Open Access

Original Article

Parkinson's Disease

Efficacy of L-dopa in Treatment of Aggression, Frontal Lobe Cognitive Functioning and Task Switching Deficits in Parkinson's Disease Patients

Amara Gul, Javed Yousaf

Islamia University of Bahawalpur, Bahawalpur Pakistan

ABSTRACT

Objectives: To assess efficacy of L-dopa treatment on aggression, frontal lobe and task switching deficits in patients with Parkinson's disease (PD).

Study Design: Prospective comparative study.

Place and Duration of Study: Bahawal Victoria Hospital and Civil Hospital Bahawalpur, Pakistan, from Apr 2016 to Oct 2017.

Methodology: Seventy-five healthy individuals and seventy-five PD patients participated in the study. This study was completed in two testing sessions. Healthy participants had single testing session whereas patients were tested twice (pre and post L-dopa treatment). Participants completed Frontal Assessment Battery, part B TMT, and Buss-Perry Aggression Questionnaire.

Results: PD patients (6.13 ± 0.81) showed deficient frontal lobe functioning F (1,48)=14489.66, p<0.001, $\eta p2$=0.99 than healthy individuals (17.93 ± 0.25). Patients (283.05 ± 6.02) had inferior task switching abilities F (1, 48) = 65397.85, p<0.001, $\eta p2$=0.99 than healthy individuals (78.37 ± 3.43). The level of aggression was higher F (1,48)=2369.24, p<0.001, $\eta p2$=0.94 in patients (131.12 ± 12.57) compared with healthy individuals (43.33 ± 9.26). Post L-dopa treatment testing session showed significant improvement in frontal lobe functioning (6.13 ± 0.81 vs. 13.46 ± 1.45), task switching abilities (216.80 ± 13.74 vs. 283.05 ± 6.02) in patients. In addition, aggression was reduced in patients (106.06 ± 1.07 vs. 131.12 ± 12.57).

Conclusion: L-dopa was found beneficial to reduce aggression, frontal lobe cognitive and task switching deficits in patients with PD.

Keywords: Aggression, Cognition, Frontal lobe, Levodopa, Parkinson's disease, Task switching.

How to Cite This Article: *Gul A, Yousaf J. Efficacy of L-dopa in Treatment of Aggression, Frontal Lobe Cognitive Functioning and Task Switching Deficits in Parkinson's Disease Patients. Pak Armed Forces Med J 2022; 72(Suppl-2): S132-135 DOI: https://10.51253/pafmj.v72iSUPPL-2.3354*

INTRODUCTION

Parkinson's Disease (PD) is characterized byselective loss of dopaminergic neurons and abnormalities in functional interaction of cortico striatal network.[1] Cognitive decline has been identified as a significant marker of disease progression in patients with PD.[2] Levodopa (L-dopa),[1,3,4] dihydroxy phenylalanine, is a building block which is converted into dopamine by human body. L-dopa can cross blood brain barrier and replaces dopamine being its precursor. Among medical therapies, L-dopa is the most effective treatment to manage symptoms of PD,[3,4] including frontal cortical and subcortical functioning of the brain.[5,6]

The rationale of thisstudy was to compare aggression, frontal lobe and task switching performance between PD patients and healthy individuals. Moreover, to assess the effect of L-dopa treatment on aggression, frontal lobe and task switching performance in patients with PD. It was hypothesized that patients with PD would show frontal lobe cognitive functioning and task swit-ching deficits in contrast with healthy individuals. Fur-ther, patients with PD would show higher aggression compared with healthy individuals. Given that the neuronal network modulating these parameters over-lap, it was hypothesized that L-dopa treatment would be beneficial in reducing aggression, frontal lobe cogni-tive functioning and task switching deficits in patients with PD.

METHODOLOGY

This study had a prospective comparative design conducted at Bahawal Victoria Hospital and Civil Hospital Bahawalpur, Pakistan, from April 2016 to October 2017 and was approved by board of studies of The Islamia University of Bahawalpur, Pakistan. The sample size was calculated with anticipated effect size=0.5, desired statistical power=0.8, probability level=0.05 resulted in minimum sample size per group=64. Purposive sampling technique was used. Seventy-five patients diagnosed with idiopathic PD and Seventy five healthy individuals from local community took part in the study.

