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Depression and Anxiety in Parkinson's Disease, Metric Properties of the Beck´s Depression and Anxiety Inventories. A K2 Factorial Design

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Abstract

Background: Study to investigate the concurrent validity of the Beck Depression Inventory and Beck Anxiety Inventory evaluation scales against the ICD-10.
Methods: A K2 factorial design for studying the metrics properties of the BDI and BAI in parkinsonian outpatients.
Results: 147 parkinsonian patients were included; 44 patients has anxiety and depression; only depression 19; only anxiety 31; finally 53 subjects don't have depression or anxiety. The BDI AUC was [0.858]. The BAI AUC was of [0.907]. The cut score was of 14/15 for the BDI and 13/14 for the BAI. The factorial design resulted in the two factors (depression and anxiety) has the best functional correlation in the regression.
Conclusions: The results we present bear out this lack of dimensionality, since we found that the BDI AUC-measured discriminative ability for anxiety was [0.739]. With regard to the BAI, this is employed to discriminate the depressed, AUC values of [0.771].

Keywords: Parkinson's disease, Depression, Anxiety, Metric properties, Psychometric properties

Introduction

Depression and anxiety disorders are highly prevalent conditions in Parkinson´s disease (PD) and constitute a global burden. Among patients in neurological clinics, concomitant anxiety syndromes with depression were present in 75% of cases.1 Some authors consider that significant anxiety in combination with depression may represent a specific depressive subtype in PD.2 The average prevalence rate of depression in PD has been calculated around of 40%,3 while the prevalence of anxiety ranges widely from 5.3% to 40%.4 Though anxiety is a common problem in PD, relatively little attention has been paid to the phenomenon.5

Depression and anxiety are common in the elderly population.6 When anxiety disorders occur later in life they tend to be associated with medical and neurological conditions.1 In the WHO Collaborative Study, depression was found to be 9 times more likely in patients with anxiety disorders. There was substantial overlapping between depressive and anxiety symptoms in this study: 39% of patients with current depression also had anxiety disorders and 44% of those with current anxiety disorders showed comorbid depression.7 In a review of anxiety in PD, Richard et al.8 noted that up to 60% of patients with depressive symptoms also suffered from anxiety.

Recently, several factors have led to suggestions that anxiety and depression are the same disease. Briefly, they frequently co-exist, there are overlapping symptoms between the two afflictions, the same neurotransmitters are involved in both these mental states9,10,11 and, finally, similar agents can be used to treat them both.

In a recent paper of the NINDS/NIMH Work Group, the authors suggested the need for research on comorbilities between anxiety and depression.12 The recent report of the the Movement Disorder Society commissioned a task force to assess the clinimetric properties of these scales in PD: "No scales met the criteria to be ''recommended,'' and all scales were classified as ''suggested.'' Essential clinimetric information is missing for all scales. Because several scales exist and have been used in PD, the task force recommends further studies of these instruments. If these studies show that the clinimetric properties of existing scales are inadequate, development of a new scale to assess anxiety in PD should be considered.13"

Our study was designed to investigate the concurrent validity of the Beck Depression Inventory (BDI) and Beck Anxiety Inventory (BAI) evaluation scales. We evaluated both scales against the International Classification of Diseases version 10 (ICD-10) criteria (as the gold standard)14 for major depressive disorders (MDD) and for generalized anxiety disorders (GAD). A second objective of this study was to examine how effectively the BDI and the BAI differentiate MDD and GAD, as diagnosed using the ICD-10. Finally, another fundamental objective of this work was to analyze the interdependency of anxiety and depression. To this end, we did a study with a K2 factorial design to analyze correlations between the two conditions.

Patients, Materials and Methods

Design. This was an observational, analytical crosssectional, one-point-in-time evaluation with a K2 factorial design.

