Motor and non-motor symptoms in cervical dystonia

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CHAPTER 2

2

Psychiatric co-morbidity is highly prevalent in idiopathic cervical dystonia and significantly influences health-related quality of life: results of a controlled study

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ABSTRACT

Introduction: The aim of this study was to systematically investigate the prevalence of psychiatric disorders and factors influencing health-related quality of life (HR-QoL) in cervical dystonia (CD) patients, in the context of objective dystonia motor severity.

Methods: We studied 50 CD patients and 50 matched healthy controls. Psychiatric assessment included the MINI–PLUS interview and quantitative questionnaires. Dystonia motor severity (based on video evaluation), pain and disability were determined with the TWSTRS rating scale. In addition, severity of tremor and jerks was evaluated with the 7-point CGI-S scale. HR-QoL was determined with the RAND-36 item Health Survey and predictors of HR-QoL were assessed using multiple regression analysis.

Results: In CD patients, the MINI-PLUS revealed a significantly higher prevalence of psychiatric disorders (64% vs. 28%, p=0.001), with substantially more depression (32% vs. 14%) and anxiety disorders (42% vs. 8%). This was confirmed by the quantitative rating scales. Disease characteristics did not differ between patients with and without a psychiatric diagnosis. HR-QoL in dystonia patients was significantly lowered. The most important predictors of HR-QoL appeared severity of depressive symptoms, pain and disability, but not severity of motor symptoms.

Conclusion: Psychiatric co-morbidity is highly prevalent and is an important predictor of HR-QoL in CD patients, rather than dystonia motor severity. Our findings support the theory of a shared neurobiology for motor and non-motor features and highlight the need for systematic research into psychiatric disorders in dystonia. Adequate treatment of psychiatric symptoms could significantly contribute to better overall quality of life of CD patients.

INTRODUCTION

Cervical dystonia (CD) is a hyperkinetic movement disorder characterized by sustained or intermittent contractions of the cervical musculature, leading to abnormal head postures. It is the most common form of adult-onset focal dystonia, with a prevalence ranging between 28-183 cases per million people [1].

Growing evidence suggests that the phenotype of CD also includes an important non-motor component, with psychiatric co-morbidity being most prevalent. The lifetime prevalence of psychiatric disorders can reach up to 91.4% in CD patients, compared with 35% in the general population [2]. Susceptibility for specific psychiatric disorders differed between studies with either a high prevalence of depressive symptoms [3–8], anxiety symptoms/ panic disorders [2,5–7], obsessive-compulsive symptoms [7,8] or substance abuse [7].

Importantly, some studies even showed that psychiatric co-morbidity is the most important predictor of poorer health-related quality of life (HR-QoL) in CD patients [9–11]. However, methodological limitations were noted in these studies; an appropriate control group and an objective CD motor score were not systematically applied. Importantly, a systematic interview assessing all axis 1 DSM-IV diagnoses complemented with specific questionnaires for the most prevalent disorders was also lacking.

The recognition of psychiatric co-morbidity in CD still raises the question whether this is part of the phenotype of dystonia or the result of living with a chronic motor disorder. A strong argument in favor of a shared pathophysiology hypothesis is that approximately 70% of the diagnosed psychiatric disorders manifested before the onset of motor symptoms [4,6,7]. Moreover, studies comparing CD with other chronic disorders with pain and/or disability such as cervical spondylosis [3] or alopecia areata [5] showed higher prevalence's of psychiatric disorders in dystonia patients, also implying a primary phenotype.

In order to systematically investigate the prevalence of psychiatric disorders, HR-QoL and factors influencing HR-QoL in CD patients, we examined motor severity, psychiatric co-morbidity and HR-QoL in 50 CD patients and compared it with 50 matched healthy controls. The prevalence of psychiatric disorders was assessed through a structured interview based on the DSM-IV criteria, supplemented by specific questionnaires regarding depression, anxiety and obsessive-compulsive disorders. The relative timing of onset of motor symptoms and psychiatric symptoms was another focus point.