Correspondence: Dr Amara Gul, Dept of Applied Psychology, Islamia University of Bahawalpur, Bahawalpur-Pakistan

Received: 15 Oct 2019; revision received: 22 Feb 2020; accepted: 24 Feb 2020

Inclusion Criteria: PD patients of age range 20-40 years with disease duration of 7-13 years and having daily L-dopa dose 400-480 mg.The inclusion criteria for healthy individuals was,age range 20-40 years, not having any physical/mental illness.

Exclusion Criteria: Participants were excluded if they have other than the mentioned parameters in inclusion criteria.

Informed consent was obtained from all the participants. Seventy-five PD patients were included from mentioned hospitals and seventy-five healthy individuals were included in the study from local community through advertisement.Participants were screened for dementia through Mini Mental Status Examination (cut off score ≤23).[6] Healthy individuals had a single testing session whereas patients had two testing sessions. One as a baseline (pre-treatment) and second testing session was conducted post 3 months of L-dopa therapy. Participants were administered Buss-Perry Aggression Questionnaire, Frontal assessment battery and Trail Making test part B.

Buss-Perry Aggression twenty-nine statement Questionnaire,[7,8] was used to assess aggression. Frontal lobe cognitive functioning was assessed through Frontal assessment battery.[8] Part B of the Trail Making Test was used to measure task switching ability. Task switching deficit is the time greater than 273 seconds whereas on average it takes approx. 75 seconds to perform part B.[9,10] The statistical analysis was conducted through SPSS-20. Mean ± SD were calculated for quantitative variables. Frequency and percentages were calculated for qualitative variables. T-test was calculated for comparison of groups. The *p*-value ≤0.05 considered significant.

RESULTS

Data of seventy-five (50%) PD patients and seventy five (50%) healthy individuals was assessed. Mean age of PD patients was 30.36 ± 6.98 yearsand healthy individuals was 32.74 ± 6.21 yearsand gender (male: female ratio was 50% in each group) (Table-I).

Mean scores of patients (6.13 ± 0.81) were lower than healthy individuals (17.93 ± 0.25) on Frontal Assessment Battery t(74)=115.42, $p<0.001$. Patients (283.05 ± 6.02) took greater time to perform part B TMT than healthy individuals (78.37 ± 3.43), t(74)=222.31, $p<0.001$. Patients (131.12 ± 12.57) showed higher aggression than healthy individuals (43.33 ± 9.26) on Buss-Perry Aggression Questionnaire t(74)=50.42, $p<0.001$ (Table-II).

Table-I: Demographic and Clinical Characteristicsof Patients and Healthy Individuals.

	Patients	Healthy Controls	*p*-value
	Mean ± SD	Mean ± SD	
Age (20-40 Years)	30.36 ± 6.98	32.74 ± 6.21	0.032
Male/Female (n)	35 (50%)	35 (50%)	
Disease duration (7-13 Years)	9.56 ± 1.58		
Daily L-Dopa dose (400-480 mg)	437.86 ± 22.09		

Table-II: Scores of patients (n=75) and healthy individuals (n=75) on FAB, Part-B-TMT and BPAQ.

	Patients	Healthy Controls	*p*-value
	Mean ± SD	Mean ± SD	
FAB	6.13 ± 0.81	17.93 ± 0.25	t (74)=115.42, $p<0.001$
Part-BTMT	283.05 ± 6.02	78.37 ± 3.43	t (74)= 222.31, $p<0.001$
BPAQ	131.12 ± 12.57	43.33 ± 9.26	t (74)=50.42, $p<0.001$

Read FAB as Frontal Assessment Battery; Part-B-TMT as Part B Trail Making Test; BPAQ as Buss-Perry Aggression Questionnaire

Differences between pre L-dopa treatment (6.13 ± 0.81) and post L-dopa treatment (13.46 ± 1.45) showed significant improvement in performance of patients on Frontal Assessment Battery t(74)=39.35, $p<0.001$. Patients took lesser time (216.80 ± 13.74) to perform part B TMT post L-dopa treatment than pre-treatment performance time (283.05 ± 6.02), t(74)=35.75, $p<0.001$.