Patients. One hundred and forty-seven consecutively included patients diagnosed with PD as per United Kingdom PD Society Brain Bank criteria,15 in stages 1 to 5 of the Hoehn and Yahr scale (HY),16 were regularly treated and followed-up as outpatients at the Movement Disorders Unit of the Carlos Andrade Marin Hospital (HCAM) Neurology Service in Quito, Ecuador.

The exclusion criteria were severe cognitive impairment (with a score of over 5/10 as evaluated by Pfeiffer's Short Portable Mental Status Questionnaire – SPMSQ17), illiteracy, serious concomitant illness, blindness, hypoacusis, or limb amputation. This study was approved by the HCAM Department of Research and Teaching and all patients involved provided prior written informed consent.

Assessment Procedure. Demographic data (age and gender) and historical data (age at onset of PD, duration of disease, years in treatment with levodopa and dose employed) were recorded. Neurologist-based assessments were HY stage,16 Schwab and England scale (SES),18 and Unified Parkinson's Disease Rating Scale sections 1 to 3 (UPDRS).19 Alternatively scales used as evaluation tools by a second researcher were the BDI (Spanish version by Sanz et al.)20 and the BAI (Spanish version by Sanz et al.)21 Measurements were applied during the "ON" state in the case of patients with fluctuations.

Seven days after the first evaluation, a third researcher evaluated patients with the ICD-10 criteria for MDD and GAD. All the authors remained blind to ongoing test results during psychometric patient evaluations.

Data Analysis. The following metric characteristics of the BDI and BAI were explored:

Acceptability. This indicates the extent to which score distributions adequately represent the true distribution of health status in the sample. This was determined by comparing observed to possible score ranges, the proximity of means to medians, floor and ceiling effects (with <15% accepted as satisfactory), and skewness of score distributions (accepted limits: -1 to +1).22

Discrimination. The discriminative capacity of each scale was statistically analyzed with ROC (receiver operating characteristic) curves and AUC (area under the curve).23 A cutoff point was established to determine the Quality Index of Sensitivity (chance corrected index of sensitivity = k (1,0)); Quality Index of Specificity (chance corrected index of specificity = k (0,0)); Efficiency (correct classification rate; proportion of positives and negatives classified correctly by the test = EFF); Efficiency of a Random Test (correct classification rate that would be expected by chance alone = EFF_RAN);24 Prevalence & Bias Adjusted Kappa (Kappa adjusted to take account of differences in perceived prevalence and the relative frequency of positive and negative observations = PABAK);25 Odds Ratio (Haldane's estimator; this estimator of the odds ratio and its standard error have desirable properties, particularly when cell frequencies are zero or small = OR');26 Positive Likelihood Ratio (LR+) and Negative Likelihood Ratio (LR-), as well as their 95% confidence intervals (95% CI) to obtain post-test probabilities.27 K2 Factorial Design.28 Several special cases of the general factorial design are important because they are widely used in research work. The most important of these special cases is that of K factors, each at only two levels. These levels may be quantitative or they may be qualitative, and may be owing to the presence or absence of a factor. A complete replicate of such a design requires 2 x 2 x...x 2 = 2K observations and is called 2K factorial design. We planned to examine the magnitude and direction of factor effects to determine which variables were likely to be important. The results of the experiment are easily expressed in terms of a regression model.

Results

The 147-patient sample was composed of 106 males (72.1%). The mean age of patients was 68.66 years, and their mean illness duration was 6.81 years. They had been on L-dopa treatment for a mean of 5.19 years and were receiving an average dose of 721.53 mg/day. Eight patients were in stage 1; 40 in stage 2; 92 in stage 3; 6 in stage 4 and just 1 in stage 5, according to the H&Y scale (see Table 1). For analytical purposes, the single stage-5 patient was included in the stage-four group.

According to the ICD-10 criteria, 75 patients (51%) experienced anxiety and 63 (43%) had depression (12 mild, 28 moderate, and 23 severe). The mean score on the BDI was 17.44 points and it was 16.18 on the BAI. Scores differed according to the H&Y stage, with a tendency toward bimodality for both the BDI and the BAI; the highest scores were seen in stages 1 and 4 (see Table 2).

