

Articles

The Prevalence and Correlation of Non-motor Symptoms in Adult Patients with Idiopathic Focal or Segmental Dystonia

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Abstract

Background: Idiopathic focal dystonia is a motor syndrome associated with dysfunction of basal ganglia circuits. Observations have suggested that many other non-motor symptoms may also be part of the clinical picture. The aim was to assess the prevalence and correlation of non-motor symptoms in patients with common idiopathic focal or segmental dystonia.

Methods: In a single-center cross-sectional case–control study, we evaluated the presence of pain, neuropsychiatric symptoms, and sleep alterations in 28 patients with blepharospasm, 28 patients with cervical dystonia, 24 patients with writer’s cramp, and 80 control subjects matched for sex, age, and schooling. We obtained clinical and demographic data, and evaluated patients using the Fahn–Marsden Dystonia Rating Scale and other specific scales for dystonia. All subjects completed the following questionnaires: Beck Depression Inventory, Beck Anxiety Inventory, Social Phobia Inventory, Apathy Scale, Epworth Sleepiness Scale, Pittsburgh Sleep Quality Index, Brief Pain Scale, and the World Health Organization Quality of Life brief scale.

Results: The patients presented more symptoms of depression, anxiety, and apathy than the control subjects. They also reported worse quality of sleep and more pain complaints. Patients with blepharospasm were the most symptomatic subgroup. The patients had worse quality of life, and the presence of pain and symptoms of apathy and depression were the main influences for these findings, but not the severity of motor symptoms.

Discussion: Patients with dystonia, especially those with blepharospasm, showed higher prevalence of symptoms of depression, anxiety, apathy, worse quality of sleep, and pain. These symptoms had a negative impact on their quality of life.

Keywords: Dystonia, non-motor symptoms, depression, apathy, sleep, pain

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Introduction

Dystonia is a movement disorder characterized by sustained and/or intermittent muscle contractions causing abnormal, often repetitive, movements, postures, or both.¹ Focal isolated dystonia is the most common form of dystonia in adulthood, with symptom onset usually in the fifth decade of life. Most of these cases are idiopathic and may present as cervical dystonia, blepharospasm, or writer’s cramp.² Idiopathic focal dystonia in adults rarely progresses to

generalized dystonia, but may spread to contiguous regions and become a segmental form.³ Despite the localized distribution of abnormal movements, focal dystonia affects functional aspects of daily living and social functioning, and significantly impairs quality of life.⁴

Although dystonia presents characteristically as a clinical motor problem, many studies have suggested that several non-motor symptoms can often be observed in these patients and may be relevant predictors

of their quality of life.^{4,5} Among these, some neuropsychiatric symptoms such as depression, anxiety, apathy, and obsessive-compulsive behaviors can be highlighted. Additionally, these patients also report having sleep disorders and pain.⁶⁻⁸ These non-motor symptoms might be because dystonia may cause functional disability and negative body perception, which could lead to the appearance of symptoms of anxiety and depression. On the other hand, non-motor symptoms may relate primarily to the pathophysiology of dystonia itself.

The pathophysiology of dystonia is not completely understood, but is considered to be related to dysfunctions of the basal ganglia system and its connections, mainly to the thalamus and brainstem.⁹ It has also been correlated with dysfunction of the cerebellum, one of the most prominent brain structures associated with motor control.¹⁰ Furthermore, several non-motor symptoms of dystonia may be due to abnormal functioning of cortical, limbic, basal ganglionic, and cerebellar loops.

Most studies published so far have focused only on a specific group of non-motor symptoms, without assessing the correlations between the most prevalent ones, and some have reported contrary findings.¹¹ Since these symptoms can significantly influence patients' quality of life, it is extremely important to gain better understanding of this issue. The present study aimed to evaluate the prevalence of neuropsychiatric symptoms, sleep disturbances, and pain in a sample of patients with idiopathic focal or segmental dystonia, and to investigate correlations between these symptoms and their impact on quality of life.

Methods

Participants

This was a case-control cross-sectional single-center study conducted on Brazilian patients. For our study, we initially recruited 160 participants. Out of that group, 80 were control subjects. The remaining 80 participants were consecutive patients with various forms of idiopathic focal or segmental dystonia. All participants were over 18 years old. The exclusion criteria in both groups were the presence of dementia, any other neurological disorder or any serious or decompensated systemic disease.

Patients were recruited from the outpatient clinic for movement disorders at the Ribeirão Preto School of Medicine. All participants agreed to participate in this study. They were all diagnosed with a common form of adult-onset idiopathic focal or segmental dystonia, with confirmation from a movement disorder specialist. All patients who were regularly undergoing treatment with botulinum toxin type A were evaluated at least 13 weeks after the last application. In addition, if the patient was using any other medication for dystonia, the treatment was continued.