L-dopa treatment showed significant reduction in aggression of patients (106.06 ± 1.07)compared with pretreatment self-reported aggression (131.12 ± 12.57), t(74)=15.11, $p<0.001$ (Table-III).

Table-III: L-Dopa Pre and Post-treatment Scores of Patients (n=75) on FAB, Part-B-TMT and BPAQ.

	Pre-Treatment	Post-Treatment	*p*-value
	Mean ± SD	Mean ± SD	
FAB	6.13 ± 0.81	13.46 ± 1.45	t (74)=39.35, $p<0.001$
Part-BTMT	283.05 ± 6.02	216.80 ± 13.74	t (74)=35.75, $p<0.001$
BPAQ	131.12 ± 12.57	106.06 ± 1.07	t (74)= 15.11, $p<0.001$

Read FAB as Frontal Assessment Battery; Part-B-TMT as Part B Trail Making Test; BPAQ as Buss-Perry Aggression Questionnaire.

DISCUSSION

Main result of the study showed that PD patients had frontal lobe cognitive functioning and task switching deficits in contrast these deficits were not observed among healthy individuals. PD patients

reported greater level of aggression than healthy individuals. These results were consistent with previous studies which showed that cognitive functioning deficits prevail in patients with PD2 associated with dopamine deficiency in brain.[11,12,13]

Second importantresult of this study showed that frontal lobe cognitive functioning and task switching ability of PD patients showed improvement in post L-dopa therapy. Alongside, aggression of PD patients was reduced post L-dopa therapy. L-dopa treatment was also found beneficial for personality disorders and higher order cognitive deficits,[14,15] associated with functional abnormality of the brain which is normalized due to L-dopa intake. For instance, the gap in functional connectedness between cortico-striatal pathway gets normalized.[16] These results can be implicated in clinical practice for better patient care.

This study was conducted to assess two main objectives. First objective was to compare whether any differences exist between PD patients and healthy individuals on task switching, frontal lobe cognitive functioning and aggressive impulses. The second objecttive was to examine effectiveness of the L-dopa therapy for frontal lobe cognitive deficits, aggression and task switching deficiencies in patients with idiopathic PD. It was hypothesized that PD patients would show weaker frontal lobe cognitive functioning and task switching abilities than healthy individuals. On contrary, higher aggression would be reported by the patients than healthy individuals. Our results showed that PD patients had frontal lobe cognitive functioning and task switching deficits in contrast these deficits were not observed among healthy individuals. PD patients reported greater level of aggression than healthy individuals. These results were consistent with previous studies which showed that cognitive functioning deficits prevail in patients with PD. These deficits were prominent in almost all areas of higher order cognition such as executive functions, memory, attention, etc.[16] It was also observed that PD patients were deficient in their skills of set-shifting,[17] which is an essential ability required to switch between tasks. These deficits have been linked with dopamine deficiency in brain.[18]

The second hypothesis of this study was confirmed with the result that frontal lobe cognitive functioning and task switching ability of PD patients showed improvement in post L-dopa therapy. Apart from this, aggression of PD patients was reduced post L-dopa therapy. These results are consistent with studies showing improvement in cognition, quality of life and fatigue severity of PD patients with L-dopa medication.[18] L-dopa treatment was also found beneficial for disturbances in personality and higher order cognitive deficits. These changes are associated with functional abnormality of the brain which is normalized due to L-dopa intake. For instance the gap in functional connectedness between corticostriatal path way gets normalized. These results can be implycated in clinical practice for better patient care.

CONCLUSION

Three months of L-dopa therapy can improve frontal lobe cognitive and task switching performance and reduce aggression in patients with PD.

ACKNOWLEDGEMENTS

We were grateful to participants of the study and hospital staff of the Bahawal Victoria hospital and civil hospital Bahawalpur Pakistan who assisted in data collection.

LIMITATION OF STUDY

The sample of this study was small which effected generalizability of results. Thus, future studies might include larger sample size.

Conflict of Interest: None.

Author's Contribution

AG: Idea conceived, Paper writing, Data collection, Data Analysis, Literature review, JY: Data collection, Literature review.