We found that 44 subjects (30%) showed depression and anxiety criteria. There were 19 (12.9%) who suffered depression without anxiety symptoms and 31 (21%) who had anxiety without depression. Finally, 53 patients (36%) experienced neither anxiety nor depression (Table 2). Concerning the acceptability of both scales, appropriate scores and statistics were achieved, thus assuring data quality.

Using the ICD-10 criteria as the gold standard, we did the BDI's ROC curves and the respective AUC and found that its ability to discriminate mild depression was 12 Revista Ecuatoriana de Neurología / Vol. 18, N o3, 2009 low [0.476 (0.384—0.568)]. We got values of [0.740 (0.656—0.825)] for moderate depression and [0.897 (0.835—0.959)] for severe depression. When we grouped the entire depressed population, the BDI showed the following values: [0.858 (0.800—0.916)] (Graph 1). The BAI's ROC curve and AUC were [0.907 (0.860—0.955)] (Graph 2).

To obtain the previously mentioned values, we analyzed the various cut-off points that enable the best discriminative qualities for both scales and got cut-off points of 14/15 for the BDI and 13/14 for the BAI (Table 3). Important values were obtained for the prior probability and posterior probability (odds) for those cut-off points (Table 4).

Finally, we decided to use the BDI to assess anxious patients (ICD-10 criteria) and the BAI to assess depressed patients (ICD-10 criteria). The ROC curves and the AUC were [0.739 (0.658—0.819)] and [0.771 (0.695-0.847) , respectively (Graphs 3 and 4). Center points were added to the K2 factorial design, which showed a clear functional dependency between both factors (Table 5).

The main concern in the use of two-level factorial design is the assumption of linearity in the factor effects. Of course, perfect linearity is unnecessary and the K2 system will work quite well even if the linearity assumption holds only very approximately. In fact, we have noted that if interaction terms are added to the main effects in the first-order model, we get:

Which is a model capable of representing any curvature in

$$y = \beta_0 + \sum_{j=1}^{k} \beta_j x_j + \sum \sum_{i<j} \beta_{ij} x_i x_j + \varepsilon$$

the response function. This curvature, of course, comes from the turn in the plane induced by the interaction of the terms βijχiχj. In our case, this first design revealed (i) that each factor (anxiety or depression) makes the intercept negative with values of -6.415 and -17.085, respectively; (ii) the presence of both places this value at 8.415.

There are going to be situations where the curvature in the response function is not adequately modeled. In such cases, a logical model to consider is: where βij represents pure second-order or quadratic effects.

$$y = \beta_0 + \sum_{j=1}^{k} \beta_j x_j + \sum \sum_{i<j} \beta_{ij} x_i x_j + \sum_{j=1}^{k} \beta_{jj} x_j^2 + \varepsilon$$

This equation is called a second-order response surface model. The method consists in adding center points to the K2 design.

yF = the average of the four factorial points; nc = the number of observations at the center (0,0), and yc = the average of the nc center points. If the yF - yc difference is small, the center points run near the plane that passes through the factorial points, and there is no quadratic curve. On the other hand, if the yF - yc difference is large, a quadratic curve is present.

The sum of squares of the pure quadratic curve has one degree of freedom and is rendered by:

The sum obtained may be compared with the mean

$$SC_{ccp} = \frac{n_F n_C (\overline{y}_F - \overline{y}_C)^2}{n_F + n_C}$$

quadratic error. More specifically, when we add points to the center of the 2K design, the curvature test becomes a hypothesis test:

$$H_0 = \sum_{j=1}^{k} \beta_{jj} = 0$$

$$H_A = \sum_{j=1}^{k} \beta_{jj} \neq 0$$

Furthermore, if the factorial points of the design have not been replicated, the nc midpoints may be used to construct an error estimate with nc - 1 degrees of freedom.