METHODS

Subjects

This study included 50 patients (mean age 54 years, range 20-80 years) with a clinically diagnosed idiopathic cervical dystonia, based on neurological examination, and 50 age- and sex-matched controls (mean age 54 years, range 24-83 years).

For all participants, exclusion criteria were relevant neurological co-morbidity and the use of serotonergic drugs or other antidepressants. An additional exclusion criterion for the CD patients was onset of CD before adulthood (<18yr, based on the classification of Albanese et al. [12], and an additional exclusion criterion for the healthy controls consisted of a positive first- or second-degree family history of dystonia. Due to the exclusion of subjects using serotonergic drugs, eight CD patients could not be included in the study. Furthermore, several additional patients within the different hospitals were not asked to participate because of known medication use, and two patients did not want to participate because of severe psychiatric complaints.

Patients were recruited via several outpatient clinics and via the dystonia patient association. Controls were recruited by open advertisements or were acquaintances of patients and investigators.

The number of 50 subjects in both the patient and control group was based on a sample size calculation performed prior to the study. We used psychiatric co-morbidity in myoclonus-dystonia (MD) patients as a reference [13,14]. In these studies a power of 0.85 is retained, using a two-sided Z test with a pooled variance and an α-value of 0.05. The results within the two studies pointed towards 23 [13] and 44 [14] subjects per group. As we anticipated that only 85% of included participants would complete the study protocol 50 subjects were included into each group.

Informed consent was obtained from all participants and the study was approved by the local ethics committee.

Motor Assessment

Motor assessment was performed using a systematic video protocol. If patients were treated with botulinum toxin, neurological assessment was performed between two weeks prior to or one week after the treatment (based on the individual treatment response time), in order to obtain the least influenced dystonia motor score. Based on the video, severity of dystonia was independently scored by two experts (MS, VH). The Toronto Western Spasmodic Torticollis Rating Scale (TWSTRS) [15] was used to assess cervical dystonia severity, pain (not explained by other conditions) and disability. We hypothesized that psychiatric co-morbidity could be dependent of the CD subtype, like predominant dystonia or predominant tremor/jerks. Therefore, overall clinical severity of

dystonia and severity of jerks and tremor were separately evaluated by using the 7-point Clinical Global Impression Scale (CGI-S) [16].

Psychiatric assessment and health-related quality of life

The presence of current/previous psychiatric disorders, as defined in the Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition (DSM-IV), was assessed using the Mini International Neuropsychiatric Interview – PLUS (MINI-PLUS), Dutch version 5.0.0 [17]. With regard to quantitative psychiatric assessment, the severity of depression, anxiety and obsessive-compulsive disorder was assessed in all subjects using the Beck Depression Inventory (BDI) [18], the Beck Anxiety Inventory (BAI) [19], and the Yale Brown Obsessive Compulsive Scale (Y-BOCS) [20]. For both the BDI and BAI guidelines are recommended for the interpretation of the total score. With regard to the BDI, scores between 0-9 could be interpreted as minimal depressive symptoms, 10-18 as mild, 19-29 as moderate and 30-63 as severe depressive symptoms [21]. The BAI could be interpreted as follows: 0-9 normal or no anxiety, 10-18 mild-moderate, 19-29 moderate to severe and 30-63 as severe anxiety [22].

HR-QoL was assessed with the RAND-36 item Health Survey (RAND-36) [23].

Statistical analysis

Statistical analysis was performed using PASW Statistics 22 for Windows (SPSS Statistics, Chicago IL, USA), and differences were considered significant at $p<0.05$.

In the patient group, we assessed interobserver agreement of the dystonia rating scales between the two independent raters by the Intraclass Correlation Coefficient (ICC).

A Pearson Chi-square test or Fisher's Exact Test was used to assess the differences in demographic features and the presence of DSM-IV diagnoses between patients and healthy controls. A Mann-Whitney U test was used to assess group differences among quantitative psychiatric rating scales and the nine domains of HR-QoL.