The control group was matched for sex, age, and years of education (schooling). Control participants were selected from among the individuals who accompanied the patients with movement disorders to their appointments and from among hospital staff members. The objective of the study was explained to these individuals and they were asked if they were willing to voluntarily collaborate in the study as a control group to be compared with the patients in the study. The exclusion criteria were the same as in the group of patients, but individuals with

pathological conditions were not excluded, even if chronic, if that condition was adequately controlled; those with previous psychiatric conditions were not excluded. If a participant in the control group presented altered scores on the scales evaluated, this individual would be referred for medical follow-up.

This study was approved by the local Ethics Committee of the Ribeirão Preto School of Medicine hospital (protocol number 12736/2011) and was conducted in accordance with the ethical principles of the Declaration of Helsinki. All subjects signed an informed consent statement before participating.

Measurements

A clinical evaluation was conducted by a neurologist who was a specialist in movement disorders in order to obtain clinical and demographic data from the patients and control subjects. The severity of dystonia was determined using the Fahn-Marsden Dystonia Rating Scale.¹² We evaluated patients with blepharospasm using the Jankovic Rating Scale and the Blepharospasm Disability Index,¹³ patients with cervical dystonia using the Tsui Rating Scale,¹⁴ and patients with writer's cramp using the Writer's Cramp Rating Scale and the Arm Dystonia Disability Scale.^{15,16}

We assessed non-motor symptoms using clinical scales that had been validated for the Brazilian population. Cognition was assessed by means of the Mini Mental State Examination.¹⁷ The Beck Depression Inventory (BDI) and Beck Anxiety Inventory (BAI) were used to determine self-reported levels of depression and anxiety.^{18,19} The Social Phobia Inventory was used to identify subjects with suspected social phobia.²⁰ Symptoms of apathy were evaluated using the Apathy Scale (AS).²¹

Excessive daytime sleepiness was assessed using the Epworth Sleepiness Scale.²² Sleep quality was evaluated using the Pittsburgh Sleep Quality Index (PSQI).²³

We evaluated the presence of pain over the previous 3 months by using a structured questionnaire based on the Brief Pain Scale²⁴ (prevalence, monthly frequency, intensity according to a numerical visual scale, and site affected according to a drawing of the specific location). The World Health Organization Quality of Life brief scale (WHOQOL-BREF) was used to evaluate quality of life.²⁵

All subjects were evaluated in either one or two sessions. They were initially instructed to provide self-reported responses to the questionnaires. The examiner then checked the responses and, if necessary (in cases in which patients were unable to respond to all the questions or if there were any doubts), the questionnaire was reapplied. In cases of inability to use self-reported scales (due to severe dystonia or low education levels), a trained examiner applied the instruments to the subject.

Statistics

We performed descriptive analysis on all the clinical data. For comparisons between groups, two comparative analyses were performed.

Firstly, we compared all the patients versus the control group. To compare numerical variables, we used analysis of variance, followed by the Bonferroni post hoc test when appropriate. For categorical data,

we used the exact chi-square test and odds ratio estimates through binary logistic regression.

We then compared all three subtypes of dystonia with the controls, simultaneously. Non-adjustment was made with regard to matching for sex, age, and schooling levels between these groups. In this analysis, we used multivariate analysis of covariance, followed by the Bonferroni post hoc test when appropriate. The factors analyzed were groups and sex, as categorical variables, and age and schooling as numerical covariates. For the categorical data, we used the exact chi-square test and odds ratio estimates through binary logistic regression.

The Spearman rank correlation test was used to evaluate associations between the motor scales.

The data were expressed as mean \pm SD, and $p < 0.05$ was assumed to be statistically significant. The data were analyzed using SPSS 17.0 statistical software (IBM, USA).

Results

We evaluated 80 patients and 80 control subjects. The patients group consisted of 28 patients with blepharospasm, including five patients with cranial dystonia (group 1); 28 patients with cervical dystonia, including five patients with craniocervical dystonia (group 2); and 24 patients with limb dystonia, including 22 with writer's cramp, one with leg dystonia and one with arm dystonia (group 3). Table 1 presents the clinical characteristics and demographic data on all the patients and control subjects.

Comparing all the patients with the control group, there were no significant differences between the groups according to age, gender, schooling, or Mini-Mental State Examination scores. The patients had presented dystonia for 10–15 years and were using antidepressants more frequently than were the controls ($p = 0.038$).