Adding midpoints produced significant values, so

$$MC_E = \frac{SC_E}{n_C - 1}$$

H0 is acceptable, and HA is rejected. That is, there is a linear relationship between both regressors (Table 5).

Discussion

Our study investigated the concurrent validity of the scales compared to the ICD-10 and our results are similar to those obtained by other authors.

Regarding the discriminative ability of the scales employed, the AUC result obtained [0.858 (0.800—0.916)] in our sample with the BDI was similar to the 0.8567 obtained by Leentjens et al. in Parkinson´s patients, even though they used the DSM-IV as the gold standard.29

Using the DSM-III-R in a population of hospitalized neurological patients, Lykouras et al. found that values for the AUC differed depending on the cutoff points, reaching 0.925 with 20 points and 0.94 with 29 points.30

In another study,31 an AUC of 0.88 was obtained and the cutscore with the greatest sensitivity (0.715) and greatest specificity (0.90) was 14/15. Again, these authors used the DSM-IV as the gold standard. We obtained an identical cutscore in our study.

With regard to the BAI, its metric properties have not been measured in Parkinson´s patients, as far as we

know. Hoyer et al.32 used it in an epidemiological study in young

Table 1. Statistics descriptives of the sample

No. 147

	Mean (+/- SD)	Median	Skewness	Minimun	Maximun
Age (years)	68.66 (10.75)	70	-0,131	41	95
Disease (years)	6.81 (4.97)	6	1,39	1	25
Treatment (L-dopa, in years)	5.19 (4.43)	5	1,35	0	20
Dose L-Dopa (mg/day)	721.53 (407.67)	750	-0,016	0	1500
UPDRS I	5.16 (2.63)	5	0,23	0	13
II	19.09 (7.04)	19	0,463	5	41
III	42.15 (12.27)	43	-0,01	15	70
Total	66.39 (20.35)	68	0,154	25	122
S&E	68.44 (14.97)	70	-0,796	20	90
SPMSQ	1.46 (1.76)	1	1,52	0	5
BDI	17.44 (9.8)	17	0,68	0	47
BAI	16.18 (10.7)	14	0,84	0	50

UPDRS = Unified Parkinson's Disease Rating Scale.
S&E = Schwab and England scale
SPMQSQ = Short Portable Mental Status Questionnaire
BDI = Beck Depression Inventory
BAI = Beck Anxiety Inventory

Table 2. Anxiety and depression scores and diagnosis according H&Y staging

H&Y	1	2	3	4	TOTAL	MEAN
No.	8	40	92	7	147	
BDI score	22 (16.6)	13.28 (9)	18.03 (8.93)	28.29 (5.21)		17.44 (9.8)
CIE-10 DEPRESSION						
LIGHT	0	2	10	0	12	
MILD	1	5	20	2	28	
SEVERE	2	3	14	4	23	
TOTAL WITH DEPRESSION	3 (37.5%)	10 (25%)	44 (47.8%)	6 (85.7%)	63 (42.8%)	
NON DEPRESSION	5	30	48	1	84	
BAI score	20.75 (12.89)	12.73 (9.1)	16.52 (10.43)	29.26 (14.19)		16.18 (10.7)
CIE-10 ANXIETY	5(62.5%)	13 (32.5%)	52 (56.5%)	5 (71.4%)	75 (51.02%)	
NON ANXIETY	3	27	40	2	72	
ANXIETY (+), DEPRESSION (+)	3	6	31	4	44	
ANXIETY (-), DEPRESSION (-)	3	23	27	0	53	
ANXIETY (+), DEPRESSION (-)	2	7	21	1	31	
ANXIETY (-), DEPRESSION (+)	0	4	13	2	19	