Because we had a relative small number of patients, we used the Spearman's rho test to assess the correlation between the domains of HR-QoL and clinical characteristics in the patient group. For the discrete dichotomous variables the correlation was assessed as point-biserial correlation with the Spearman *r* test. With multiple regression analysis, we determined the influence of variables with a p-value of <0.20 in the univariate analysis using backward elimination. The data fulfilled the assumption of normal distribution in order to perform a linear regression analysis and there was no multicollinearity between variables.

RESULTS

Participants characteristics

The fifty patients with cervical dystonia included in this study had a mean total TWSTRS score of 34.85 (SD=12.75) (mean subscores: motor severity 16.02 (SD=4.88), disability 10.52 (SD=5.37), pain 8.31 (SD=5.97)), a mean CGI-S dystonia score of 3.91 (SD=1.39) and a mean CGI-S jerks/tremor score of 2.43 (SD=1.32).

Four patients had a clear positive family history of cervical dystonia in first or second degree family members. In 14 patients a positive family history was suspected.

Motor assessment showed almost perfect intraclass correlation coefficients between raters [24]. The interobserver agreement scores for the TWSTRS severity scale, the CGI-S dystonia scale en the CGI-S-jerks/tremor scale were 0.84, 0.87 and 0.91 respectively.

Psychiatric disorders and quantitative psychiatric rating scales

Results of the structured interview assessing the presence of a DSM-IV diagnosis are shown in table 1. Overall, the patient group showed a significantly higher prevalence of psychiatric disorders (64% vs. 28%, p=0.001), with profoundly more depressive disorders (32% vs. 14%, p=0.03) and anxiety disorders (42% vs. 8%, p<0.001). Other DSM-IV diagnoses were not significantly increased in CD patients.

Additionally, on the quantitative rating scales, patients scored significantly worse on both depression (10.62 vs. 4.38, p<0.001) and anxiety rating scales (10.00 vs. 3.76, p<0.001). Based on the subdivision as described in the methods section, 23 patients (46%) had aberrant scores on the BDI (13 mild, 10 moderate) in comparison to 12% (n=6: 5 mild, 1 moderate, p<0.001) in the healthy control group. With regards to the BAI, 20 patients (40%) had aberrant scores (13 mild, 6 moderate, 1 severe) compared to 8% (n=4, 3 mild, 1 moderate, p<0.001) in the healthy control group. The Y-BOCS rating scale showed higher total scores in the patients compared with controls (0.92 vs 0.08, p=0.02). However, except for one subject (total score 12 out of 40), all scores were within the subclinical range.

Of the 32 patients who fulfilled the criteria of a psychiatric disorder according to the DSM-IV criteria, 20 patients (62.5%) suffered from psychiatric illness before onset of motor symptoms.

Comparing the disease characteristics of the patients who fulfilled the criteria of a DSM-IV diagnosis with the patients without a DSM-IV diagnosis did not reveal any differences (Table 2). Duration of dystonia (12.91yr vs. 13.89yr, p=0.78), a positive family history (3.1% vs. 16.7%, p=0.13) or scores on the dystonia rating scales (TWSTRS total score: 36.67 vs. 31.62, p=0.22; CGI-S dystonia score: 3.97 vs. 3.81, p=0.86 and CGI-S jerks/tremor score: 2.34 vs. 2.58, p=0.94) were not significantly different between the two groups.

