Exploring the Effects of Dopamine on Sensorimotor Inhibition and Mobility in Older Adults

Douglas N. Martini, PhD[1, 2*], Rosie Morris, PhD[1,3], Graham Harker, MPH[1], Valerie E. Kelly, PhD[4], John G. Nutt, MD[1], and Fay B. Horak, PhD, PT [1]

[1] *Department of Neurology, Oregon Health and Science University, Portland, OR, USA*

[2] *Department of Kinesiology, University of Massachusetts Amherst, Amherst, MA, USA*

[3] *Department of Sport, Exercise, and Rehabilitation, Northumbria University, Newcastle, UK*

[4] *Department of Rehabilitation Medicine, University of Washington School of Medicine, Seattle, WA, USA*

***Corresponding Author:**
Dr. Douglas N Martini
Assistant Professor
Department of Kinesiology
University of Massachusetts Amherst
30 Eastman Lane
Amherst, Massachusetts, USA, 01003
Email: dmartini@umass.edu

Abstract

Background: Dopaminergic activity decreases in older adults (OAs) with normal aging and is further reduced in Parkinson's disease (PD), affecting cortical motor and sensorimotor pathways. Levodopa is the prevailing therapy to counter dopamine loss in PD, though not all PD motor signs improve with levodopa. The purpose of this preliminary study was to explore the effects of levodopa on sensorimotor inhibition, gait and quiet standing in OAs and to investigate the relationships between sensorimotor inhibition and both gait and standing balance both OFF- and ON-levodopa.

Methods: Fifteen OA males completed a gait, balance and sensorimotor assessments before and one hour after they were given a 100mg dose of levodopa. Short-latency afferent inhibition quantified sensorimotor inhibition. Wearable sensors characterized gait (two-minute walk) and standing balance (one-minute stance).

Results: No sensorimotor inhibition, gait, or standing balance measures changed from OFF- to ON-levodopa. When OFF-levodopa, worse inhibition significantly related to increased double stance ($r=0.62$; $p=0.01$), increased jerkiness of sway ($r=0.57$; $p=0.03$) and sway area ($r=0.58$; $p=0.02$). While ON-levodopa, worse inhibition related to increased arm swing range of motion ($r=0.63$; $p=0.01$) and jerkiness of sway ($r=0.53$; $p=0.04$). The relationship between SAI and arm swing excursion significantly changed from OFF- to ON-levodopa ($z = -3.05$; $p = 0.002$; 95% confidence interval = -0.95 - -0.21).

Conclusion: Sensorimotor inhibition relationships to both gait and balance may be affected by dopamine in OAs. Cortical restructuring due to the loss of dopamine may be responsible for the heterogeneity of levodopa effect in people with PD and OAs.

Key words: Gait; Balance; Short-Latency Afferent Inhibition; Drug Related

1. Introduction

Dopaminergic activity decreases in normal aging, with an exacerbated decrease observed in Parkinson's disease (PD).[1] In PD, dopaminergic denervation may result in cortical restructuring that alters the roles of neurotransmitters in motor pathways.[2] Evidence from rodent stroke indicate that dopamine has a role in sensorimotor integration in the somatosensory cortex.[3] Altered motor and sensory pathways following a decrease in dopaminergic activity manifests as gait and balance impairments in people with PD. Levodopa, a dopamine replacement medication, is the prevailing therapy to treat motor signs and symptoms of PD. However, not all PD motor signs and symptoms improve with levodopa. Some components of gait and standing balance deteriorate from OFF- to ON-levodopa states in people with PD,(Curtze and others 2015; Wilson and others 2020) but the reasons that levodopa negatively impacts some motor functions remain unclear.