Table 3. Cut-score for the best capability of sensibility and specificity

CUT/SCORE	κ(1,0)	κ(0,0)	EFF	EFF_RAN	PABAK	OR'
BECK DEPRESSION INVENTORY						
12/13	0,66	0,96	0,89	0,52	0,79	190,03
13/14	0,79	0,96	0,93	0,51	0,87	363,47
14/15	**0,97**	**0,89**	**0,96**	**0,50**	**0,93**	**745,37**
15/16	0,96	0,60	0,87	0,49	0,74	149,77
16/17	0,96	0,62	0,87	0,49	0,75	160,71
17/18	0,96	0,80	0,93	0,50	0,87	375,00
18/19	0,96	0,57	0,85	0,49	0,71	131,09
19/20	0,95	0,45	0,80	0,48	0,60	82,60
20/21	0,95	0,38	0,76	0,47	0,52	60,99
BECK ANXIETY INVENTORY						
10/11	0,96	0,58	0,86	0,50	0,72	136,26
11/12	0,96	0,60	0,87	0,50	0,74	146,31
12/13	0,96	0,80	0,93	0,50	0,87	376,88
13/14	**0,97**	**0,94**	**0,97**	**0,50**	**0,95**	**1400,60**
14/15	0,87	0,97	0,95	0,49	0,91	611,00
15/16	0,77	0,96	0,93	0,49	0,86	333,66
16/17	0,73	0,96	0,91	0,49	0,83	267,34
17/18	0,54	0,82	0,82	0,49	0,65	33,22
18/19	0,53	0,96	0,84	0,49	0,68	113,34

κ(1,0) = Quality index of sensitivity
κ(0,0) = Quality index of specificity
EFF = Efficiency (Correct classification rate)
EFF_RAN = Efficiency of a random test
PABAK = Prevalence & Bias Adjusted Kappa
OR' = Odds ratio (Haldane's estimator)

Table 4. Cut-score for the best capability of determination of the Prior probability and Posterior probability

BECK DEPRESSION INVENTORY. Prior probability (odds): 43% (0.8)				
	POSITIVE TEST		NEGATIVE TEST	
CUT/SCORE	LHR(+) (95%CI)	Posterior probability (odds) (95%CI)	LHR(-) (95%CI)	Posterior probability (odds) (95%CI)
12/13	65 (9.27–460)	98% (48.8) (87–100)	0.22 (0.14–0.36)	14% (0.2) (10%–21%)
13/14	73 (10–516)	98% (54.8) (88%–100%)	0.13 (0.07–0.25)	9% (0.1) (5%–16%)
14/15	**21 (7.94–54)**	**94% (15.8) (86%–98%)**	**0.02 (0.00–0.12)**	**1% (0.0) (0%-8%)**
15/16	4.59 (3.05–6.93)	78% (3.4) (70%–84%)	0.02 (0.00-0.14)	1% (0.0) (0%–10%)
16/17	4.86 (3.18–7.44)	79% (3.7) (70%–85%)	0.02 (0.00-0.14)	1% (0.0) (0%–10%)
17/18	10 (5.34–20)	88% (7.5) (80%–94%)	0.02 (0.00-0.12)	1% (0.0) (0%–8%)
18/19	4.13 (2.82–6.07)	76% (3.1) (68%–82%)	0.02 (0.00-0.15)	1% (0.0) (0%–10%)
19/20	2.95 (2.18–4.00)	69% (2.2) (62%–75%)	0.02 (0.00-0.17)	1% (0.0) (0%–11%)
20/21	2.43 (1.87–3.16)	65% (1.8) (58%–70%)	0.03 (0.00-0.19)	2% (0.0) (0%–12%)
BECK ANXIETY INVENTORY. Prior probability (odds): 51% (1.0)				
10/11	3.74 (2.54–5.50)	80% (3.9) (73%–85%)	0.02 (0.00–0.13)	2% (0.0) (0%–12%)
11/12	3.95 (2.64–5.89)	80% (4.1) (73%–86%)	0.02 (0.00-0.13)	2% (0.0) (0%–12%)
12/13	8.88 (4.62–17)	90% (9.2) (83%–95%)	0.01 (0.00-0.11)	1% (0.0) (0%–10%)
13/14	**36 (9.05–139)**	**97% (37.5) (90%–99%)**	**0.01 (0.00-0.10)**	**1% (0.0) (0%–9%)**
14/15	67 (9.59–171)	99% (69.7) (91%-100%)	0.07 (0.03–0.16)	7% (0.1) (3%–14%)
15/16	63 (9.03–445)	98% (65.6) (90%–100%)	0.12 (0.07–0.22)	11% (0.1) (7%–19%)
16/17	61 (8.75–431)	98% (63.5) (90%–100%)	0.15 (0.09–0.26)	14% (0.2) (9%–21%)
17/18	11 (4.48–25)	92% (11.4) (82%–96%)	0.29 (0.20–0.42)	23% (0.3) (17%–30%)

