movement either target (nose or finger). Rate the highest amplitude seen. No tremor. Tremor is present but less than 1 cm in amplitude. Tremor is at least 1 but less than 3 cm in amplitude. Tremor is at least 3 but less than 10 cm in amplitude. Tremor is at least 10 cm in amplitude.	 R L

3.17 REST TREMOR

AMPLITUDE

Instructions to examiner

This and the next item have been placed purposefully at the end of the examination to allow the rater to gather observations on rest tremor that may appear at any time during the exam, including when quietly sitting, during walking and during activities when some body parts are moving but others are at rest. Score the maximum amplitude that is seen at any time as a Rate only the amplitude. As part of the final score. and not the persistence or the intermittency of the this rating, the patient should sit quietly in a chair with the hands placed (not in the lap) and on the arms of the chair. e with the feet comfortably supported on the floor for 10 seconds directives. Rest tremor is assessed separately for all four limbs and also for the lip/jaw. Rate only the maximum amplitude that is seen at any time as the final rating.

RUE

LUE

RLE

LLE

Lip/Jaw

Extremity ratings

0: Normal: No tremor.

1: Slight.: ≤ 1 cm in maximal amplitude.

2: Mild: > 1 cm but < 3 cm in maximal amplitude.

3: Moderate: 3 - 10 cm in maximal amplitude.

4: Severe: > 10 cm in maximal amplitude.

Lip/Jaw ratings

0: Normal: No tremor.

1: Slight: ≤ 1 cm in maximal amplitude.

2: Mild: > 1 cm but ≤ 2 cm in maximal amplitude.

3: Moderate: > 2 cm but ≤ 3 cm in maximal amplitude.

4: Severe: > 3 cm in maximal amplitude.

3.18 CONSTANCY OF REST TREMOR	SCORE
Instructions to examiner: This item receives one rating for all rest tremor and focuses on the constancy of rest tremor during the examination period when different body parts are variously at rest. It is rated purposefully at the end of the examination so that several minutes of information can be coalesced into the rating. 0: Normal: No tremor. 1: Slight: Tremor at rest is present ≤ 25% of the entire examination period. 2: Mild: Tremor at rest is present 26-50% of the entire examination period. 3: Moderate: Tremor at rest is present 51-75% of the entire examination period. 4: Severe: Tremor at rest is present > 75% of the entire examination period.	☐

DYSKINESIA IMPACT ON PART III RATINGS	
A. Were dyskinesias (chorea or dystonia) present during examination?	☐ No ☐ Yes
B. If yes, did these movements interfere with your ratings?	☐ No ☐ Yes

HOEHN AND YAHR STAGE

0: Asymptomatic.

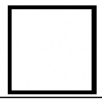
1: Unilateral involvement only.

2: Bilateral involvement without impairment of balance.

3: Mile to moderate involvement; some postural instability but physically independent; needs assistance to recover from pull test.

4: Severe disability; still able to walk or stand unassisted.

5: Wheelchair bound or bedridden unless aided.



4.2 FUNCTIONAL IMPACT OF DYSKINESIAS	SCORE
Instructions to examiner: Determine the degree to which dyskinesias impact on the patient's daily function in terms of activities and social interactions. Use the patient's and caregiver's response to your question and your own observations during the office visit to arrive at the best answer. *Instructions to patient [and caregiver]: Over the past week, did you usually have trouble doing things or being with people when these jerking movements occurred? Did they stop you from doing things or from being with people?* 0: Normal: No dyskinesias or no impact by dyskinesias on activities or social interactions. 1: Slight: Dyskinesias impact on a few activities, but the patient usually performs all activities and participates in all social interactions during dyskinetic periods. 2: Mild: Dyskinesias impact on many activities, but the patient usually performs all activities and participates in all social interactions during dyskinetic periods. 3: Moderate: Dyskinesias impact on activities to the point that the patient usually does not perform some activities or does not usually participate in some social activities during dyskinetic episodes. 4: Severe: Dyskinesias impact on function to the point that the patient usually does not perform most activities or participate in most social interactions during dyskinetic episodes.	☐
B . MOTOR FLUCTUATIONS	
4.3 TIME SPENT IN THE OFF STATE Instructions to examiner: Use the number of waking hours derived from 4.1 and determine the hours spent in the "OFF" state. Calculate the percentage. If the patient has an OFF period in the office, you can point to this state as a reference. You may also use your knowledge of the patient to describe a typical OFF period. Additionally you may use your own acting skills to enact an OFF period you have seen in the patient before or show them OFF function typical of other patients. Mark down the typical number of OFF hours, because you will need this number for completing 4.6 *Instructions to patient [and caregiver]: Some patients with Parkinson's disease have a good effect from their medications throughout their awake hours*	☐

and we call that "ON" time. Other patients take their medications but still have some hours of low time, bad time, slow time or shaking time. Doctors call these low periods "OFF" time. Over the past week, you told me before that you are generally awake hrs each day. Out of these awake hours, how many hours in total do you usually have this type of
low level or OFF function (Use this number for your calculations).