Both the majority of patients ($n = 41$) and the majority of participants in the control group ($n = 55$) had at least one comorbidity ($p = 0.024$). Cardiovascular diseases were predominant in both groups with comorbidities of patients (58.5%) and control participants (63.6%) ($p = 0.612$), followed by endocrine and metabolic diseases (46.3% and 38.2%, respectively, $p = 0.422$), and neuropsychiatric diseases (39% and 23.6%, $p = 0.104$).

We found significant differences between the groups regarding their scores from the BDI, BAI, AS, PSQI, and Numerical Visual Scale for pain; however, there were no differences between the groups regarding their scores from the Social Phobia Inventory and Epworth Sleepiness Scale (Table 1).

In the BDI, the patients had higher scores than the controls. They presented more than twice the risk of having a depressive symptom ($BDI \geq 12$) ($p = 0.004$; odds ratio [OR] = 2.58; 95% confidence interval [CI] = 1.32–5.04), and more of them presented moderate and severe depressive symptoms ($BDI \geq 20$) ($p = 0.024$). They also presented higher scores in the BAI than did the controls, with a higher chance of presenting a symptom of anxiety ($BAI \geq 8$) ($p = 0.001$; OR = 3.58; 95% CI = 1.67–7.67).

From analysis of the AS, the patients showed significantly higher scores ($p = 0.002$) and their risk of apathy ($AS \geq 14$) was three times

higher than that of the controls ($p = 0.002$; OR = 2.96; 95% CI = 1.49–5.87). Moreover, they presented higher scores in the PSQI than did the controls, and their sleep quality was more frequently impaired ($PSQI > 5$) than was that of the controls ($p = 0.007$; OR = 2.37; 95% CI = 1.25–4.47). Multivariate regression analysis showed that the BDI and BAI scores ($p = 0.004$ and $p < 0.001$) influenced the PSQI scores, whereas there was no effect on pain ($p = 0.485$) or the use of antidepressants among the subjects ($p = 0.730$).

The dystonic patients presented significantly more intense and frequent pain than did the controls. They were 2.5 times more likely to complain of pain than were the controls ($p = 0.019$; OR = 2.58; CI = 1.16–5.71). Most of those with cervical dystonia (87%) and writer's cramp (76%) reported having pain at the site of their dystonic movements, while most of the patients with blepharospasm (67%) reported having pain in other parts of the body.

The patients with dystonia presented lower total scores in the WHOQOL-BREF measurement than those of the controls (Table 1). They showed lower scores in physical and psychological evaluations, but not in the social relationship or environmental domains. In multivariate analysis, the presence of pain ($p = 0.029$), BDI scores ($p < 0.001$), AS scores ($p < 0.001$), and type of dystonia ($p = 0.015$) influenced the WHOQOL-BREF total score, but there was no influence on the severity of motor symptoms measured by the Fahn–Marsden Dystonia Rating Scale ($p = 0.198$).

Comparing the patient subgroups with the control group, group 3 was the only group in which males predominated. Group 1 was significantly older, with lower schooling and lower Mini-Mental State Examination scores than either of the other two subgroups of patients or the controls. Schooling ($p < 0.001$) and age ($p = 0.046$) influenced the Mini-Mental State Examination scores of the patients, but there was no influence from the type of dystonia ($p = 0.854$).

The Fahn–Marsden Dystonia Rating Scale scores correlated significantly with the scores on the scores on the Jankovic Rating Scale ($p = 0.0001$; correlation coefficient (cc) = 0.71), Arm Dystonia Disability Scale ($p = 0.0001$; cc = -0.77), Writer's Cramp Rating Scale part B ($p = 0.01$; cc = -0.53), and Tsui Rating Scale ($p = 0.02$; cc = -0.42). However, there were no correlations with the scores on the Blepharospasm Disability Index ($p = 0.15$; cc = 0.27) or the Writer's Cramp Rating Scale part A ($p = 0.15$; cc = -0.31). These observations suggest that the scores on the Fahn–Marsden Dystonia Rating Scale generally reflected the severity of dystonia in the different groups of patients. Group 1 and group 2 did not show any difference in their Fahn–Marsden Dystonia Rating Scale scores, while group 3 presented lower scores than either of the other subgroups ($p = 0.013$).

In a group analysis, we found that the prevalence of psychiatric symptoms presented by group 3 was not as high as the prevalence among the patients in groups 1 and 2. Group 1 had higher BDI scores than those of all the other groups. They also showed higher BAI and AS scores than those of group 3 and the controls (Table 2).

Group 1 was five times more likely to experience pain than were the controls ($p = 0.006$; OR = 5.38; 95% CI = 1.63–17.78).