Table 1
Frequencies of psychiatric disorders (DSM-IV) and scores on psychiatric questionnaires

	CD (n=50)	HC (n=50)	p-value
Treatment MHC (n, %)	33 (66)	17 (34)	<0.01
DSM-IV diagnosis (n, %)			
Mood			
- Depressive episode	16 (32)	7 (14)	0.03
- Dysthymia	4 (8)	0 (0)	0.11
- Combined depression/anxiety	1 (2)	0 (0)	1
- Total	19 (38)	7 (14)	<0.01
Anxiety			
- Panic disorder	5 (10)	1 (2)	0.20
- Agoraphobia	12 (24)	1 (2)	<0.01
- Social phobia	9 (18)	0 (0)	<0.01
- Simple phobia	8 (16)	2 (4)	0.05
- Generalized anxiety disorder	6 (12)	0 (0)	0.03
- Total	21 (42)	4 (8)	<0.01
Total diagnosis	32 (64)	14 (28)	<0.01
Psychiatric rating scales (mean, SD)			
BDI	10.62 (7.34)	4.38 (4.48)	<0.01
BAI	10.00 (6.96)	3.76 (3.95)	<0.01
Y-BOCS	0.92 (2.35)	0.08 (0.40)	0.02

Values are presented as n (%) or mean (SD). CD = cervical dystonia. HC = healthy control. MHC = mental health care.

Table 2
Disease characteristics of patients with and without a DSM-IV diagnosis

	CD with DSM-IV diagnosis (n=32)	CD without DSM-IV diagnosis (n=18)	p-value
Age at onset dystonia (mean, SD)	39.81 (12.79)	43.22 (9.51)	0.22
Dystonia duration in years (mean, SD)	12.91 (10.48)	13.78 (10.68)	0.78
Positive family history[a] (n, %)	1 (3.1)	3 (16.7)	0.13
TWSTRS (mean, SD)			
- Severity	16.08 (5.31)	15.92 (4.15)	0.88
- Pain	9.41 (6.10)	6.37 (5.36)	0.09
- Disability	11.19 (5.37)	9.33 (5.31)	0.27
- Total	36.67 (13.23)	31.62 (11.50)	0.22
CGI-S dystonia (mean, SD)	3.97 (1.52)	3.81 (1.15)	0.86
CGI-S jerks/tremor (mean, SD)	2.34 (1.09)	2.58 (1.69)	0.94

Values are presented as mean (SD) or n (%). CD = cervical dystonia. HC = healthy control. [a]History of dystonia in first- or second-degree relatives.

HR-QoL and predictors of HR-QoL

The results of the scores on the nine domains of HR-QoL are shown in supplementary figure 1. The patient group scored significantly worse on the first eight domains compared to the healthy controls. Univariate analysis showed that age, fulfillment of a DSM-IV diagnosis and high scores on the BDI, BAI, YBOCS, TWSTRS pain and TWSTRS disability negatively affect the first eight domains of HR-QoL. Duration of dystonia had a mild effect on the domain expected health change ($p<0.20$) and the severity of dystonia (TWSTRS dystonia severity) had only a mild effect on the domain physical functioning ($p<0.20$), but not on the other domains of HR-QoL (Table 3).

Based on the univariate analysis, multiple regression analysis revealed that a reduced HR-QoL was significantly predicted by high scores on the BDI (domain: social functioning, role limitation emotional, mental health and vitality), by high scores on the TWSTRS pain rating (domain: role limitation emotional and pain), by high scores on the TWSTRS disability rating (domain: physical functioning) and by high scores on the BAI (domain: mental health) (Table 4).

To check if pain and disability, as important predictors of a reduced HR-QoL, were influenced mostly by motor severity or by psychiatric symptoms, we performed an additional multiple regression analysis. Univariate analyses showed that disability was associated with anxiety, depression, dystonia motor severity and pain. (Supp. table 1). Pain appeared to be associated with age, psychiatric co-morbidity, disability and dystonia motor severity. In the multiple regression analysis, severity of disability as measured by the TWSTRS disability subscale was significantly associated with pain (B 0.38, SE 0.11, β .42, $p<0.01$) and by the severity of depressive symptoms as measured by the BDI (B 0.20, SE 0.09, β .28, $p<0.05$) (R^2 adjusted 0.29). The degree of pain, as measured with the TWSTRS pain subscale, was significantly associated with the TWSTRS disability rating (B 0.47, SE 0.14, β .42, $p=0.001$) and anxiety symptoms as measured by the BAI (B 0.28, SE 0.10, β .33, $p=0.01$) (R^2 adjusted 0.32). Dystonia motor severity had no significant influence on disability or pain.

