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Influence of anxiety symptoms on quality of life in idiopathic Parkinson's disease without dementia.

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Abstract

The Parkinson's Disease (PD) is a type of neurodegenerative pathology. It has a negative impact on the Quality of Life (QOL), the patient's daily life activities, as well as the psychological stability and family activities of their immediate caregivers. Some studies show that anxiety is related to the deterioration of the quality of life.
The objective of this work is to study the influence of anxiety on the QOL in patients with idiopathic PD without dementia.
The sample was composed by 50 subjects diagnosed with idiopathic PD without dementia (33 men and 17 women), in stages I and II of Hoehn and Yahr, aged between 45 and 75 years.
It was found that depressive symptomatology, more than anxiety, cognitive functioning, or sensorimotor stage significantly affects the quality of life in patients diagnosed with idiopathic PD without dementia, with mild motor disability. Regression analysis showed that the depression and cognitive functioning explained 45.7% of the variance. The results showed that anxiety doesn't impact on QOL in PD, possibly associated with overlapping clinical depression as frequent in PD emotional alteration.
The results suggest that the identification and prompt treatment of anxiety and depression is important for the improvement of QOL in idiopathic PD without dementia.

Keywords: Anxiety, Depression, Quality of life, Parkinson's disease.

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Introduction

Parkinson's disease is pathology of neurodegenerative which is clinically characterized by motor symptoms such as bradykinesia, rigidity, tremor of rest and postural instability [1], accompanied by non-motor alterations like depression, anxiety, apathy, autonomic dysfunction, gastrointestinal symptoms, sleep problems and neurobehavioral disorders in early and advanced stages [2-4].

In terms of emotional alterations [5-7], it was found that depression is one of the most frequent neurobehavioral disorders in PD, accompanied by symptoms such as crying, low self-esteem, recurrent sleep deprivation, weight loss and deterioration of the quality of life and the functional activities of the patient [8]. With a prevalence of greater than 50% [9], depression is a predictor of the strong deterioration of the quality of life and functional involvement in subjects with PD [10].

Similarly, anxiety is another frequent in PD emotional alterations. The data obtained by some studies point out that it may be present in the premotor stage [11,12]. The symptoms range from insecurity, fear, sweating, tightness in the chest and lack of decision-making. The scientific literature indicates that 40% of patients diagnosed with PD suffer from psychosocial stress (anxiety), panic disorder and generalized anxiety [11,12].

Anxiety in PD is related to a deficit of dopaminergic and noradrenergic of limbic innervation. Also a dysfunction in serotonin transporter gene has been found [13-15].

Common disorders of anxiety to be in PD are not well characterized. Most of these clinical pictures are under diagnosed. This is possibly due to the exacerbation of the physical symptoms of the disease. In addition, it is also difficult to differentiate since anxiety is usually accompanied by depression, because the pictures of psychosocial stress and its relation with the motor cardinality of the PD tend to be quite confusing and controversial [16-18].

Anxiety has a prevalence that ranges between 3.6% and 40% [19], affecting directly the QOL, stigma, emotional well-being

and other areas of interest that the subject with PD carried out with full normality before their diagnosis.

The objective of this study is to investigate the influence of anxiety on the QOL, in idiopathic PD without dementia. Clinical variables such as depression, general cognitive functioning, the severity of the disease, age and time of diagnosis were analysed in order to identify if they affect the QOL.

Method and Materials

Participants

50 people with a diagnosis of PD idiopathic without dementia (33 men and 17 women) participated in the study. Patients were recruited from Parkinson Associations of Salamanca, Madrid, Mostoles, Valladolid and Segovia (Spain). Each patient's clinical history was reviewed, in order to confirm the diagnosis of idiopathic PD-no more than 10 years of evolution. Each of the participants signed informed consent voluntarily. None of the subjects had a history of dementia, consumption of alcohol or drugs. They should not present a history of neurological, neuropsychological and psychopathological disorders clinically demonstrable, or have been subjected to any kind of functional neurosurgery for PD treatment. Participants should be aged between 45-75 years and have a 6 year schooling level at least. Motor disability was quantified using Hoehn et al. [20]. Brief cognitive tracking Mini-Mental Parkinson (MMP) test was used [21] to assess the cognitive situation of each of the patients. A score in the MMP greater than or equal to 27 was considered suitable to participate in the study.