Table 1. Demographic and Clinical Characteristics of 80 Patients with Focal and Segmental Idiopathic Dystonia and 80 Control Subjects

| | Patients | Control Subjects | p |
|-------------------------------|----------------------------|-------------------|-------|
| | Total | Total | |
| Number | 80 | 80 | – |
| Gender (M/F) | 29/51 | 29/51 | – |
| Age (years) | 58.8 ± 14.2 | 56.5 ± 13.3 | 0.298 |
| Schooling (years) | 9.1 ± 6.1 | 9.5 ± 4.8 | 0.550 |
| % with comorbidities | 51.2 | 68.7 ^a | 0.024 |
| % with use of benzodiazepines | 18.7 | 11.2 | 0.184 |
| % with use of antidepressants | 23.7 ^a | 11.2 | 0.038 |
| Duration of disease (years) | 12.8 ± 9.7 | – | – |
| Age at disease presentation | 45.8 ± 13.3 | – | – |
| FMDRS scores | 5.5 ± 3.3 | – | – |
| MMSE | 25.90 ± 3.16 | 26.55 ± 2.93 | 0.180 |
| BDI | 12.64 ± 10.83 ^a | 9.05 ± 7.32 | 0.015 |
| BAI | 10.40 ± 9.22 ^a | 6.33 ± 8.86 | 0.005 |
| AS | 13.89 ± 8.37 ^a | 10.08 ± 6.62 | 0.002 |
| SPIN | 17.98 ± 13.63 | 14.33 ± 12.02 | 0.074 |
| ESS | 7.89 ± 4.72 | 8.85 ± 4.82 | 0.204 |
| PSQI | 7.51 ± 4.1 ^a | 5.91 ± 4.17 | 0.017 |
| Pain, NVS scores | 6.6 ± 2.5 ^a | 5.3 ± 2.4 | 0.018 |
| % with pain | 80 ^a | 50 | 0.001 |
| WHOQOL-BREF | | | |
| Total | 63.9 ± 15.5 ^a | 70.2 ± 13.3 | 0.007 |
| Physical | 62.7 ± 17.1 ^a | 73.0 ± 17.2 | 0.001 |
| Psychological | 64.9 ± 20.7 ^a | 71.2 ± 16.4 | 0.037 |
| Social relationships | 68.6 ± 47.4 | 71.5 ± 17.2 | 0.606 |
| Environmental | 64.2 ± 14.4 | 64.8 ± 15.1 | 0.780 |

Abbreviations: AS, Apathy Scale; BAI, Beck Anxiety Inventory; BDI, Beck Depression Inventory; ESS, Epworth Sleepiness Scale; FMDRS, Fahn–Marsden Dystonia Rating Scale; MMSE, Mini Mental State Examination; NVS, Numeric Visual Scale; PSQI, Pittsburgh Sleep Quality Index; SPIN, Social Phobia Inventory; WHOQOL-BREF, World Health Organization Quality of Life Brief Scale.

Data were compared using analysis of variance and chi-square.

^aDifferent from the other group ($p \leq 0.05$).

Their risk of having pain symptoms was higher than that observed for group 2 ($p = 0.005$; OR = 4.63; 95% CI = 1.59–13.49) or group 3 ($p = 0.056$; OR = 2.72; 95% CI = 0.97–1.02). The Fahn–Marsden Dystonia Rating Scale scores did not affect the results from the BDI and BAI, AS, or PSQI ($p = 0.328$), or the presence of pain ($p = 0.250$).

Group 2 showed higher BAI scores and higher AS scores than the controls. Groups 2 and 3 presented higher PSQI scores than the controls (Table 2).

From analysis on all the different subgroups, we observed that group 1 was the most affected in terms of quality of life, which includes the physical and social relationship domains. Groups 1 and 2 were equally

Table 2. Demographic and Clinical Characteristics of Subgroups of Patients with Focal and Segmental Idiopathic Dystonia and 80 Control Subjects

