Anxiety, depression, and quality of life in Parkinson’s disease: the implications of multidisciplinary treatment

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multidisciplinary rehabilitation treatment, is also generally recommended because it is able to treat both the motor and non-motor aspects of PD.

Neurorehabilitative training is an important approach to improve functional status in PD, in particular, multidisciplinary care program showed positive effect on motor and non-motor symptoms (Dockx et al., 2016; Biundo et al., 2017; Kaseda et al., 2017). In this study, we investigated changes in anxiety and depressive symptoms and quality of life in PD patients under multidisciplinary rehabilitative training.

Subjects and Methods

Subjects

One hundred PD patients hospitalized at our neurorehabilitative unit were admitted to 60 days hospitalization rehabilitative program; the recruitment time was between January 2017 and December 2018.

All subjects signed informed consent in accordance with the Declaration of Helsinki. The study was approved by Istituito di Ricovero e Cura a Carattere Scientifico (IRCCS) Centro Neurolesi “Bonino-Pulejo” Ethical Committee (approval No. 6/2016) in June 2016.

Inclusion criteria were: diagnosis of idiopathic PD according to the UK Brain Bank criteria (Lyons and Pahwa, 2011), Hoehn and Yahr stages (Hoehn and Yahr, 1996) 2–3 and stable pharmacological treatment (dopaminergic therapy: dopamine agonists and Levo-dopa both) in the last 6 weeks. Exclusion criteria were: atypical Parkinsonisms, PD with dementia according to Diagnostic and Statistical Manual of Mental Disorders (DSM-IV) criteria (American Psychiatric Association, 2013); other neurological or psychiatric disorders.

The mean age of included patients was 64.66 ± 6.85 years, the mean time of education was 10.33 ± 4.45 years, and the mean disease duration was 7.57 ± 3.46 years. The assessments were performed at the date of admission (T0 baseline visit) and 60 days later (T1).

Anxiety, depression and quality of life evaluations

Motor conditions of PD patients were evaluated by means of unified Parkinson’s disease rating scale-Part III (UPDRS) (Fahn et al., 1987) The Barthel Index rating scale (Hobart and Thompson, 2001) was used to measure performance in activities of daily living and functional independence (ADL). The neuropsychological evaluation was assessed using Addenbrooke’s Cognitive Examination-Revised (ACE-R) (Mioshi et al., 2006), a brief battery that provides evaluation of six cognitive domains: orientation and attention, memory, verbal fluency, language and visuospatial ability.

Beck Depression Inventory (BDI-II) and Hamilton Anxiety Rating Scale (HAM-A) (Hamilton, 1959) were used for evaluation of depressive and anxiety symptoms, respectively. Quality of life was evaluated by means of Parkinson’s Disease Quality of Life Questionnaire (PDQ-39) (Jenkinson et al., 1997). Speech language was assessed using the Clinical Bedside Swallowing examinations (Carnaby-Mann and Lenius, 2008) for dysphagia and Robertson dysarthria profile, clinical–perceptual methods exploring all components potentially involved in speech difficulties.

Rehabilitative program

Rehabilitative program included motor, cognitive, and speech language training. Motor training was based on task-oriented exercises; balance exercises and gait training have been carried out as they improve mobility. The cognitive training included specific exercises, paper-and-pencil or computerized tasks oriented to attention/working memory, psychomotor speed, executive functions, visuo-spatial abilities, and calculation skills. Speech language training included an intensive stimulation of speech intensity, exercises to improve verbal intelligibility, treatment of limitations to swallowing choking and slowness of chewing. Every day rehabilitative program was organized according to a predefined scheme: motor exercises (60 minutes), language exercises (60 minutes), cognitive exercises (60 minutes). The rehabilitation program lasted 8 weeks. Rehabilitation also included psychoeducation intervention once a week (60 minutes) in group setting, focused on information and explanations about the disease and the possible effects on patients’ psychological wellbeing. Four main areas were targeted: disease awareness, adherence to treatment, detection of motor and non-motor symptoms, and lifestyle regularity.

Statistical analysis

The Shapiro normality test was used to verify the distribution of variables. Data that do not follow a normal distribution are presented in median and first-third quartile.

The Mann-Whitney U test was used to compare clinical variables between two time points, while correlations between demographic characteristics and clinical variables were analyzed by Spearman’s coefficient.

For analysis, we used an open source R3.0 software package considering a confidence level of 95%, a 5% alpha error and statistical significance at P < 0.05.