Materials

Hoehn et al. [20] test which aims to evaluate the motor phase of the disease, evaluate postural instability, rigidity, tremor and bradykinesia. Stage I indicates unilateral motor involvement, stages II and III indicate bilateral involvement. The participants in the study were classified in stage I and II.

Mini mental Parkinson (MMP) [21]: It is a brief test of cognitive and specific tracing which aims to assess the psychological functions in patients diagnosed with PD. The test consists of the following sections: temporal orientation, spatial orientation, memory, attention/mind control, verbal fluency, associative memory, recognition and processing of concepts. The cut-off point for cognitive impairment is a score less than or equal to 24.

Parkinson's disease cognitive rating scale (PD-CRS) [22]: It is a specific cognitive test for PD, which evaluates immediate verbal memory, confrontation naming, sustained attention, working memory, clock copying and clock drawing, delayed verbal memory, alternating verbal fluency and action verbal fluency.

Beck depression inventory (BDI) [23]: Questionnaire that aims to measure depressive symptomatology.

Yesavage geriatric depression scale (Geriatric depression rating scales) [24]: Aims to evaluate the depressive symptoms in the elderly.

Beck anxiety inventory (BAI) [25]: Evaluates the anxious symptoms. It consists of 20 items which in turn are divided in subjective and somatic symptoms.

Hamilton anxiety scale (HRSA) [26]: It is a scale that aims to assess the severity of anxiety states, presents two sections corresponding to the psychic and somatic anxiety.

Questionnaire of quality of life in Parkinson's disease (PDQ-39) [27]: It evaluates the quality of life in patients with PD. Consists of eight sections that measure: mobility, activities of daily living, emotional well-being, stigma, social support, cognition, communication and body discomfort.

Statistical analysis

It took the total score of the PDQ-39 according to their system of punctuation [28]. Correlation coefficients were calculated to assess the direction and magnitude between the variables. An analysis of step-wise regression was made, aiming to identify the variables that from the multivariate perspective have greater predictive weight.

The procedure has been the method by steps backward, which roughly consists of introducing all the potential predicting variables and going removing those which do not provide sufficient significance to the model with better prognosis within the principle of parsimony. The final solution has contrasted with the method of successive steps forward, finding a virtually identical model.

Data analysis

It was taken as the dependent variable to the total score of the PDQ-39 according to their system of punctuation [28]. Correlation coefficients were calculated to assess the direction and magnitude between the variables. An analysis of step-wise regression was made, aiming to identify the variables that from the multivariate perspective have greater predictive weight.

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Results

Descriptive analysis

The sample is composed (N=50) by 60% of males (33) plus 34% (17) of women. With an average age 64.8 ± 6.53 years (IC 95% to the average: 63.00-66.72) within a range 47-75 with median 65.5 years. As far as the level of schooling is concerned, the majority of patients with PD (68%) (Table 1)

have elementary education, 22% of patients have secondary education, and the remaining 10% of patients have higher education (Table 1).

Table 1. *Socio-demographic characteristics in patients with PD.*

		A	SD	Range
Age Schooling		64.86	6.534	45-75
		N	%	
	Elementary	34	68.0	
	Secondary	11	22.0	
	Higher	5	10.0	
Gender		N	%	
	Male	33	66.0	
	Female	17	34.0	
Marital status		N	%	
	Single	2	4.0	
	Married	44	88.0	
	Widow/widower	4	8.9	
Handedness		N	%	
	Right-handed	50	100	

Subjects with PD have a diagnostic time of 0.5 and 10 years, with median 5. The average is 4.99 ± 2. 86 (IC 95% to the average: 4.18-5.80). In terms of the stage, 80% (40) of cases are in stage II and the remaining 20% in stage I. Regarding the drug consumption 1 subject receives a combination of levodopa/carbidopa (n=1) or in combination with dopamine agonists (n=17). 9 subjects were treated with therapy of levodopa/carbidopa/dopamine agonists and inhibitors of Monoamine Oxidase type B (MAO) (n=9), 7 subjects were treated with levodopa/carbidopa/MAO combination therapy (n=7), 11 subjects were treated with levodopa/carbidopa/ entacatapone and dopamine agonists (n=11), 1 subject received a combination therapy of levodopa/carbidopa and anticholinergics. (n=1), and 4 subjects received treatment dopamine agonists (n=4).