____

0: Normal:	No OFF time.
1: Slight:	≤ 25% of waking day.
2: Mild:	26 - 50% of waking day.
3: Moderate:	51 - 75% of waking day.
4: Severe:	> 75% of waking day.

1. Total Hours Awake: _____

2. Total Hours OFF: _____

3. % OFF = ((2/1)*100):

FLUCTUATIONS		SCORE
4.4 FUNCTIONA IMPACT OF	Determine the degree to which motor fluctuations impact on the patient's daily es and social interactions. This question concentrates on the difference	
Instructions to examiner: functio	nd the OFF state. If the patient has no OFF time, the rating must be), but if fluctuations, it is still possible to be rated 0 on this item if no impact on activities	
in terms of activiti	and caregiver's response to your question and your own	
between the ON state a patients	bservations during	
have very mild occurs. Use the	the best answer.	
patient' the office visit to arrive at	*caregiver]: Think about when those low or "OFF" periods ve occurred over u usually have more problems doing things being with people than compared to you feel your medications rking? Are there some things you usually do t you have trouble with or stop doing during a low period?*	
Instructions patient [and t past week. Do the rest of the d when during good period th	No fluctuations or No impact by fluctuations on performance of activities or social interactions.	
0: Normal:	Fluctuations impact on a few activities, but during OFF, the patient usually performs all activities and participates in all social interactions that typically occur during the ON state.	
1: Slight:	Fluctuations impact many activities, but during OFF, the patient still usually performs all activities and participates in all social interactions that typically occur during the ON state.	
2: Mild:	Fluctuations impact on the performance of activities during OFF to the point that the patient usually does not perform some activities or participate in some social interactions that are performed during ON periods.	
3: Moderate:	Fluctuations impact on function to the point that, during OFF, the patient usually does not perform most activities or participate in most social interactions that are performed during ON periods.	
4: Severe:		

4.5 COMPLEXITY OF MOTOR FLUCTUATIONS

Instructions to examiner: Determine the usual predictability of OFF function whether due to dose, time of day, food intake or other factors. Use the information provided by the patients and caregiver and supplement with your own observations. You will ask if the patient can count on them always coming at a special time, mostly coming at a special time (in which case you will probe further to separate slight from mild), only sometimes coming at a special time or are they totally unpredictable? Narrowing down the percentage will allow you to find the correct answer.

Instructions to patient [and caregiver]: For some patients, the low or "OFF" periods happen at certain times during day or when they do activities like eating or exercising. Over the past week, do you usually know when your low periods will occur? In other words, do your low periods always come at a certain time? Do they mostly come at a certain time? Do they only sometimes come at a certain time? Are your low periods totally unpredictable?"

0: Normal: No motor fluctuations.

1: Slight: OFF times are predictable all or almost all of the time (> 75%).

2: Mild: OFF times are predictable most of the time (51-75%).

3: Moderate: OFF times are predictable some of the time (26-50%).

4: Severe: OFF episodes are rarely predictable. (≤ 25%).

C. "OFF" DYSTONIA

4.6 PAINFUL OFF-STATE DYSTONIA

Instructions to examiner: For patients who have motor fluctuations, determine what proportion of the
OFF episodes usually includes painful dystonia? You have already determined the number of hours of "OFF" time (4.3). Of these hours, determine how many are associated with dystonia and calculate the percentage. If there is no OFF time, mark 0.

Instructions to patient [and caregiver]: In one of the questions I asked earlier, you said you generally have _____ hours of low or "OFF" time when your Parkinson's disease is under poor control. During these low or "OFF" periods, do you usually have painful cramps or spasms? Out of the total __hrs of this low time, if you add up all the time in a day when these painful cramps come, how many hours would this make?

0: Normal:	No dystonia OR NO OFF TIME.
1: Slight:	≤ 25% of time in OFF state.
2: Mild:	26-50% of time in OFF state.
3: Moderate:	51-75% of time in OFF state.
4: Severe:	> 75% of time in OFF state.