| | Group 1 | Group 2 | Group 3 | Group 4 | dF | F | p |
|----------------------|-------------------------|-------------|-------------------|-------------|----|-------|--------------------|
| Number | 28 | 28 | 24 | 80 | | | |
| Gender (M/F) | 23/5 | 20/8 | 8/16 ^a | 29/51 | | | 0.002 |
| Age (years) | 66.6 ± 9.1 ^a | 57.0 ± 13.1 | 51.7 ± 16.1 | 56.5 ± 13.3 | | | 0.001 |
| Schooling (years) | 5.1 ± 5.6 ^a | 10.5 ± 6.5 | 11.9 ± 3.6 | 9.5 ± 4.8 | | | 0.001 |
| MMSE | 26.1 ± 0.6 | 26.1 ± 0.5 | 26.5 ± 0.5 | 26.5 ± 0.3 | 3 | 0.259 | 0.854 |
| BDI | 16.8 ± 2.3 | 10.4 ± 1.8 | 9.4 ± 1.9 | 8.7 ± 1.0 | 3 | 3.348 | 0.021 ^a |
| BAI | 12.2 ± 2.2 | 10.1 ± 1.8 | 6.2 ± 1.9 | 5.6 ± 1.0 | 3 | 3.373 | 0.020 ^a |
| AS | 16.2 ± 1.9 | 14.1 ± 1.6 | 11.1 ± 1.6 | 10.2 ± 0.8 | 3 | 3.486 | 0.017 ^a |
| SPIN | 15.6 ± 3.2 | 18.3 ± 2.6 | 13.6 ± 2.8 | 13.8 ± 1.5 | 3 | 0.812 | 0.489 |
| ESS | 9.0 ± 1.2 | 7.4 ± 1.0 | 8.3 ± 1.1 | 8.6 ± 0.6 | 3 | 0.458 | 0.712 |
| PSQI | 8.3 ± 1.0 | 8.1 ± 0.8 | 6.7 ± 0.9 | 5.6 ± 0.5 | 3 | 3.204 | 0.025 ^a |
| WHOQOL-BREF | | | | | | | |
| Total | 57.5 ± 3.7 | 65.7 ± 2.9 | 68.5 ± 3.1 | 70.6 ± 1.7 | 3 | 3.611 | 0.015 ^a |
| Physical | 61.6 ± 4.3 | 63.8 ± 3.5 | 66.0 ± 3.7 | 73.4 ± 1.9 | 3 | 3.620 | 0.015 ^a |
| Psychological | 58.9 ± 4.7 | 66.3 ± 3.8 | 72.5 ± 4.0 | 72.2 ± 2.1 | 3 | 2.479 | 0.063 |
| Social relationships | 52.3 ± 8.9 | 69.1 ± 7.2 | 91.7 ± 7.6 | 71.6 ± 4.0 | 3 | 3.709 | 0.013 ^a |
| Environmental | 57.9 ± 3.7 | 63.7 ± 3.0 | 68.4 ± 3.1 | 65.2 ± 1.7 | 3 | 1.512 | 0.214 |

Abbreviations: AS, Apathy Scale; BAI, Beck Anxiety Inventory; BDI, Beck Depression Inventory; dF, degrees of freedom; ESS, Epworth Sleepiness Scale; F, multivariate F value; MMSE, Mini Mental State Examination; PSQI, Pittsburgh Sleep Quality Index; SPIN, Social Phobia Inventory; WHOQOL-BREF, World Health Organization Quality of Life Brief Scale.

Date were compared using multivariate analysis of covariance.

Group 1, blepharospasm patients; group 2, cervical dystonia patients; group 3, writer's cramp patients; group 4, control subjects.

^ap ≤ 0.05.

affected in regard to the physical domain compared with the controls, while group 3 was the least affected in all domains (Table 2).

Discussion

Our study confirmed previously published observations that indicated that non-motor symptoms are more prevalent in patients with idiopathic focal or segmental dystonia. Our patients with blepharospasm, cervical dystonia, and writer's cramp presented more symptoms of depression, anxiety, apathy, pain, and impaired sleep quality than did the control subjects. Nonetheless, despite having poor sleep quality, they did not complain of excessive daytime sleepiness. In addition, even though they showed more anxiety symptoms, the incidence of social phobia was not higher.

Several studies have already indicated that the prevalence of depressive symptoms in patients with dystonia is higher, thus indicating that depression is probably a common clinical problem associated with this disorder.^{6,8,11,26} However, for some authors, the association between dystonia and anxiety was not very well defined.¹¹

In our sample, patients with focal dystonia presented significantly more symptoms of anxiety than did the controls. This was also observed in some other recent studies.^{7,8,26} Only one study did not find any association between symptoms of anxiety and dystonia.⁶ Despite these contradictory findings, most recent studies corroborate the notion that there is an association between dystonia and symptoms of anxiety. We did not find higher levels of symptoms of social phobia among our patients; however, there was a statistical trend towards this. Other studies have also indicated a high frequency of social phobia among patients with cervical dystonia.^{27,28} We also observed higher prevalence of symptoms of apathy in our patients, as also described previously.²⁹

Pain and discomfort are common symptoms among patients with focal dystonia.¹¹ Most of our patients presented pain, and, in most cases, this was related to the body region affected by dystonic movements, as already described in other studies.⁵ Pain is usually evident in the body region affected by dystonia; however, pain levels do not always correlate with the objective severity of neurological signs, as we also observed in our sample.³⁰ However, treatment of dystonia through local injections of

botulinum toxin clearly reduces pain in these patients.³¹ Some studies have suggested that pain thresholds are lower in patients with dystonia than in healthy controls.³²

Voxel-based analyses showed a reduction in gamma-aminobutyric acid (GABA) receptor expression in the primary motor cortex, premotor cortex, secondary somatosensory cortex, and motor component of the cingulate gyrus in patients with early-onset generalized torsion dystonia (DYT-TOR1A) and sporadic dystonia that could lead to a lower threshold for pain.³³ We observed in our sample that more than half of our patients with blepharospasm also complained of pain that was unrelated to the site of dystonia. This finding might be related to the fact that these patients were older than the others, and other causes of pain associated with aging could be responsible for these symptoms. Further studies to clarify the mechanisms of pain associated with dystonia are needed.