Results

Clinical variables

The Mann-Whitney U test showed significant differences in almost all clinical variables between T0 and T1 (Table 1). No significant difference was found in cognition (P = 0.82), sub-item PDQ-39. Moreover, memory, verbal fluency, and visuospatial abilities, sub-items of ACE-R, remained unchanged between T0 and T1.

Correlations of anxiety, depression and quality of life with clinical features

UPDRS-III scores were significantly positively correlated with education (r = 0.21, P = 0.03) and BDI-II scores were negatively correlated with and disease duration (DD) (r = –0.28, P = 0.004). Significant correlations between Barthel Index and education (r = –0.19, P = 0.06), UPDRS and education (r = 0.18, P = 0.07), HAM-A and DD (r = –0.18, P = 0.07) were found.

Predictors

Results in Table 2 showed the significant impact of BDI-II, HAM-A and UPDRS-III scores on sub-item of PDQ-39. BDI-II and HAM-A were significant predictors of mobility, while UPDRS-III was a significant predictor of communications.

Discussion

Emotional disturbances are frequently observed in PD patients and aggravate their motor symptoms, thereby leading to increased disability, high healthcare costs, and poor quality of life. In some cases, depression and anxiety may precede the diagnosis of PD; however, the under-recognition and side effects of the pharmacological management of...
especially in prosody and vocal articulation. Cognitive improvements in attention and language performance, and gait. After rehabilitative treatment, patients showed improvement were those related to motor function, balance and discharge. Further studies with a larger population and a longer-term follow-up can allow us to confirm these results.

**Conclusion**

Although traditionally considered a pure motor disorder, PD is increasingly recognized as a complex disease process. Anxiety and depression are the most common non-motor symptoms in PD with a potential negative impact on motor disability and quality of life. Multidisciplinary rehabilitative training has potential to improve PD management.

**Author contributions:** Study design: VLB; study implementation: VLB, RP, PB, SM, GDL; data collection and analysis: SDS, MB, AG, RC, VS, FC; manuscript preparation: VLB, RP, LB, FC; approval of final version of this manuscript for publication: all authors.

**Conduct, Reporting, Editing and Publication of Scholarly Work in Medical Journals developed by the International Committee of Medical Journal Editors**

This study followed the Recommendations for the Conduct, Reporting, Editing and Publication of Scholarly Work in Medical Journals developed by the International Committee of Medical Journal Editors.

**Biostatistics statement:** The statistical methods of this study were reviewed by the biostatistician of Istituto di Ricovero e Cura a Carattere Scientifico IRCCS Centro Neurolesi “Bonino-Pulejo” Ethical Committee (approval No. 6/2016) in June 2016.

**Declaration of patient consent:** The authors certify that they have obtained all appropriate patient consent forms. In the forms, the patients have given their consent for their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity.

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References

Abbruzzese G, Marchese R, Avanzino L, Pelosi E (2016) Rehabilitation for Parkinson's disease: current outlook and future challenges. Parkinsonism Relat Disord 22 Suppl 1:560-64.

American Psychiatric Association (2013) Diagnostic and Statistical Manual of Mental Disorders. 5th ed. Washington, DC: APA.

Avanzino L, Lagravinese G, Abbuzzese G, Pelosi E (2018) Relationships between gait and emotion in Parkinson's disease: A narrative review. Gait Posture 65:57-64.

Bhat S, Acharya UR, Hagiwara Y, Dadmehr N, Adeli H (2018) Parkinson's disease: Cause factors, measurable indicators, and early diagnosis. Comput Biol Med 102:234-241.

Biundo R, Weis L, Fiorenzato E, Antonini A (2017) Cognitive rehabilitation in Parkinson's disease: is it feasible? Arch Clin Neuropsychol 32:840-860.

Carnaby-Mann G, Lenius K (2008) The bedside examination in dysphagia. Phys Med Rehabil Clin N Am 19:747-768.

Chen JJ, Marsh L (2014) Anxiety in Parkinson's disease: identification and management. Ther Adv Neurol Disord 7:52-59.

Ciurleo R, Corallo F, Bonanno L, Lo Buono V, Di Lorenzo G, Versaci R, Allone C, Palmeri R, Bramantii P, Marino S (2018) Assessment of Duodopa® effects on quality of life of patients with advanced Parkinson's disease and their caregivers. J Neurol 265:2005-2014.

Corallo F, De Cola MC, Lo Buono V, Di Lorenzo G, Bramantii P, Marino S (2017) Observational study of quality of life of Parkinson's patients and their caregivers. Psychogeriatrics 17:97-102.

Díez-Cirarda M, Ibarretxe-Bilbao N, Peña O, Ojeda N (2018) Efficacy of cognitive rehabilitation in Parkinson's disease. Neurolog Res 13:226.