Table 3
Univariate analysis between the nine domains of HR-QoL and selected variables in cervical dystonia patients.

	PF	SF	RLP	RLE	MH	V	P	GHP	EHC
Demographic characteristics									
Age	0.10	0.15	0.29*	0.19†	0.29*	0.40**	0.13	0.09	-0.02
Gender	0,05	-0,05	0,01	-0,05	-0,03	0,01	0,01	0,13	-0,07
Psychiatry									
DSM-IV diagnosis	-0,28*	-0,40**	-0,34*	-0,28†	-0,45**	-0,46**	-0,22†	-0,27†	-0,08
BDI	-0.54**	-0.65**	-0.43**	-0.61**	-0.71**	-0.62**	-0.46**	-0.47**	-0.04
BAI	-0.44**	-0.25†	-0.25†	-0.45**	-0.65**	-0.52**	-0.42**	-0.47**	-0.15
Y-BOCS	0.15	-0.19†	-0.19†	-0.14	-0.15	-0.24†	-0.20†	-0.07	0.15
Dystonia characteristics									
Dystonia duration	-0.01	0.03	0.03	-0.16	0.02	0.02	0.10	0.01	-0.23†
TWSTRS Severity	-0.25†	0.04	0.08	0.11	0.11	0.10	-0.08	-0.08	0.00
TWSTRS Disability	-0.62**	-0.36**	-0.28*	-0.18	-0.22†	-0.33*	-0.50**	-0.45**	-0.00
TWSTRS Pain	-0.52**	-0.28†	-0.37**	-0.36**	-0.25†	-0.37**	-0.59**	-0.40**	-0.14
CGI-S jerks/tremor	-0.14	0.09	-0.07	0.06	0.02	-0.07	-0.12	0.03	-0.12

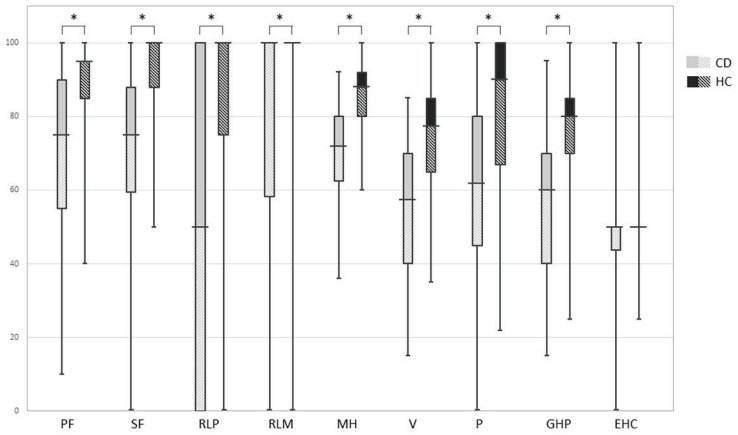
Data are shown as correlation coefficient. PF = physical functioning. SF = social functioning. RLP = role limitation physical. RLE = role limitation emotional. MH = mental health. V = vitality. P = pain. GHP = general health perception. EHC = expected health change. †p<0.20, *p<0.05, **p<0.01.

Table 4
Significant predictors of a reduced HR-QoL

Domain	Predictor(s)	Adjusted R Square	B°	β	p-value
Physical functioning	TWSTRS disability	0.36	-2.61 (0.49)	-.61	<0.001
Social functioning	BDI	0.43	-2.11 (0.34)	-.67	<0.001
Role limitation physical	-				
Role limitation emotional	BDI TWSTRS pain	0.47	-2.84 (0.58) -2.30 (0.71)	-.53 -.35	<0.001 <0.001
Mental health	BDI BAI	0.59	-1.10 (0.22) -0.57 (0.23)	-.57 -.28	<0.001 0.02
Vitality	BDI	0.42	-1.52 (0.25)	-.65	<0.001
Pain	TWSTRS pain	0.33	-2.40 (0.48)	-.58	<0.001
General health perception	-				
Expected health change	-				

Multiple linear regression analysis for the effect of predictors with a p-value of <0.20 in the univariate analysis. For the significant predictors, we calculated the adjusted R square, the B° (unstandardized coefficient with standard error in parenthesis) and β (standardized regression coefficient).