The average score direct for the PDQ-39 was 33.27 (DS: 12.014). The average anxiety score was 29.24 (DS: 11.821) in the BAI and 29.16 (DS: 10.767) in HRSA. The average scores for depression in BDI and Yesavage were: 18.12 (DS: 6.423) and 13.72 (DS: 4.504) respectively. The average for MMP was 30.06 (DS: 1.361), and the average for PD-CRS was: 76.10 (DS: 7.260).

Correlation analysis results

Sensorimotor stage, age, duration of disease, anxiety, depression and global cognitive functioning, are variables that have affected the quality of life (Table 2). PDQ-39 direct score was correlated significantly and directly with the anxiety measured by BAI (R=0.344; P=0.014) and HRSA (R=0.367; P=0.009), as well as with depression measured by BDI (R=0.464; P=0.001) and Yesavage (R=0.507; P=0.000). PDQ-39 is also inversely related cognitive functioning global (PDCRS) (R=- 0.359; P=0.011). It is necessary to be noted that none of the participants complied with the criteria for the diagnosis of dementia, including MMP scores. Subjects that suffer from major symptoms of anxiety and depression, have a worse deterioration in their quality of life. Age of onset of the disease (R=0.257; P=0.072), current age (R=0.089; P=0.538) and sensorimotor stage (R=0.111; P=0.443) were not significantly correlated with QOL.

Table 2. *Correlation matrix of variables associated with the deterioration of the QOL in PD.*

Measuring instrument	Rho	P
Age	0.089	0.538
Diagnostic time	0.257	0.072
Stage of disease	0.111	0.443
BAI	0.344	0.014
HRSA	0.367	0.009
BDI	0.464	0.001
Yesavage	0.507	0.000
PD-CRS	-0.359	0.011

Multiple regression analysis

The predict-dependent variable is the total scale score for CDV-PDQ-39. Predictors initially considered are: BAI (anxiety), HRSA (anxiety) and BDI (depression), Yesavage (depression), stage of disease, age, time of diagnosis, MMP and PD-CRS (cognitive function).

It has been taken into account that BAI and HRSA measure the same construct: anxiety, such as it is the case with Yesavage and BDI for depression. That is why these two pairs of instruments are correlated each other in an elevated way (r =0.837; p=0.000 in anxiety; and r=0.820; p=0.000 in the case of depression). This implies a high collinearity among them in case of being introduced simultaneously in the prediction model. Therefore, all possible combinations have been tested with one of the instruments of each pair and all the other predictor variables. They are not exposed the entire collection of results in each phase and each step, but only a summary of the best solution found.

In all cases, several backward steps have been taken, excluding the variables according to their degree of inefficiency as significant predictors (con $p<0.05$), and the coefficients at each of these steps have been reset.

The best found model (Table 3), within various solutions that would be feasible, has a degree of adjustment R2 45.7% (percentage of explained variance), which can be considered as high and it is equivalent to a very large effect size. The multivariate model has excluded the two instruments that

measured anxiety, while univariate form that could have been considered as predictors, given its significant relationship (Table 2) as discussed. On the other hand, it includes significantly effective predictors in the following order: Yesavage (T=3.28; P=0.002) and cognitive PD-CRS (T=-2.20; P=0.033). The sign of the respective regression coefficients (Table 3) indicates that the PDQ-39 relationship with Yesavage is direct. In other words, the score is increased by PDQ39 as the coefficients score more in depression; it is reverse with PD-CRS, because the value is increased in PDQ-39 as it decreases the score in this predictor. The tolerance values of both predictors are acceptable, indicating a sufficient degree of independence among them. This model is therefore independent of the anxiety level of patients.

They have been excluded from the model. Although due to their proximity to the significance, they are notable with a view to future research with higher sample size, age and time of diagnosis on a first step, and anxiety with HRSA in the background. What it seems reasonably safe from a multivariate perspective, is the absence of predictive capacity of the other variables: Stage, BDI, BAI and MMP.

Table 3. Multiple linear regressions of total score in PDQ-39. Methods adjusted by backward steps.