D'iorio A, Vitale C, Piscopo F, Baiano C, Falanga A, Longo K, Amboni M, Diez-Cirarda M, Ibarretxe-Bilbao N, Peña J, Ojeda N (2018) Efficacy of cognitive rehabilitation in Parkinson's disease: is it feasible? Arch Clin Neuropsychol 32:840-860.

Dissanayaka NWW, White E, O'Sullivan JD, Marsh R, Silburn PA, Copland DA, D'Iorio A, Vitale C, Piscopo F, Baiano C, Falanga A, Longo K, Amboni M, Diez-Cirarda M, Ibarretxe-Bilbao N, Peña J, Ojeda N (2018) Efficacy of intensive multidisciplinary rehabilitation in Parkinson's disease. Cochrane Database Syst Rev 12:CD010760.

Ellis T, Katz DI, Marsh L (2014) Anxiety in Parkinson's disease: identification and management. Ther Adv Neurol Disord 7:52-59.

Kaseda Y, Ikeda J, Sugihara K, Yamawaki T, Kohriyama T, Matsumoto M (2017) Therapeutic effects of intensive inpatient rehabilitation in advanced Parkinson's disease. Neurol Clin Neurosci 5:18-21.

Lauterbach EC, Freeman A, Vogel RL (2003) Correlates of generalized anxiety and panic attacks in dystonia and Parkinson disease. Cogn Behav Neurol 16:225-233.

Lerman SF, Bronner G, Cohen OS, Elinix-Benizri S, Strauss H, Yahalom G, Hassin-Baer S (2019) Catastrophizing mediates the relationship between non-motor symptoms and quality of life in Parkinson's disease. Disabil Health J 12:673-678.

Liu L, Luo XG, Dy CL, Ren Y, Feng Y, Yu HM, Shang H, He ZY (2015) Characteristics of language impairment in Parkinson's disease and its influencing factors. Transl Neurodegener 4:2.

Lyons KE, Patel R (2011) Diagnosis and initiation of treatment in Parkinson's disease. Int J Neurosci 121 Suppl 2:77-36.

Misho E, Dawson K, Mitchell J, Arnold R, Hodges JR (2006) The Addenbrooke's Cognitive Examination Revised (ACE-R): a brief cognitive test battery for dementia screening. Int J Geriatr Psychiatry 21:1078-1085.

Pachana NA, Egan Si, Laidlaw K, Dissanayaka N, Byrne GJ, Brockman S, Marsh R, Starkstein S (2013) Clinical issues in the treatment of depression and anxiety in older adults with Parkinson’s disease. Mov Disord 28:1930-1934.

Palmeri R, Lo Buono V, Corallo F, Foti M, Di Lorenzo G, Bramantii P, Marino S (2017) Nonmotor symptoms in Parkinson disease: a descriptive review on social cognition ability. J Geriatr Psychiatry Neurol 24:168-178.

Petersen RC, Caracciolo B, Brynec G, Gauthier S, Jelic, V, Fratiglioni L (2014) Mild cognitive impairment: a concept in evolution. J Intern Med 275:214-228.

Pekus AJ, Filoteo JV, Schiehser DM, Gomez ME, Petzinger G (2019) Worse cognitive performance predicts increased anxiety and depressive symptoms in patients with Parkinson's disease: A bidirectional analysis, Neuropsychology 33:35.

Schrag A, Taddei RN (2017) Depression and anxiety in Parkinson's disease. Int Rev Neurobiol 133:623-655.

Starkstein SE, Preziosi TJ, Berthier ML, Bolduc PL, Mayberg HS, Robinson RG (1989) Depression and cognitive impairment in Parkinson’s disease. Brain 112:1141-1153.

van der Mark MA, Bloem BR, Born GF, Overeem S, Munneke M, Guttman M (2013) Effectiveness of multidisciplinary care for Parkinson's disease: a randomized, controlled trial. Mov Disord 28:605-611.

van Laar AD, Jain S (2004) Non-motor symptoms of Parkinson disease: update on the diagnosis and treatment. Neurologist 10:185.

Wee N, Wen MC, Kandiah N, Chandler RJ, Ng A, Au WL, Tan LC (2016) Neural correlates of anxiety symptoms in mild Parkinson’s disease: A prospective longitudinal voxel-based morphometry study. J Neurol Sci 371:131-136.

Zhou L, Lhost J, Watabe I, Torromino G, Amalric M (2018) Striatal cholinergic interneurons regulate cognitive and affective dysfunction in partially dopamine-depleted mice. Eur J Neurosci 48:2988-3004.

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