1. Total Hours Off: _____
2. Total Off Hours w/Dystonia: _____
3. % Off Dystonia = ((2/1)*100):

☐

Rating Scale Permissions

Thank you. The information you submitted appears below.

MDS Rating Scale Permissions Request Form

Name: Joseph DeSouza
Company / Organization Name: Centre for Vision Research - York University
Address: 4700 Keele St
Dept of Psychology | Centre for Vision Research
City: Toronto
State: Ontario
Zip: M3J 1P3
Country: Canada
Telephone: 4167362100 x22946
Fax:
Email: desouza@yorku.ca

Intended use of materials: We are using the UPDRS for categorizing people with PD to correlate motor and non-motor tests with EEG, fMRI and MRI

Unified Parkinson's Disease Rating Scale (MDS-UPDRS)
No Financial Support (No charge)
Protocol number: e2013-313

Total: $0 USD

By submitting this request to MDS, you agree to the following:
I understand that all of the International Parkinson and Movement Disorder Society (MDS) Rating Scales may only be used for the purposes described above. I also understand that reproduction, translation, modification, sale, or distribution of any portion of the MDS Rating Scales is strictly prohibited and, specifically, that the MDS Rating Scales may not be incorporated into clinical trials, training or certification programs or materials, software programs, or otherwise except through use of

Appendix C: Medication Questionnaire

Initials: _____ Date: _____

Medication Questionnaire

Please circle or answer the following questions as accurately as possible.

1. Are you taking any medications? Yes / No

   If yes, which medication(s)? Please list the medication name(s) and dosage(s).

_____

_____

_____

2. Do you take any medication(s) to be "on" for class? Yes / No

   If yes,

   a) What time do you take your medication for the 10 am class? _____
   b) What time does it become effective? _____
   c) What time does it wear off? _____

   If you participated in any of the pre- or post- class testing sessions,

   d) Did you take your medication(s) to be "on" for the test session? Yes / No
   e) What time did you take your medication for the test session? _____
   f) What time does it become effective? _____
   g) What time does it wear off? _____
   h) If you were tested before and after class, do you think your medication was equally effective before and after class? Yes / No
      If no, please explain_____
      _____

3. Has your medication or dosage recently changed? Yes / No

4. If yes above, when did the change occur? _____

5. Is there any other information you would like to share with us about medication and performance on the motor tasks?

_____

_____

_____

Date: _____

Questionnaire

Please circle or answer the following questions as accurately as possible.

1. What are the initials of your first and last name? _____

2. Age: _____

3. At what age did you learn you had Parkinson's disease? _____

4. Sex: female / male

5. With which hand do you do the following actions?

- Throw a ball R / L
- Brush your teeth R / L
- Eat soup with a spoon R / L
- Comb your hair R / L
- Cut bread with a knife R / L
- Swing a racquet or bat R / L
- Point accurately R / L
- Write your name R / L
- Hammer a nail R / L
- Is there anything you do consistently with your left hand? _____

6. How many hours of sleep do you get per night? _____

7. Extend both arms in front of your body and place the hands together so as to make a small triangle between your thumbs and the first knuckle. With both of your eyes open, look through the triangle and focus on a specific small object. Close your left eye. If the object remains in view, you are right eye dominant. If your hands appear to move off the object and move to the left, then you are left eye dominant

Eye dominance: R-eye / L-eye

Date: _____

8. Can you wink with your left eye? _____

Can you wink with your right eye? _____

9. Corrected vision? Yes / No

10. Are you taking any medications? Yes / No

If yes, which medication(s)? _____

What is/are the dosage (s)? _____

At which time(s) do you take your medication _____

11. Have you ever taken a dance class? Yes / No

12. If yes, what kind of dance class(es)? _____

At which age did you start? _____

At which age did you stop? _____

13. Have you ever participated in a dance for Parkinson's program? Yes / No

14. If yes, which program? _____

Where was it held? _____

Are you still participating in this program? Yes / No

If yes, how many time per week? _____

15. Do you participate in any physical exercise programs besides dance? Yes / No

16. If yes, what kind of physical exercise (s) do you do? _____

How many hours per week? _____

17. How many Dance for Parkinson's classes have you attended at Canada's National Ballet School? _____

Date: _____

18. Of the classes you attended, were you able to participate fully in them? Yes / No

If no, how often did you have to sit out? _____

19. How many times per week do you practice visualizing the steps of the dance you are learning? _____

20. For how many minutes do you visualize? _____