Short-latency afferent inhibition (SAI), a surrogate for sensorimotor inhibition, was initially linked to cholinergic activity because the cortical inhibition quantified by SAI improved with a cholinergic agonist.[6] Other studies subsequently observed effects of gamma aminobutyric acid agonists and levodopa on SAI.(Di Lazzaro and others 2005; Di Lazzaro and others 2002; Sailer and others 2003) SAI worsens in the ON-levodopa state in people with PD.[9] Cumulatively, the implication is that SAI results from complex neurophysiological interactions controlling inhibition in the sensorimotor pathway. The reduction of sensorimotor inhibition in the ON-levodopa state may contribute to the observed heterogenous effects of levodopa on gait and balance in PD.

Although gait speed improves with dopamine in PD, postural stability during walking (double support time) and standing balance (sway area, frequency, smoothness) are unaffected or worsen with dopaminergic medication in PD.(Curtze and others 2015; Wilson and others 2020)

Both gait and standing balance relate to the amount of sensorimotor inhibition quantified by SAI in people with PD, older adults (OA), and OA fallers.(Martini and others 2020; Martini and others 2021; Pelosin and others 2016; Rochester and others 2012) Specifically, abnormal postural sway or slower gait are associated with worse SAI is in these populations.(Martini and others 2020; Martini and others 2021; Pelosin and others 2016; Rochester and others 2012) Despite established dopaminergic decreases with aging, the effect of levodopa on these relationships is not known.[1] Establishing the relationships among levodopa, sensorimotor inhibition, and mobility in OAs could provide greater insight into the heterogeneous effects of levodopa on mobility in PD.

The purpose of this exploratory investigation was to examine the effects of levodopa on sensorimotor inhibition and mobility in OAs. Specifically, we aimed to investigate the effects of levodopa on sensorimotor inhibition, gait, and quiet standing balance in OAs. Further, we aimed to explore the relationships between sensorimotor inhibition and both gait and standing balance in OAs OFF- and ON-levodopa. We hypothesized that sensorimotor inhibition, gait stability and standing balance will be worse, while other characteristics of gait will remain unchanged from the OFF- to ON-levodopa state, consistent with the aforementioned heterogeneous effect of levodopa on gait in the PD literature. Finally, we hypothesize that worse gait stability and standing balance measures will correlate to worse sensorimotor inhibition.

2. Methods

The Oregon Health & Science University Institutional Review Board approved this study. All participants reviewed the study purpose and procedures involved before signing the informed consent.

2.1 Participants

Fifteen healthy OA males were recruited from an ongoing Pacific Udall Center project at Oregon Health & Science University. Participants were screened for TMS eligibility before enrollment. Inclusion criteria included the ability to stand unsupported for 30 seconds. Exclusion criteria included: inability to walk for two minutes without an assistive device, any TMS contraindication, any musculoskeletal injury that would affect mobility, any neurological disorder, a failed medical screen (completed by JGN) for taking levodopa, or any cholinergic mediation. A single 100/25 mg dose of levodopa/carbidopa was given to each participant after completing the “OFF-levodopa medication state” assessment. No participant reported an adverse event as a result of ingesting a single 100/25 mg dose of levodopa/carbidopa.

Each participant completed the following clinical assessments: Montreal Cognitive Assessment (MoCA; range=0-30), Activities Balance Confidence (ABC; range=0-100) scale, and the Falls Efficacy Scale (FES; range=0-100). The participants completed the MoCA prior to the OFF-levodopa state sensorimotor inhibition and mobility assessments. Upon completing the OFF-levodopa state assessments, participants were given their single 100/25 mg tablet (levodopa/carbidopa) with carbonated water and an option of fruit. Participants waited an hour before starting the “ON-levodopa state” assessments. During the wait, participants completed the ABC and FES scales. After one hour, participants completed the ON-levodopa state sensorimotor inhibition and mobility assessment in the same order as the OFF-levodopa state assessment.

2.2 Transcranial Magnetic Stimulation (TMS)

TMS of the motor cortex was performed with a Magstim 200 (Magstim Co.). A figure-of-eight coil (external loop diameter of 9cm) was positioned over the hemisphere associated with the

dominant hand. Motor-evoked potentials (MEPs) were recorded from the first dorsal interosseous muscle through disposable, Ag/AgCl surface electrodes. Samples were amplified (gain: 2000) and bandpass filtered (100Hz-5kHz) using BIOPAC MP150 system (BIOPAC Systems, Inc). Resting motor threshold was determined as the percentage of the minimum stimulator output to elicit an MEP of 50μV in five out of ten trials.