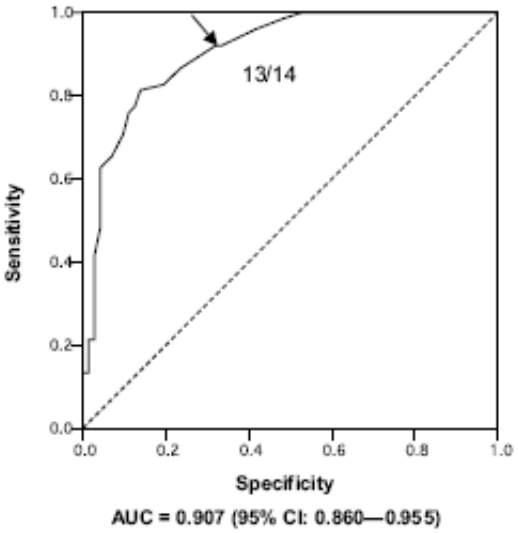
Table 5. Analysis of variance for factorial experiment with central points

Source of variation	Grades of freedom	Sum of squares	Mean of the sum of squares	*F*	*p*
Anxiety	1	0,02083333	0,02083333	0,13	0,72
Depression	1	0,28009259	0,28009259	1,79	0,21
Anxiety and depression	1	19,1689815	19,1689815	122,68	0,0004
Sum of squares of the pure quadratic curvature	1	1100,13889	1100,13889	7040,88	0,0005
Error	4	0,625	0,15625		
Total	8				

High (+) 63	b	19	44	ab
Depression		central points: 15,5 / 15 / 14,5 / 14 / 13,5		
Low (-) 84	1	53	31	a
		Low (-) 72 — Anxiety — High (+) 75 A		147

GRAPHIC 1

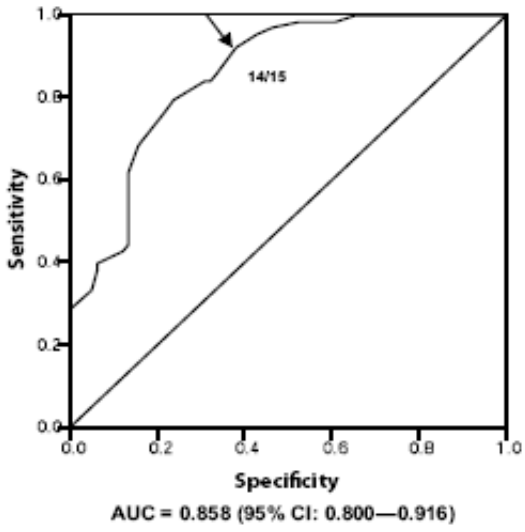
ROC Curve: BAI vs CIE-10 Criteria



AUC = 0.907 (95% CI: 0.860—0.955)

GRAPHIC 2

ROC Curve: BDI vs CIE-10 Criteria



AUC = 0.858 (95% CI: 0.800—0.916)

GRAPHIC 3

GRAPHIC 4

adult women, and Kabacoff et al.33 used it to evaluate elderly psychiatric outpatients. In any case, our results are not comparable to those from these studies. Indeed, one of the limitations of our study is that we cannot compare our results because we have used a different gold standard.