Our patients presented lower sleep quality than that of the control subjects. Nevertheless, they did not show higher rates of daytime sleepiness. Other studies found the same results.^{11,34,35} The authors of a systematic review on sleep disorders in cases of dystonia suggested that sleep disturbances among these patients could have many origins, such as the same pathophysiological mechanisms that produce dystonia, medications, pain, the abnormal movements themselves, or psychosocial stress.³⁶ In our sample, symptoms of anxiety and depression especially influenced sleep quality, but not pain or the use of antidepressants. Our findings support the hypothesis that psychiatric disorders may be a significant factor related to the worsened quality of sleep of patients with dystonia.

One of the major difficulties in studying non-motor symptoms in movement disorders is the high prevalence of comorbidities and the interaction between these diseases and their symptoms. Just as insomnia can be a disease by itself, it can also be a symptom of depression or secondary to pain. Studying various non-motor symptoms together may be one way to evaluate these interactions and better understand what would be related to the pathophysiology of dystonia and what would be the consequence of this chronic disease.

Patients with dystonia may present non-motor symptoms for several reasons. In addition, some non-motor symptoms may interact with each other to cause or worsen other symptoms. Some of these might mainly be consequences of psychosocial effects relating to dystonia itself; however, dysfunctions in the basal ganglia circuits could be the cause of several of these non-motor symptoms.

We did not design our study to answer these questions, and further studies are needed in order to understand the mechanisms underlying these effects. However, our findings suggest that physical alterations caused by dystonia might also have been responsible for some of our patients' psychiatric complaints, as such complaints were more frequent among patients with blepharospasm and cervical dystonia than among those with writer's cramp. Among patients with blepharospasm, some authors have suggested that depression may be a cause of the facial feedback.³⁷

A recent study sought to assess correlations between psychiatric symptoms and dopaminergic dysfunction in movement disorders. It was found that patients with dystonia presented an inverse association

between the severity of depressive and anxiety symptoms and the availability of dopaminergic transporter in the left putamen.³⁸ Striatum connections such as the prefrontal cortex, amygdala, and locus coeruleus connect neuronal networks relating to the pathophysiology of anxiety. Thus, it is possible that the psychiatric symptoms found in these patients were, in part, secondary to striatal pathway dysfunction. It can therefore be seen that the pathophysiology of non-motor symptoms in cases of dystonia is complex and depends on the interplay between various clinical factors and underlying abnormalities of the functioning of the basal ganglia.

Nevertheless, the negative impact of non-motor symptoms on the quality of life indicates the importance of investigating their presence in patients with dystonia, in order to plan individualized treatments. As shown in previous studies, we also observed that patients with common focal dystonia presented worse quality of life than that of control subjects.^{4,39} The domains most affected were physical and psychological. The severity of motor symptoms as measured using the Fahn–Marsden Dystonia Rating Scale was not a relevant predictor of quality of life in the way that some non-motor symptoms were, especially pain and depression. Additionally, we observed that there was a difference in the quality of life depending on the clinical form of focal dystonia. We believe that discrimination through these non-motor symptoms explains this observation.

This study was the first Brazilian study evaluating and correlating the non-motor symptoms among patients with idiopathic focal and segmental dystonia. We included a relatively large and selected sample, and used clinical scales that had been validated for the Brazilian population. However, we only included a small number of patients with each different subtype of dystonia and the patients were not subjected to psychiatric evaluation or polysomnography for a more detailed clinical analysis.

In conclusion, our study reinforces previous observations, thus indicating that there was higher prevalence of symptoms of depression, anxiety, apathy and pain, and poorer quality of sleep, among patients with focal dystonia. This study also showed that these symptoms could influence one another.