2.3 Short-Latency Afferent Inhibition

SAI was performed using a modified version of a protocol previously described.(Martini and others 2020; Martini and others 2021) Participants were instructed to remain at rest, sitting as still as possible, and refrain from keeping their eyes closed. A peripheral, electric conditioning stimulus was applied over the median nerve followed by the central test stimulus, TMS. The intensity of the conditioning stimulus was set at the amplitude required to elicit a visible twitch of the first dorsal interosseous muscle. For the purpose of this investigation, we used 20ms as the N20 latency across all participants.(Martini and others 2020; Martini and others 2021) The interstimulus intervals (ISI) were randomly applied from N20+0ms to N20+5ms, in 1ms increments. Ten trials were collected and the conditioned peak-to-peak MEP magnitudes were averaged for each ISI. The grand mean of the ISIs is expressed as the percentage of the unconditioned MEP magnitudes. A SAI grand mean around 100% indicates minimal or no sensorimotor inhibition (worse), as this indicates that the peripheral nerve stimulation ascending signal provides limited inhibition of the descending motor signal.

2.4 Mobility Assessment

Inertial sensors (Opals, APDM Inc.) were placed on each wrist and foot, around the waist, and over the sternum to characterize gait and standing balance using Mobility Lab software (APDM, Inc).[14] Gait was characterized during a two-minute walk, back-and-forth over a seven-meter

path, requiring 180 degree turns at the ends of the marked path. Participants were instructed to walk at a comfortable, self-selected pace. Gait variables of interest were double limb support (% of gait cycle), speed (meters/second [m/s]), stride time (s), stride length (m), arm swing excursion (degrees [d]), and turn velocity (d/s). Standing balance was characterized while participants stood quietly for one minute looking straight ahead with foot position standardized by a template. The balance variables of interest were jerkiness of sway, root mean square (RMS) relative to the mean sway, sway velocity, and sway area.

2.5 Statistical Analyses

Data were inspected for normality using histograms and the Kolmogorov-Smirnov test. Balance variables were not normally distributed, so they were natural log transformed to improve normality. Paired samples t-tests were used to compare medication state differences in SAI, gait and balance variables. Pearson's correlations assessed the relationships between SAI and mobility variables. For significant relationships between SAI and mobility variables, the magnitude of Pearson's correlations were statistically compared using the R statistics package cocor and Fisher's z transformation of overlapping variables (e.g. OFF and ON-levodopa).[15, 16] Cohen's *d* effect sizes were calculated to characterize the magnitude of the medication effect and were interpreted as weak (<0.50), moderate (0.50-0.79) or strong (≥0.80).[17] Alpha was set *a priori* to $p < 0.05$. IBM SPSS version 27 was used for statistical analyses. Data are presented as mean(standard deviation), unless otherwise indicated.

3. Results

3.1 Participants

The 15 OA males that participated in this study were 65.8(6.5) years-old, with an average height of 175.1(9.4) cm and mass of 81.1(7.8) kg. The average MoCA score was 27.8(1.5), indicating no cognitive impairment. The average FES was 10.3(0.7) and the ABC was 98.3(1.9), indicating no fear of falling.

3.2 SAI in the OFF- versus ON-levodopa states

There was no significant difference in SAI between the OFF- and ON-medication states (t=0.56; *p*=0.59; Cohen's *d*=0.14). The average OFF-levodopa state SAI was 66.5(17.3)% and the average ON-levodopa state SAI was 64.4(16.3)% (**Figure 1**). Average SAI values in both OFF- and ON-levodopa states for these OAs are similar to previously reported values in OAs.(Martini and others 2020; Martini and others 2021; Pelosin and others 2016; Rochester and others 2012)

3.3 Gait and Standing Balance Differences Between Medication States

Levodopa had no significant effect on gait or postural sway variables (**Table 1**). Though not significant, arm swing excursion had a moderate effect size (Cohen's *d*=0.50), with less arm swing excursion in the ON-levodopa compared to the OFF-levodopa state.

