The Effects of Caffeine versus Placebo on Motor Performance in Parkinson's Disease

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Abstract

Parkinson's disease (PD) is a neurodegenerative disease caused by the loss of dopaminergic neurons in the substantia nigra. The disease is characterized by a decline in motor quality such as speed of movements, slowness and stiffness of movement, postural instability, and increased risk of falling. Though there is currently no cure, the current standard of treatment for PD is symptom management with a medication called levodopa, which works by supplementing dopamine in the brain. This medication, while helpful, can have significant side effects and lose its efficacy over time. To improve the management of PD and maximize the potential of levodopa, researchers have been investigating additional therapies. Caffeine, which is known to have many neuroprotective effects, is one such therapy. Caffeine acts as an antagonist of the adenosine A_{2A} receptor, which helps modulate the amount of dopamine in the substantia nigra. This modulatory effect may be used to improve motor performance at peak dose of levodopa therapy. The purpose of this study is to investigate the acute effects of caffeine on motor performance in PD. This is done through a series of tests, such as handwriting and the Purdue Pegboard test, before and after the ingestion of the pill containing caffeine or a placebo. The effects of such an inexpensive and accessible therapy have the potential to drastically improve the well-being of patients with PD.

Introduction

Parkinson's Disease (PD) is one of the most common neurodegenerative diseases affecting 1% of the population greater than 60 years. PD is characterized by a loss of dopaminergic neurons in the substantia nigra of the basal ganglia, resulting in a loss of dopamine. Dopamine deficiency produces motor symptoms, specifically tremors, bradykinesia (or slowness of movement), and instability. Many clinical trials are active, but currently, no cure for PD exists. The leading therapy for PD is dopamine replacement therapy with levodopa. This medication helps to reduce the symptom burden, but it can have significant side effects (e.g. dyskinesia) and it becomes increasingly ineffective over time. To improve the efficacy and longevity of Levodopa therapy, researchers are investigating additional supplements and medications.

Literature has consistently demonstrated that caffeine has many neuroprotective effects, particularly due to its activity as an antagonist of the adenosine A_{2A} receptor. The inhibition of A_{2A} receptors by caffeine could have downregulatory effects on the disease process, slowing the progression of PD and potentially providing an acute improvement in motor performance, particularly when combined with dopamine replacement therapy. Though there have been studies investigating the short-term therapeutic potential of caffeine in PD, to date there have not been sufficient trials investigating the acute effects of caffeine. This study seeks to investigate the motor effects of caffeine within 30-60 minutes of consumption on PD patients at peak dose levodopa therapy. The accessibility of caffeine as an adjuvant therapy for PD could have significant, positive impacts on the quality of life of PD patients.

Figure 1:
Purdue Pegboard, used to assess fine motor skills.
Left hand, right hand, and bimanual performance assessed individually.

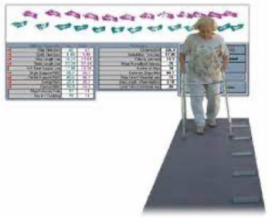
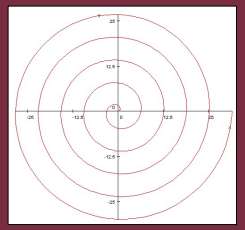


Figure 2:
GAITRight platform, used to analyze gait and assess falls risk (FAP score).



The quick brown fox jumped over the lazy dog.

Figure 3: Sentence for handwriting sample.
Figure 4: Archimedes Spiral example drawing.

Sample Schedule

00:00 - 00:05: Blood Pressure, Heart Rate
00:05 - 00:25: UPDRS parts 2 and 3
00:25 - 00:30: GAITRite: 2 baseline walks
00:30 - 00:35: GAITRite: 2 cognitive load (alphanumeric sequencing) walks
00:35 - 00:40: Freiburg CSVA computer test
00:40 - 01:05: Fine and gross motor performance (Purdue Pegboard, handwriting test, spiral)
01:05 - 01:35: Consume Caffeine or Placebo (3mg/kg) based on a randomly created algorithm
01:35 - 01:40 Blood Pressure, Pulse
01:40 - 01:50: UPDRS part 3
01:50 - 01:55: GAITRite: 2 baseline walks
01:55 - 02:00: GAITRite: 2 cognitive load (alphanumeric sequencing) walks
02:00 - 02:05: Freiburg CSVA computer test
02:05 - 02:30: Fine and gross motor performance (Purdue Pegboard, handwriting test, spiral)