REFERENCES

1. Zhai S, Tanimura A, Graves SM, Shen W, Surmeier DJ. Striatal synapses, circuits, and Parkinson's disease. Curr Opin Neurobiol 2018; 48(1): 9–16.
2. Roheger M, Kalbe E, Liepelt-Scarfone I. Progression of cognitive decline in Parkinson's disease. J Parkinson's Dis 2018; 8(2): 183–193. doi:10.3233/JPD-181306.
3. Gul A, Yousaf J. L-Dopa response to cortical dysfunctions, health related quality of life and fatigue severity in Idiopathic Parkinson's disease. Pak J Med Sci 2018; 34(4): 1014-1018.
4. Syed NM, Bertoni J, Bhatti DE. Deep brain stimulation for Parkinson's disease in Pakistan: Current status, opportunities and challenges. J Pak Med Assoc 2020; 70(12 A): 2247-2254.
5. Gul A, Yousaf J. Effect of levodopa on frontal-subcortical and posterior cortical functioningin patients with Parkinson's disease. Singapore Med J 2019; 60(8): 414-417. doi: https://-doi.org/10.11622/smedj.2018116
6. Folstein MF, Folstein SE, McHugh PR. "Mini-mental status". A practical method for grading the cognitive state of patients for the clinician. J Psych Res 1975; 12(3): 189–198.doi:10.1016/0022-3956(75)90026-6.
7. Buss AH, Perry MP. The aggression questionnaire. J Pers Soc Psychol 1992; 63(1): 452-459.
8. Dubois B, SlachevskyA, Litvan I, Pillon B.The FAB: a Frontal assessment battery at bedside. Neurol 2000; 55(1): 1621-1626.
9. Reitan RM. Validity of the Trail Making Test as an indicator of organic brain damage. Percept Mot Skills 1958; 8(1): 271-276.

10. Trojano L, Papagno C. Cognitive and behavioral disorders in Parkinson's disease: an update. II: behavioral disorders. Neurol Sci 2018; 39(1): 53-61. doi: 10.1007/s10072-017-3155-7.
11. Skibsted AP, Cunha-Bang SD, Carre' JM, Hansen AE, Beliveau V, Knudsen GM . Aggression-related brain function assessed with the Point Subtraction Aggression Paradigm in fMRI. Aggress Behav. 2017; 43(6): 601-610. doi: 10.1002/ab.21718.
12. Lawrence AD, Goerendt IK, Brooks DJ. Impaired recognition of facial expressions of anger in Parkinson's disease patients acutely withdrawn from dopamine replacement therapy. Neurol 2007; 45(1): 65-74.
13. Ricciardi L, Visco-Comandini F, Erro R, Morgante F, Bologna M.Facial emotion recognition and expression in Parkinson's disease: An emotional mirror mechanism? PLoS One 2017; 12(1): e0169110.
14. Mäkinen E, Joutsa J, Jaakkola E, Noponen, T, Johansson, J, Pitkonen M, et al. Individual parkinsonian motor signs and striatal dopamine transporter deficiency: A study with [I-123]FP-CIT SPECT. J Neurol 2019; 266(4): 826–834.
15. Delaveau P, Salgado-Pineda P, Witjas T, Micallef-Roll J, Fakra E, Azulay JP, Blin O. Dopaminergic modulation of amygdala activity during emotion recognition in patients with Parkinson disease. J Clin Psychopharmacol 2009; 29(6): 548-554.
16. Martinez-Fernandez R, Kibleur A, Chabardes S, Fraix V, Castrioto A, Lhommee E. Different effects of levodopa and subthalamic stimulation on emotional conflict in Parkinson's disease. Hum Brain Mapp 2018; 39(12): 5014-5027.
17. Fleury V, Cousin E, Czernecki V, Schmitt E, Lhommée E, Poncet A. Dopaminergic modulation of emotional conflict in Parkinson's disease. Front. Aging Neurosci 2014; 6(1): 164.
18. Gul A, Yousaf J. Effect of Levodopa on frontal-subcortical and posterior cortical functioning in patients with Parkinson's Disease. Singapore Med J 2019; 60(8): 1-4. doi: 10.11622/ smedj. 2018116.