3.4 Correlations Between SAI and Mobility

Worse SAI in the OFF-levodopa state significantly related to increased double limb support, jerkiness of sway, and sway area (**Figure 2**). SAI OFF was not significantly related to OFF: gait speed (r = -0.34), stride time (r = 0.24), stride length (r = -0.19), arm swing excursion (r = 0.16), turn velocity (r = -0.23), RMS Sway (r = 0.38), or sway velocity (r = 0.19). Worse SAI in the ON-levodopa state significantly related to increased arm swing excursion and jerkiness of sway (**Figure 2**). SAI ON was not significantly related to ON: double limb support (r = 0.45), gait speed (r = -0.12), stride time (r = 0.19), stride length (r = -0.01), turn velocity (r = 0.04), RMS

Sway (r = 0.14), sway velocity (r = -0.27), or sway area (r = 0.23). There were no significant relationships between the change in SAI and the change in gait or balance measures from OFF- to ON-levodopa states. The relationship between SAI and arm swing excursion significantly changed from OFF- to ON-levodopa (z = -3.05; p = 0.002; 95% confidence interval for the difference in Person's r = -0.95 - -0.21).

4. Discussion

The aim of this study was to quantify gait, standing balance, and sensorimotor inhibition in OAs in OFF- and ON-levodopa states. We aimed to explore the impact of levodopa on mobility and SAI in healthy OAs to gain more insight into the impact of dopamine on mobility and sensorimotor inhibition in people with PD. Unlike findings in PD cohorts, our preliminary findings suggest that levodopa has no effect on either mobility or SAI in OAs. However, levodopa-dependent relationships were observed between mobility and SAI. In the OFF-levodopa state, worse SAI significantly correlated with worse performance for specific aspects of gait and balance. Since increased double limb support reflects a decreased ability to balance on one foot, the OFF-levodopa state SAI-mobility relationships reflect a role for sensorimotor inhibition in gait stability of OAs. This early observation is mirrored for OFF-levodopa state balance, with worse stability (e.g. increased jerkiness of sway and sway area) related to worse sensorimotor inhibition. Unlike the OFF-levodopa state, the ON-levodopa state resulted in significant relationships between worse SAI and increased arm swing excursion (gait) and worse jerkiness of sway (balance). The increased arm excursion with worse SAI is interesting, as the worse sensorimotor inhibition indicated by higher SAI may result in larger arm excursion while walking, but only when ON-levodopa. Further, the relationship between SAI and arm swing excursion significantly changed from OFF- to ON-levodopa and a moderate effect (Cohen's *d* = 0.50). This observation is particularly interesting because levodopa can result in large, dyskinetic arm excursion while walking in patients with PD.(Curtze and others 2015)

There were no changes in gait or balance performance after taking a 100mg dose of levodopa. In contrast, fine motor skill speed has been reported to improve in healthy OAs with three, 100mg doses of levodopa over a 24-hour period.[18] The observed improvement in fine motor skill was not observed in healthy young adults, suggesting that exposure to levodopa can improve fine motor performance in healthy OAs.[18] The dosage used to improve fine motor skill was selected based on the minimum levodopa dose to induce cognitive change in the subjects.[18] However, more recent studies established that a single, 100mg dose of levodopa induced cognitive deficits in young and older adults.[19, 20] The difference in effects of brief levodopa exposure on cognitive versus motor performance could be related to the different dopaminergic pathways involved in cognition and mobility. While the nigrostriatal pathway (substantia nigra to striatum) plays a role in motor function, the mesolimbic/cortical dopaminergic pathway (ventral tegmental area to amygdala/hippocampal and frontal cortex) likely plays a role in cognition. Additional research is needed to determine why a single dose of levodopa appears to differentially affect the two dopaminergic pathways.