References

Sample Dataset B Day

	B Day					
	Pre			Post		
HR (BPM)	65			60		
BP (mmHg)	121/65			141/74		
FAP w/o load 1	91			92		
FAP w/o load 2	93			92		
FAP w/ load 1	62			55		
FAP w/ load 2	53			64		
UPDRS P 3	Avg	Invest 1	Invest 2	Avg	Invest 1	Invest 2
Total	32	32	32	29.5	30	29
Speech	1	1	1	1.5	1	2
Facial Expression	2	2	2	2	2	2
Rigidity - Neck	0	0	0	0	0	0
Rigidy - RUE	1	1	1	1	1	1
Rigidity - LUE	1	1	1	0.5	1	0
Rigidity - RLE	1	1	1	1	1	1
Rigidity - LLE	1	1	1	1	0	2
Finger Tap R	3	3	3	3	3	3
Finger Tap L	3	3	3	3	3	3
Hand Movement R	2	2	2	2	2	2
Hand Movement L	2	2	2	2	2	2
Pronation-Supination R	1	1	1	2	2	2
Pronation-Supination L	1	1	1	1	1	1
Toe Tap R	3	3	3	3	3	3
Toe Tap L	3	3	3	2.5	3	2
Leg Agility R	1	1	1	1.5	1	2
Leg Agility L	1	1	1	1	1	1
Arising from Chair	1	1	1	0.5	1	0
Gait	1	1	1	0.5	1	0
Freezing of Gait	0	0	0	0	0	0
Postural Stability	0	0	0	0	0	0
Posture	1	1	1	0	0	0
Body Bradykinesia	0	0	0	0	0	0
Postural Tremor Hand R	0	0	0	0	0	0
Postural Tremor Hand L	1	1	1	0.5	1	0
Kinetic Tremor Hand R	0	0	0	0	0	0
Kinetic Tremor Hand L	0	0	0	0	0	0
Rest Tremor Amplitude RUE	0	0	0	0	0	0
Rest Tremor Amplitude LUE	0	0	0	0	0	0
Rest Tremor Amplitude RLE	0	0	0	0	0	0
Rest Tremor Amplitude LLE	0	0	0	0	0	0
Rest Tremor Amplitude Lip/Jaw	0	0	0	0	0	0
Constancy of Resting Tremor	1.	1.	1.	0	0	0
Pegboard R	7			7		
Pegboard L	6			8		
Handwriting avg change in letter height						
Spiral avg space						
Spiral # Rings						
Spiral # overlaps						
Visual Acuity Assessment LogMAR	-0.3			-0.3		
Visual Acuity Assessment decVA	2.0			2.0		
Contrast Sensitivity	1.75			1.76		
Contrast Sensitivity logCs(Weber)	1.79%			1.76%		

Methodology

This study is a double-blinded crossover study using randomized placebo intervention to assess the effect of caffeine on motor performance. Subjects will include individuals on dopamine replacement therapy for Parkinsonism stages 1-4 on the Hoehn and Yahr scale.

This study will take place over two separate evaluation days. Subjects will be evaluated each day at peak dose both before and 30 min after the administration of caffeine or placebo for comparison to baseline.

Gross motor function and falls risk will be assessed using the GAITRite platform. There will be two baseline walks and two walks with cognitive load (alphanumeric sequencing).

Fine motor performance will be assessed using the Purdue Pegboard (pictured Figure 1), a handwriting assessment for micrographia, drawing of Archimedes Spiral in 10 seconds, and UPDRS part 3 measurements. Contrast sensitivity and visual acuity will also be assessed via the Freiburg Test.

Preliminary Results

Our data is currently under preliminary analysis by a statistician. We will also be paying particular attention to the effects of caffeine on patients' tremors and whether it improves, worsens, or has no effect at all. We expect these results to be available for discussion and further implications of research in the near future.

Future Direction of Research

The future of this particular study includes finalizing data analysis and determining whether or not caffeine has acute effects on motor performance in patients with PD. In the future, the study should be improved by working with a larger population of patients, and the inclusion of additional fine motor assessments and more objective tremor assessments. A larger study could allow for stratification of results based on medication dosages and the average amount of caffeine each patient consumes daily. Additional studies could also investigate the efficacy of other methods of caffeine delivery that avoid the gastrointestinal tract, such as caffeine patches and increase variation of the time the data is collected.

Generally, results will address a hole in the literature regarding the acute effects of caffeine on motor performance. This could have significant quality-of-life implications for patients, as caffeine is both accessible and affordable. If caffeine can be used in acute settings to improve peak motor performance on levodopa, it could delay the need for patients to add adjuvant medications or increase levodopa dose, reducing the risk of developing side effects or medication tolerance.

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