Introduced variables	Coefficient B	E.T. (B)	IC at 95% of B	T Value	P-value	Value of R	Partial R	Tolerance
Yesavage depression	1.214	0.37	0.469; 1.959	3.284		0.606	0.44	0.628
PD-CRS cognitive	-0.493	0.225	-0.945; -0.041	-2.196	0.033*	-0.369	-0.311	0.656
Constant	72.798	29.362	13.659; 131.937	2.479	0.017*	-	-	-
Variation source	**Sum of squares**	**g. l.**	**Root mean square value**	**F**	**P-value**	**Coefficient of determination**	**Effect size**	**Estimate standard error**	**Durbin-Watson**
Regression	3229.85	2	1614.92	19.75	0.000**	0.457	0.842	9.240	2.122
Residual	3842.29	47	81.75						
Excluded variables	**Coefficient B**	**T-value**	**p-value**	**Partial R**	**Tolerance**			
Age	-0.398	-1.621	0.112 NS					
Diagnostic time	0.564	0.883	0.383 NS	0.14	0.569			
HRSA Anxiety	0.197	0.753	0.456 NS	0.12	0.627			
Stage of disease	-1.243	-0.279	0.782 NS	-0.045	0.589			
BDI Depression	0.056	0.149	0.882 NS	0.022	0.323			
BAI Anxiety	-0.023	-0.1	0.921 NS	-0.016	0.595			
MMP	0.022	0.017	0.987 NS	0.003	0.587			

Discussions and Conclusions

Data obtained in the study show that anxious symptoms do not affect QOL in subjects with idiopathic PD without dementia, unlike depressive symptomatology, where we can find that more than anxiety, cognitive functioning and sensorimotor stage affect QOL in this type of patients.

Despite several studies [29-31] indicate that anxiety impacts the quality of life in patients with PD, in our study we did not find anxiety affecting emotional well-being, stigma, cognition and individuality in patients with this diagnosis.

This may be due to the following variables:

1. Clinical depression overlaps as frequent emotional disturbance in PD.
2. The imprecision of the diagnosis of anxiety and the superposition of motor symptoms.
3. The size of the sample is not representative for this type of analysis. Therefore, it is not possible to determine the impact of anxiety on QOL in patients with idiopathic PD without dementia.

Anxiety in subjects with PD is usually fluctuating (mixed clinical pictures accompanied by depression) and heterogeneous. This leads to that their clinical picture cannot be explained as a secondary entity, but as a primary entity to their diagnosis, or that it is preceded to their motor cardinality [11,12].

This leads us to suggest and rethink the creation and use of tools of a specific nature which can measure states of anxiety in PD, do it in an individualized manner, with the aim of finding the relationship of anxiety with motor fluctuations, cognitive functioning and QOL particularly.

What we know so far is that anxiety arises from a distressing way and that is associated with the deterioration of the quality of life and the pathology [29-31]. The fact that we have not found it does not mean that it does not impact, it really does.

But because of inaccuracies previously commented, they have allowed that these strange variables cannot be controlled.

What was found in our study points out that depression and not anxiety explains up to 50% on the results of the PDQ-39 [32,33].

As mentioned above, it is possible that anxiety and depression overlap clinically in PD [34], since the materials used to identify depression and anxiety are not able to differentiate between these features, especially the relationship that occurs in both emotional alterations.

This study failed to demonstrate the impact that anxiety has on the quality of life, but on the depression [35-37] in PD and the impact that it has on the functional activity of the subjects, related to the low production of dopamine and serotonin [38,39].

With 45.7% of variance in the quality of life explained by depression and cognitive functioning, this study highlights the importance of treating depression, aiming to improve the social, individual and familiar dimensions of the subjects with idiopathic PD without dementia. However, it is necessary to focus the intervention works and research in anxiety since there are several studies showing the impact that anxiety has on the QOL [29-31]. Regardless of our results, anxiety contributes to the morbidity of PD associated with the physical and psychological affectation of the caregiver and the deterioration of emotional well-being, social support and the stigma of each of the subjects.

A relationship was not found between anxiety, QOL, sensorimotor stage, age and the time of the diagnosis. A larger sample can give different results in these variables.

It is also relevant to note that when anxiety and depression occur together, they are associated with further deterioration that becomes chronic and progressive of worse evolution [40,41]. In PD data from different studies suggest that anxiety often appears with symptoms of depression [42-43]. It is necessary to carry out research that aims at emotional alterations in PD and its direct impact on QOL.

Future Research

The absence of relationship that arises between anxiety, QOL and cognitive performance suggests the need for research involving a larger number of participants with different stages of the disease, their pathophysiology and factors of risk, in order to investigate different therapeutic lines that allow improving the QOL in patients with idiopathic PD without dementia.

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