Contrary to the PD-SAI literature,[9] there appears to be no effect of levodopa on SAI in OAs without PD. The nigrostriatal dopaminergic pathway in OAs is largely intact and therefore may be unaffected by a single or multiple doses of levodopa. Deficiency in the dopaminergic nigrostriatal pathway is related to the motor impairments in people with PD. The motor changes observed from the OFF- to ON-levodopa in PD is attributed to the conversion of levodopa to dopamine. The increased dopaminergic activity could positively and negatively affect compensatory mechanisms adopted for sensorimotor inhibition deficiencies in people with PD. A possible compensatory mechanism for nigrostriatal dopamine deficiency in people with PD proposes an upregulation of cholinergic activity,[2] which may partially explain why a single dose of cholinergic drugs can improve SAI.[6] However, this effect of cholinergic drugs on SAI is

complicated since prolonged exposure (six weeks) to an acetylcholinesterase inhibitor results in no change in SAI in people with PD.[21]

To date, only gait characteristics in the pace domain significantly related to sensorimotor inhibition in OAs.(Martini and others 2021; Pelosin and others 2016) Specifically, gait speed and stride length were slower and shorter, respectively, with worse SAI.[13] The results herein expand on these findings with the observations that SAI was significantly related to spatiotemporal gait characteristics and postural sway characteristics, both in the OFF- and ON-levodopa states in healthy OAs. While no gait pace domain variable significantly related to SAI in this OA cohort, dynamic (gait) and quasi-static (quiet standing) stability variables were significantly related to SAI, such that worse SAI related to worse stability during gait and standing balance. The different relationships between mobility and SAI from OFF- to ON-levodopa states of the OAs herein could portend different relationships between SAI and mobility in the OFF-levodopa state for people with PD. To date, the relationships between SAI and mobility in people with PD are reported in the ON-levodopa state, limiting the ability to differentiate the effects of disease and drug on the relationships between SAI and mobility in people with PD. The identification of these different relationships could explain some of the heterogeneity in gait and balance responsiveness to levodopa in PD.

Limitations to this study include the small sample size and the dosing of levodopa. A single, 100/25 mg dose of levodopa/carbidopa may not have been strong enough to induce neurophysiological changes in some OAs without a known nigrostriatal dopaminergic deficit. However, this design was previously used with success in establishing changes in cognitive performance in both young and older adult populations.[19, 20] Another limitation is the limited characterization of cognition. A comprehensive cognitive assessment could determine if levodopa has similar effects on cognition as shown previously. The lack of a placebo might limit

the interpretation of the relationship between SAI and gait OFF- and ON-levodopa. Additionally, there were no females in this study, limiting the generalizability of these findings. Finally, using neuronavigation for the TMS procedure could reduce MEP variability, resulting in greater consistency between TMS sessions (OFF- and ON- levodopa).[22]

5. Conclusion

A single dose of levodopa does not appear to affect cortical sensorimotor inhibition or mobility in OAs. However, sensorimotor cortical inhibition is related to balance and gait performance in OAs, and these relationships appear to be affected by levodopa. Combined with the established effects of levodopa on mobility and SAI in people with PD, our preliminary results suggest that an underlying cortical restructuring due to the loss of dopamine activity and levodopa, a disease-drug interaction, is responsible for the heterogeneous effects of levodopa in PD. Future investigations that implement a double-blind, crossover design with a placebo, in a larger population of OAs and young adults is the clear next step to explain the heterogeneity of balance and gait performance in OAs and the heterogeneous effect levodopa has on gait and balance in PD.

Financial Disclosures: OHSU and Dr Horak have a significant financial interest in APDM Wearable Technologies, a Clario company, that may have a commercial interest in the results of this research and technology. This potential conflict has been reviewed and managed by OHSU. No other author has a financial disclosure to claim.

