



## 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.

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### 1. 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 and 183 cases per million people [1].

Growing evidence suggests that the phenotype of CD also includes an important non-motor component, with psychiatric comorbidity 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 comorbidity 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 prevalences 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.

## 2. Methods

### 2.1. 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 (<18 yr, 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  $\alpha$ -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.

### 2.2. 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 comorbidity 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].

### 2.3. 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 and 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].

### 2.4. 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

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