Supplementary figure 1
Health-related quality of life in CD patients and healthy controls.



Median values of the nine domains of HR-QoL (wide stripe), including interquartile ranges and minimum and maximum scores. CD = cervical dystonia. HC = healthy control. PF = physical functioning. SF = social functioning. RLP = role limitation physical. RLE = role limitation emotional. MH = mental health. V = vitality. P = pain. GHP = general health perception. EHC = expected health change. *p<0.001.

Supplementary table 1
Univariate analysis between the TWSTRS disability score and TWSTRS pain score and selected variables in cervical dystonia patients.

	TWSTRS disability	**TWSTRS pain**
Demographic		
Age	-0.16	-0.28*
Gender	-0.03	0.16
Psychiatry		
Total DSM-IV diagnosis	0.17	0.25†
BDI	0.38**	0.29*
BAI	0.24†	0.42**
Y-BOCS	0.11	0.24†
Motor		
Dystonia duration	-0.05	-0.12
TWSTRS Severity	0.47**	0.34**
TWSTRS Disability	NA	0.51**
TWSTRS Pain	0.51**	NA
CGI-S dystonia	0.38**	0.23†
CGI-S jerks/tremor	0.17	-0.03

Data are shown as correlation coefficient. NA = not applicable. †p<0.20, *p<0.05, **p<0.01.

DISCUSSION

In this study, we showed that a lifetime prevalence of psychiatric disorders, particularly depression and anxiety disorders, was significantly higher in CD patients compared to matched healthy controls. Notably, the prevalence found in our study is likely an underestimation, as patients using antidepressant medication were excluded. Furthermore, the first eight domains of HR-QoL were significantly lower in dystonia patients compared to healthy controls and this strongly related to the presence of depressive and anxiety symptoms, pain and disability, while there was no significant correlation with the objective severity of motor symptoms.

The higher prevalence of psychiatric disorders in CD patients was documented by the structured interview regarding DSM-IV axis 1 diagnostic categories, as well as the self-reported levels of depressive and anxiety symptoms using the BDI and BAI. Several other studies also found similar high prevalences of depressive disorders [2–5,7,8] and anxiety disorders [2,5–7] in CD patients, indicating an important non-motor component. The Y-BOCS rating scale showed a higher total score in the patients compared with the healthy controls. However, except for one subject (total score of 12 out of 40), all scores were within the subclinical range. Two previous studies have used the Y-BOCS in order to quantify obsessive-compulsive symptoms in CD patients. One study found similar scores on the Y-BOCS in CD patients [4]. However, of the 34 patients included, 44% used several anxiolytics and anti-depressive agents, which possibly caused lower scores on the Y-BOCS. In contrast, Bihari et al. found significantly higher and clinically relevant Y-BOCS scores in CD patients, even in a smaller sample size [8]. Influence of the rater on scoring the Y-BOCS could possibly have contributed to the higher scores, as the healthy controls in the cohort of Bihari et al. also had higher Y-BOCS scores. However, our study results compliment the study of Bihari et al., suggesting higher levels of obsessive compulsive symptoms in CD patients compared to control subjects.