Funding: This work was supported by the National Institutes of Neurological Disorders and Stroke (P50 NS062684), the U.S. Department of Veterans Affairs (101 CX001702), and the Medical Research Foundation of Oregon (ANEUR0967).

Acknowledgements: This publication was possible due to the work and effort of each listed co-author. DNM, FBH, and JGN conceptualized and received funding; DNM, RM and GH contributed to recruitment and data collection; DNM and GH contributed to data processing and analyses; Each author contributed to interpretation; DNM wrote the initial draft, RM, VEK, JGN and FBH contributed to editing and review.

References

Bohnen, N.I.; Kanel, P.; Müller, M.L. Molecular imaging of the cholinergic system in Parkinson's disease. International review of neurobiology. 141:211-250; 2018

Cohen, J. Statistical power analysis for the behavioral sciences (rev: Lawrence Erlbaum Associates, Inc; 1977

Curtze, C.; Nutt, J.G.; Carlson-Kuhta, P.; Mancini, M.; Horak, F.B. Levodopa Is a Double-Edged Sword for Balance and Gait in People With Parkinson's Disease. Mov Disord. 30:1361-1370; 2015

Di Lazzaro, V.; Oliviero, A.; Profice, P.; Pennisi, M.; Di Giovanni, S.; Zito, G.; Tonali, P.; Rothwell, J. Muscarinic receptor blockade has differential effects on the excitability of intracortical circuits in the human motor cortex. Experimental brain research. 135:455-461; 2000

Di Lazzaro, V.; Oliviero, A.; Saturno, E.; Dileone, M.; Pilato, F.; Nardone, R.; Ranieri, F.; Musumeci, G.; Fiorilla, T.; Tonali, P. Effects of lorazepam on short latency afferent inhibition and short latency intracortical inhibition in humans. J Physiol. 564:661-668; 2005

Di Lazzaro, V.; Oliviero, A.; Tonali, P.A.; Marra, C.; Daniele, A.; Profice, P.; Saturno, E.; Pilato, F.; Masullo, C.; Rothwell, J.C. Noninvasive in vivo assessment of cholinergic cortical circuits in AD using transcranial magnetic stimulation. Neurology. 59:392-397; 2002

Diedenhofen, B.; Musch, J. cocor: A comprehensive solution for the statistical comparison of correlations. PloS one. 10:e0121945; 2015

Floel, A.; Vomhof, P.; Lorenzen, A.; Roesser, N.; Breitenstein, C.; Knecht, S. Levodopa improves skilled hand functions in the elderly. European Journal of Neuroscience. 27:1301-1307; 2008

Julkunen, P.; Säisänen, L.; Danner, N.; Niskanen, E.; Hukkanen, T.; Mervaala, E.; Könönen, M. Comparison of navigated and non-navigated transcranial magnetic stimulation for motor cortex mapping, motor threshold and motor evoked potentials. Neuroimage. 44:790-795; 2009

Linssen, A.; Sambeth, A.; Vuurman, E.; Riedel, W. Cognitive effects of methylphenidate and levodopa in healthy volunteers. European Neuropsychopharmacology. 24:200-206; 2014

Luo, Y.; Roth, G.S. The roles of dopamine oxidative stress and dopamine receptor signaling in aging and age-related neurodegeneration. Antioxidants and Redox Signaling. 2:449-460; 2000

Mancini, M.; Chung, K.; Zajack, A.; Martini, D.N.; Ramsey, K.; Lapidus, J.; Horak, F.B.; Nutt, J.G. Effects of augmenting cholinergic neurotransmission on balance in Parkinson's disease. Parkinsonism & related disorders. 69:40-47; 2019

Mancini, M.; King, L.; Salarian, A.; Holmstrom, L.; McNames, J.; Horak, F.B. Mobility Lab to Assess Balance and Gait with Synchronized Body-worn Sensors. J Bioeng Biomed Sci. Suppl 1:007; 2011