References

1. Albanese A, Bhatia K, Bressman SB, Delong MR, Fahn S, Fung VS, et al. Phenomenology and classification of dystonia: a consensus update. *Mov Disord* 2013;28:863–873. doi: 10.1002/mds.25475
2. Epidemiological Study of Dystonia in Europe (ESDE) Collaborative Group. A prevalence study of primary dystonia in eight European countries. *J Neurol* 2000;247:787–792. doi: 10.1007/s004150070094
3. Stanley F, Jankovic J, Hallett M, Principles and practice of movement disorders. Philadelphia: Saunders; 2011 (2nd edition).
4. Page D, Butler A, Jahanshahi M, Quality of life in focal, segmental, and generalized dystonia. *Mov Disord* 2007;22:341–347. doi: 10.1002/mds.21234
5. Pekmezovic T, Svetel M, Ivanovic N, Dragasevic N, Petrovic I, Tepavcevic DK, et al. Quality of life in patients with focal dystonia. *Clin Neurol Neurosurg* 2009;111:161–164. doi: 10.1016/j.clineuro.2008.09.023

6. Fabbrini G, Berardelli I, Moretti G, Pasquini M, Bloise M, Colosimo C, et al. Psychiatric disorders in adult-onset focal dystonia: a case-control study. *Mov Disord* 2010;25:459–465. doi: 10.1002/mds.22983
7. Barahona-Corrêa B, Bugalho P, Guimarães J, Xavier M. Obsessive-compulsive symptoms in primary focal dystonia: a controlled study. *Mov Disord* 2011;26:2274–2278. doi: 10.1002/mds.23906
8. Lehn A, Mellick G, Boyle R. Psychiatric disorders in idiopathic-isolated focal dystonia. *J Neurol* 2014; 261:668–674. doi: 10.1007/s00415-014-7244-8
9. Defazio G, Berardelli A, Hallett M. Do primary adult-onset focal dystonias share aetiological factors? *Brain* 2007;130:1183–1193. doi: 10.1093/brain/awl355
10. Jinnah HA, Hess EJ. A new twist on the anatomy of dystonia: the basal ganglia and the cerebellum? *Neurology* 2006;67:1740–1741. doi: 10.1212/01.wnl.0000246112.19504.61
11. Stamelou M, Edwards MJ, Hallett M, Bhatia KP. The non-motor syndrome of primary dystonia: clinical and pathophysiological implications. *Brain* 2012;135:1668–1681. doi: 10.1093/brain/awr224
12. Burke RE, Fahn S, Marsden CD, Bressman SB, Moskowitz C, Friedman J. Validity and reliability of a rating scale for the primary torsion dystonias. *Neurology* 1985;35:73–77. doi: 10.1212/WNL.35.1.73
13. Jankovic J, Kenney C, Grafe S, Goertelmeyer R, Comes G. Relationship between various clinical outcome assessments in patients with blepharospasm. *Mov Disord* 2009;24:407–413. doi: 10.1002/mds.22368
14. Tsui JK, Eisen A, Stoessel AJ, Calne S, Calne DB. Double-blind study of botulinum toxin in spasmodic torticollis. *Lancet* 1986;2:245–247. doi: 10.1016/S0140-6736(86)92070-2
15. Wissel J, Kabus C, Wenzel R, Klepsch S, Schwarz U, Nebe A, et al. Botulinum toxin in writer's cramp: objective response evaluation in 31 patients. *J Neurol Neurosurg Psychiatry* 1996;61:172–175. doi: 10.1136/jnnp.61.2.172
16. Fahn S. Assessment of the primary dystonias. In: Munsat TL, editor. Quantification of neurologic deficit. Oxford: Butterworths; 1989. p. 241–270.
17. Bertolucci PH, Brucki SM, Campacci SR, Juliano Y. The Mini-Mental State Examination in an outpatient population: influence of literacy. *Arq Neuropsiquiatr* 1994;52:1–7. doi: 10.1590/S0004-282X1994000100001
18. Gomes-Oliveira MH, Gorenstein C, Neto FL, Andrade LH, Wang YP. Validation of the Brazilian Portuguese Version of the Beck Depression Inventory-II in a community sample. *Rev Bras Psiquiatr* 2012;34:389–394. doi: 10.1016/j.rbp.2012.03.005
19. Cunha JA. Manual da versão em português das Escalas Beck. São Paulo: Casa do Psicólogo; 2001.
20. de L. Osório F, Crippa JAS, Loureiro SR. Cross-cultural validation of the Brazilian Portuguese version of the Social Phobia Inventory (SPIN): study of the items and internal consistency. *Rev Bras Psiquiatr* 2009;31:25–29.
21. Guimaraes HC, Fialho PPA, Carvalho VA, dos Santos EL, Caramelli P. Brazilian caregiver version of the Apathy Scale. *Dement Neuropsychol* 2009;3:321–326. doi: 10.1590/S1980-57642009DN30400010