Interestingly, in 20 patients (40% of the total group, 62.5% of the group with a DSM-IV diagnosis) the structured interview revealed the presence of psychiatric disorders before the onset of dystonia (mean age of onset 41 years), which is similar to the prevalence found in other dystonia studies [4,6,7]. This percentage reflects the total lifetime prevalence of psychiatric illnesses in the general Dutch population (41.2%) [25], suggestive of an earlier higher prevalence in dystonia patients. The occurrence of psychiatric symptoms before the motor symptoms is suggestive for a shared neurobiology instead of a reactive mechanism. Moreover, no relation was found between the presence or severity of psychiatric disorders and the severity of motor symptoms, which is a further indication that the psychiatric symptoms are not solely a response to motor symptoms. These findings support the hypothesis of psychiatric co-morbidity as part of the phenotype of dystonia. Possibly, disturbances in networks related to the dystonia pathophysiology could lead to both motor- and NMS. However, the retrospective design of the study is not suitable to

draw firm conclusions about a primary and/or secondary cause of psychiatric disorders in dystonia patients.

Our second finding comprised that the first eight domains of HR-QoL were significantly lower in dystonia patients compared with healthy controls. This effect was caused by the presence and severity of depressive and anxiety symptoms, pain and disability, while there was no significant correlation with the objective severity of motor symptoms scored on the several CD rating scales. Typically, the degree of disability was only predicted by the degree of pain and depressive symptoms and pain was mostly associated with disability and anxiety symptoms. The finding of psychiatric co-morbidity as the most important predictor of a decreased HR-QoL was supported by other studies [9–11]. However, in these studies the effect of dystonia motor severity was not systematically examined. With our study we confirmed the lack of correlation between motor severity and a decreased HR-QoL. This finding argues against a decreased HR-QoL as a sole consequence of living with a chronic, visible and disabling movement disorder, and emphasizes the need for systematic screening for psychiatric disorders in dystonia patients.

The increasing recognition of psychiatric co-morbidity as part of the phenotype of dystonia suggests a shared pathophysiology. Basal ganglia networks are involved in the pathophysiology of dystonic motor symptoms, and changes in plasticity in these networks are thought to play a causative role. The finding of psychiatric co-morbidity may point to a role of neurotransmitters like dopamine and serotonin in both motor- as well as NMS. Disruption of serotonergic function is known to be involved in many psychophysiologic processes and early life serotonergic dysregulation is associated with a wide spectrum of psychiatric disorders. Furthermore, during gestation, serotonin is involved in the formation of cortical circuits and in modulating plasticity, which in turn is known to be involved in the pathophysiology of dystonia [26–28]. Thus, involvement of basal ganglia neurotransmitter changes in dystonia needs further study.

Our study had several limitations. First, as mentioned before, retrospectively assessing psychiatric disorders is difficult and likely caused an underestimation of the prevalence of psychiatric disorders. The underestimation was further strengthened by the exclusion of subjects using antidepressant medication. Second, as described previously, the cross-sectional design of the study does not allow firm conclusions to be drawn about a primary or secondary cause of psychiatric disorders in dystonia patients, although the onset of psychiatric disorders before onset of motor symptoms suggests a primary cause. Third, personality profile and coping style were not investigated in our study, but might have influenced the results, as these factors are also associated with the prevalence of psychiatric complaints in the general population. In future research, it would be interesting to elucidate the influence of these factors on the phenotype of dystonia.

In conclusion, a higher rate of several psychiatric disorders in CD patients was confirmed in this study and suggests there is an important non-motor component of this disorder. In particular, mood and anxiety disorders were more prevalent in CD patients, albeit patients using antidepressant medication were excluded from the study. Quite often psychiatric complaints preceded the motor symptoms, suggestive of a shared neurobiology. Prospective studies could further elucidate the question whether psychiatric disorders are part of the phenotype of dystonia or a secondary mechanism in response to motor symptoms. The most important predictors of HR-QoL were the severity of depressive symptoms, pain and disability, but not the severity of motor symptoms. This finding highlights the need for systematic research into psychiatric disorders in dystonia patients. We plead for attention to NMS as an integral part of the care for patients with CD. Adequate treatment of these disorders could significantly contribute to better physical and mental quality of life of CD patients.

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