Our findings on the prevalence of depression (42.8%) are similar to others reported by our group,34 and the prevalence of anxiety (51%) falls within the range reported by some authors,8 although we are aware that the BAI may over-assess the presence of anxiety, as described by Higginson et al.35

It has been persistently stated that scales such as the HDRS or BDI are not unidimensional and that they involve too many somatization items that are confused with the selfsame symptoms of Parkinson´s disease.36,37 The results we present bear out this lack of dimensionality, since we found that the BDI´s AUC-measured discriminative ability for anxiety was [0.739 (0.658—0.819)]. With regard to the BAI, which is employed to discriminate the depressed, AUC values of [0.771 (0.695-0.847)] were obtained.

We believe our results show, as do others, the defects of both scales. As de Gruijter DNM and van der Kamp38 say, “A depression inventory, for example, may not merely tap depression as the intended trait to measure, but also anxiety. In this case, a reasonable decomposition of observed scores on the depression inventory would be:

$Z = \tau + E_D + E_U$ where X is the observed score, τ is the true score, ED is the systematic error due to the anxiety component, and EU is the combined effect of unsystematic error”. This, in our opinion, is due to what Bond TG and Fox CM39 have clearly stated, “… one’s philosophy of measurement leads one to use a statistical analysis model that will guide the development and selection of items –the statistical model is being used as a means of quality control of the items. This is in contrast to the most common alternate approach where the statistical model is augmented by parameters that are designed to accommodate the characteristics of the item set—one could say that the statistical model is being used to describe the items.”

Additionally, our results clearly show the presence of both entities – depression and anxiety – as a continuum, which is borne out by refinement of the design models. This coexistence of depression and anxiety has been reported in a number of studies. In general practice, for example, 39% of depressed patients suffered anxiety and 44% of anxiety patients suffered depression.7 Dual prevalence is also well known in the elderly.6 In fact, one of the first reports of the coexistence of both entities in Parkinson´s patients, Menza et al.40 found that 92% of those suffering anxiety had comorbility with depressive disorder and that 67% of depressed PD patients also suffered from anxiety. Another article adds that Parkinson´s patients with anxiety got higher scores on the HDRS.41

More recently, Nuti et al.42 reported that 19.3% of their subject sample with Parkinson´s suffered depressive illness and anxiety.

Despite the extensive literature on anxiety and depression, there is still disagreement about whether these two syndromes represent distinct clinical disorders, as evidenced in Anxiety and Depression: Individual Entities or Two Sides of the Same Coin?.9 This conception of their being two sides of the same coin is

based on the widely observed coexistence of both entities in populations studied, and the fact that they both respond to the same drugs, the SSRIs. Finally, we should consider the monoaminergic circuits as paradigmatically responsible for depression symptoms.43

On the other hand, it has been suggested that the hypothesis for anxiety disorders would be the presence of a reverberating circuit that arises in the orbitofrontal cortex and projects to the striate, from this to the thalamus, and from there returns to the prefrontal cortex.44

By unifying these hypotheses, we would conclude that the monoamines serotonin, noradrenalin, and dopamine are involved in the parallel circuitry that runs from the prefrontal regions to the caudal regions of the basal ganglia, and from these to the thalamus, from whence they return to the cortical regions.45

In addition, studies suggest that anxiety disorders may be particularly difficult to distinguish from depression46 and that different clusters of symptoms are reported by depressed and anxious patients on clinical and self- ating scales.47 Thus, we may also consider that these are very deeply interpenetrating entities, just as we have shown.

One of the reasons for studying these correlations is to see the degree of dependence or independence of the variables. Since neither of the two – depression and anxiety, or anxiety and depression – can be taken as an independent regressor while the other is dependent, it is then essential, in our opinion, to determine the degree of interdependence between both variables. We believe we have demonstrated that the combination of anxiety and depression is, statistically, more significant than the presence of either one alone. In other words, they may be elements of one and the same continuum.

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