Martini, D.N.; Morris, R.; Kelly, V.E.; Hiller, A.; Chung, K.A.; Hu, S.-C.; Zabetian, C.P.; Oakley, J.; Poston, K.; Mata, I.F. Sensorimotor Inhibition and Mobility in Genetic Subgroups of Parkinson's Disease. Frontiers in Neurology. 11:893; 2020

Martini, D.N.; Morris, R.; Madhyastha, T.M.; Grabowski, T.J.; Oakley, J.; Hu, S.-C.; Zabetian, C.P.; Edwards, K.L.; Hiller, A.; Chung, K. Relationship between Sensorimotor Inhibition and Mobility in Older Adults with and without Parkinson’s Disease. The Journals of Gerontology: Series A. 76:630-637; 2021

Meng, X.-L.; Rosenthal, R.; Rubin, D.B. Comparing correlated correlation coefficients. Psychological bulletin. 111:172; 1992

Obi, K.; Amano, I.; Takatsuru, Y. Role of dopamine on functional recovery in the contralateral hemisphere after focal stroke in the somatosensory cortex. Brain research. 1678:146-152; 2018

Pelosin, E.; Ogliastro, C.; Lagravinese, G.; Bonassi, G.; Mirelman, A.; Hausdorff, J.M.; Abbruzzese, G.; Avanzino, L. Attentional Control of Gait and Falls: Is Cholinergic Dysfunction a Common Substrate in the Elderly and Parkinson's Disease? Front Aging Neurosci. 8:104; 2016

Rochester, L.; Yarnall, A.J.; Baker, M.R.; David, R.V.; Lord, S.; Galna, B.; Burn, D.J. Cholinergic dysfunction contributes to gait disturbance in early Parkinson's disease. Brain. 135:2779-2788; 2012

Sailer, A.; Molnar, G.F.; Paradiso, G.; Gunraj, C.A.; Lang, A.E.; Chen, R. Short and long latency afferent inhibition in Parkinson's disease. Brain. 126:1883-1894; 2003

Vo, A.; Seergobin, K.N.; MacDonald, P.A. Independent effects of age and levodopa on reversal learning in healthy volunteers. Neurobiology of aging. 69:129-139; 2018

Wilson, J.; Alcock, L.; Yarnall, A.J.; Lord, S.; Lawson, R.A.; Morris, R.; Taylor, J.-P.; Burn, D.J.; Rochester, L.; Galna, B. Gait progression over 6 years in Parkinson’s disease: Effects of age, medication, and pathology. Frontiers in aging neuroscience. 12; 2020

Figure Legends

Figure 1: Levodopa Effects on SAI. Box and scatter plot of SAI during OFF and ON levodopa states. Grey dashed lines indicate the direction of change in SAI for individual. Black dashed line indicates group mean.

Figure 2: Top Row: Scatter plots highlighting the Pearson correlations between SAI and gait during the OFF (blue) and ON (red) levodopa states. Bottom Row: Scatter plots highlighting the Pearson correlations between SAI and standing posture during the OFF (blue) and ON (red) levodopa states. Sway data presented as natural log transformed data. Solid gray line represents the best fit line.

Table 1: Mobility

		OFF	ON	Cohen's *d*
Gait	Double Support (%)	19.1(2.6)	19.1(2.7)	0.03
	Stride Time (s)	1.1(0.1)	1.1(0.1)	0.34
	Gait Speed (m/s)	1.2(0.1)	1.2(0.1)	-0.12
	Stride Length (m)	1.3(0.1)	1.3(0.1)	0.09
	Arm Swing (d)	48.6(9.0)	45.8(10.1)	0.50
	Turn Velocity (d/s)	184.8(33.6)	179.2(31.0)	0.22
Postural Sway	Jerk	-2.3(0.8)	-2.2(0.7)	-0.11
	RMS	-2.6(0.5)	-2.6(0.4)	-0.01
	Velocity	-1.4(0.6)	-1.4(0.7)	-0.002
	Sway Area	-6.0(0.8)	-5.9(0.8)	-0.19

Mean(standard deviation). Postural sway variables are natural log transformed.