22. Bertolazi AN, Fagundes SC, Hoff LS, Pedro VD, Barreto SS. Portuguese-language version of the Epworth sleepiness scale: validation for use in Brazil. *J Bras Pneumol* 2009;35:877–883. doi: 10.1590/S1806-37132009000900009
23. Bertolazi AN, Fagundes SC, Hoff LS, Dartora EG, Miozzo IC, de Barba ME, et al. Validation of the Brazilian Portuguese version of the Pittsburgh Sleep Quality Index. *Sleep Med* 2011;12:70–75. doi: 10.1016/j.sleep.2010.04.020
24. Ferreira KA, Teixeira MJ, Mendonza TR, Cleland CS. Validation of brief pain inventory to Brazilian patients with pain. *Support Care Cancer* 2011;19:505–511. doi: 10.1007/s00520-010-0844-7
25. Fleck MP, Louzada S, Xavier M, Chachamovich E, Vieira G, Santos L, et al. Application of the Portuguese version of the abbreviated instrument of quality life WHOQOL-BREF. *Rev Saude Publica* 2000;34:178–183. doi: 10.1590/S0034-89102000000200012
26. Yang J, Shao N, Song W, Wei Q, Ou R, Wu Y, et al. Nonmotor symptoms in primary adult-onset cervical dystonia and blepharospasm. *Brain Behav* 2016;7:e00592. doi: 10.1002/brb3.592
27. Lauterbach EC, Freeman A, Vogel RL. Differential DSM-III psychiatric disorder prevalence profiles in dystonia and Parkinson's disease. *J. Neuropsychiatry Clin Neurosci* 2004;16:29–36. doi: 10.1176/jnp.16.1.29
28. Lencer R, Steinlechner S, Stahlberg J, Rehling H, Orth M, Baeumer T, et al. Primary focal dystonia: evidence for distinct neuropsychiatric and personality profiles. *J Neurol Neurosurg Psychiatry* 2009;80:1176–1179. doi: 10.1136/jnnp.2008.170191
29. Louis ED, Huey ED, Gerbin M, Viner AS. Apathy in essential tremor, dystonia, and Parkinson's disease: a comparison with normal controls. *Mov Disord* 2012;27:432–434. doi: 10.1002/mds.24049
30. Kutvonen O, Dastidar P, Nurmikko T. Pain in spasmodic torticollis. *Pain* 1997;69:279–286. doi: 10.1016/S0304-3959(96)03296-4
31. Camargo CH, Cattai L, Teive HA. Pain relief in cervical dystonia with botulinum toxin treatment. *Toxins (Basel)* 2015;7:2321–2335. doi: 10.3390/toxins7062321
32. Lobbezoo F, Tanguay R, Thon MT, Lavigne GJ. Pain perception in idiopathic cervical dystonia (spasmodic torticollis). *Pain* 1996;67:483–491. doi: 10.1016/0304-3959(96)03153-3
33. Garibotto V, Romito LM, Elia AE, Soliveri P, Panzacchi A, Carpinelli A, et al. Perani D. In vivo evidence for GABAA receptor changes in the sensorimotor system in primary dystonia. *Mov Disord* 2011;26:852–857. doi: 10.1002/mds.23553
34. Eichenseer SR, Stebbins GT, Comella CL. Beyond a motor disorder: a prospective evaluation of sleep quality in cervical dystonia. *Parkinsonism Relat Disord* 2014;20:405–408. doi: 10.1016/j.parkreldis.2014.01.004
35. Paus S, Gross J, Moll-Müller M, Hentschel F, Spottke A, Wabbels B, et al. Impaired sleep quality and restless legs syndrome in idiopathic focal dystonia: a controlled study. *J Neurol* 2011;258:1835–1840. doi: 10.1007/s00415-011-6029-6
36. Hertenstein E, Tang NKY, Bernstein CJ, Nissen C, Underwood MR, Sandhu HK. Sleep in patients with primary dystonia: A systematic review on the state of research and perspectives. *Sleep Med Rev* 2015;26:95–107. doi: 10.1016/j.smrv.2015.04.004
37. Bedarf JR, Kebir S, Michelis JP, Wabbels B, Paus S. Depression in blepharospasm: a question of facial feedback? *Neuropsychiatr Dis Treat* 2017;14:1861–1865. doi: 10.2147/NDT.S141066
38. Di Giuda D, Camardese G, Coccilillo F, Fasano A. Dopaminergic dysfunction and psychiatric symptoms in movement disorders: a 123I-FP-CIT SPECT study. *Eur J Nucl Med Mol Imaging* 2012;39:1937–1948. doi: 10.1007/s00259-012-2232-7
39. Basurovic N, Svetel M, Pekmezovic T, Kostic V. Evaluation of the quality of life in patients with segmental dystonia. *Vojnosanit Pregl* 2012;69:759–764. doi: 10.2298/VSP1209759B