Figure 1

Click here to access/download;Figure;Figure1.tif

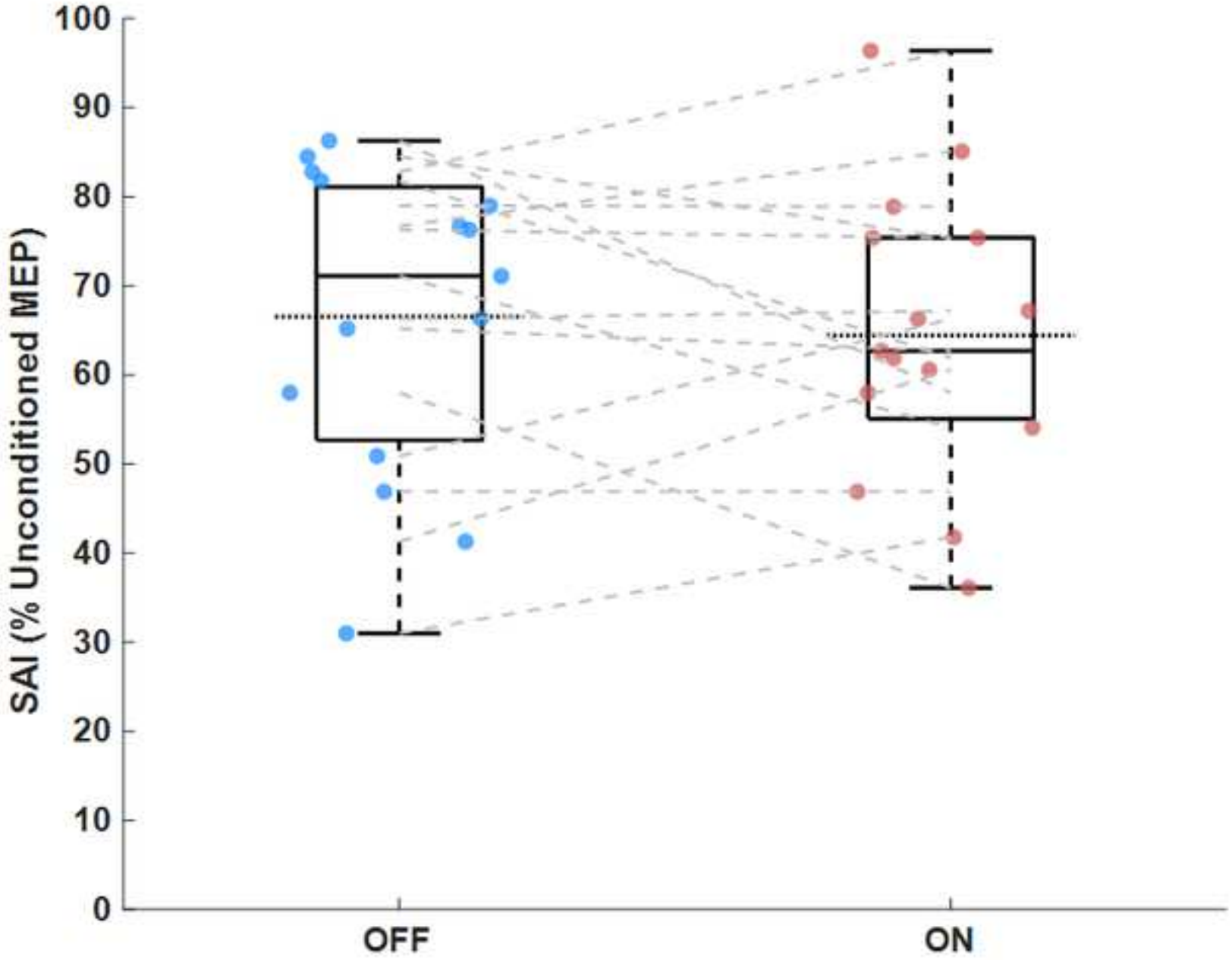

Figure 2