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Psychiatric Comorbidities in Dystonia: Emerging Concepts

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Abstract

Psychiatric disorders are highly prevalent in patients with dystonia and have a profound effect on quality of life. Patients with dystonia frequently meet criteria for anxiety disorders, especially social phobia, and major depressive disorder. Deficits in emotional processing have also been demonstrated in some dystonia populations. Onset of psychiatric disturbances in patients with dystonia often precedes onset of motor symptoms suggesting that the pathophysiology of dystonia itself contributes to the genesis of psychiatric disturbances. This article examines the hypothesis that mood and anxiety disorders are intrinsic to the neurobiology of dystonia, citing the available literature, which is derived mostly from research on focal isolated dystonias. Limitations of studies are identified and the role of emotional reactivity, especially in the context of pain secondary to dystonia, is recognized. Available evidence underscores the need to develop dystonia assessment tools that incorporate psychiatric measures. Such tools would allow for a better understanding of the full spectrum of dystonia presentations and facilitate research on the treatment of dystonia as well as the treatment of psychiatric illnesses in the context of dystonia.

Keywords
dystonia; psychiatry; depression; anxiety; social phobia

This paper, solicited for a special Movement Disorders issue on novel research findings and emerging concepts in dystonia, addresses the following issues:

1. To what extent are psychiatric disturbances related to the pathophysiology of dystonia?
2. What is the impact of psychiatric disturbances on outcome measures of current assessment tools for dystonia?
3. How do psychiatric comorbidities influence the treatment of dystonia?

Answers to these questions will lead to an increased appreciation of psychiatric disorders in dystonia, a better understanding of brain physiology, more nuanced research questions pertaining to this population, better clinical scales that can be used to further patient management and research, and improved patient outcomes.

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Dystonia is “a movement disorder characterized by sustained or intermittent muscle contractions causing abnormal, often repetitive, movements, postures, or both. Dystonic movements are typically patterned, twisting, and may be tremulous.” This review focuses primarily on dystonias whose cause is unknown or genetic. Greatest emphasis is placed on focal isolated dystonias with onset in adulthood, the most common form of dystonia and most thoroughly investigated from the psychiatric perspective.

Historically, the diagnostic classification of focal dystonia has oscillated between the poles of being regarded as a disorder involving coarse brain disease on the one hand (i.e., an ‘organic’ or neurological disorder), versus a ‘functional’ or psychiatric disturbance on the other. Functional disorders were not attributed to a brain abnormality, but to an underlying psychiatric syndrome caused by an attempt to resolve an unconscious psychological conflict. For example, a possible psychoanalytic interpretation for a woman with cervical dystonia (CD) whose symptoms involved turning her head to the right might have been that she was conflicted about looking at the woman working to her left because that woman’s husband was having an extramarital relationship with the patient.

In addition to the association of meaningful and distressing life events with the onset of symptoms, several other reasons were regarded as supportive of a ‘functional’ basis for focal dystonias: the bizarre nature of the movements; female preponderance; relief of dystonic postures by use of a sensory trick, i.e., ‘geste antagoniste’; improvement of dystonia through relaxation, sedation and hypnosis; sensitivity of postures and movements to social and mental stress; the occurrence of spontaneous remissions; task specificity of some forms of dystonia such as the writer’s and musician’s cramps; and the absence of any identifiable anatomic, physiologic, or biochemical abnormalities that explained the movement abnormalities.

A paradigm shift occurred in 1975 at the International Symposium on Dystonia. It was at that meeting that the movement disorder community made strong and concerted arguments to recognize focal dystonias as a product of basal ganglia dysfunction, and not psychological conflict, therefore emphasizing the organic nature of these illnesses. As a result, focal dystonia became classified as a movement disorder not caused by a functional, or psychiatric dysfunction. However, the subsequent marked progress in neuroscience, including increased recognition that psychiatric illnesses are a product of both mind and brain, has led to a more integrated view of these illnesses by the turn of the century. New data demonstrated that, in addition to the influence of everyday stressors on the intensity of dystonic symptoms, comorbid psychiatric disturbances cause significant morbidity and reduce quality of life independent of the motor aspects of dystonia.

Psychiatric illness in dystonia

Whereas all dystonias share the common denominator of abnormal and sustained muscular contractions, dystonia is otherwise clinically diverse. Some dystonias are focal and involve only one group of muscles at a single site in the body; others are generalized, impacting virtually every movement; some have onset in early childhood, others only become manifest in midlife. Similarly, the various dystonia syndromes are not uniform in their manifestations of psychiatric illness. As such they are not clinically uniform and, from the standpoint of understanding their association to psychiatric illnesses, should not be grouped together as one disorder, as has occurred all too frequently in many research studies.

The gold standard for establishing psychiatric diagnoses in any given patient population is for an experienced psychiatrist to conduct a clinical diagnostic interview and mental status
examination along with a review of historical information and an interview with a reliable informant. In research studies, this process is approximated using two strategies. The first involves the use of diagnostic tools, such as the Structured Clinical Interview for Diagnosis and Statistical Manual (SCID) for mental disorders. The SCID uses standardized questions to establish psychiatric diagnoses, based on the Diagnostic and Statistical Manual (DSM) criteria, within one month of the interview (point prevalence); the SCID can also be used to determine retrospective or lifetime diagnoses based on the information provided by the patient, informants and chart review. However, the SCID is not a substitute for a clinical diagnostic interview; in part, this is because its questions correspond to DSM criteria and can be used as a simple ‘checklist’ to establish a diagnosis, thus missing nuances of patient presentation. The SCID also does not have questions related to all neuropsychiatric disturbances, e.g. impulse control disorders or apathy.

A second, and much less labor intensive, approach to making psychiatric diagnoses is to use patient or clinician rated scales to determine the point prevalence of clinically significant psychiatric disturbances, e.g. a diagnosis of ‘depression’ as defined by a cutoff point on the scale. This approach amounts to a symptom check list regardless of symptom origin. Therefore, a sleep or appetite disturbance secondary to pain, or medication would still be captured and counted, resulting in an increased score especially in the medically ill population. Consequently, as with the SCID, scales are not to be regarded as substitutes for formal clinical diagnostic interviews. Currently, the psychometric properties of scales for predicting psychiatric illness are not established in dystonia and diagnostic cut-off points are typically based on values from the general population or other medical illnesses. However, despite methodological differences, including the variety of different scales used that render it difficult to compare studies, the collective data using either research diagnostic approach demonstrate an increased prevalence of psychiatric illness in many dystonia populations.

In the cervical dystonia (CD) population, the likelihood of meeting criteria for a current or lifetime diagnosis of a psychiatric illness of any type is as high as 91.4%, as compared to 35% in the general population. The magnitude of this difference is less when comparing CD patients to those with other chronic illnesses. In terms of specific diagnoses associated with CD, lifetime and point prevalence of major depression are increased, as is the risk for anxiety disorders, especially social phobia and panic disorder. The lifetime risk for patients with CD meeting diagnostic criteria for depression ranges from 15% to 53.4%. The rates of anxiety disorders are also increased ranging from 26.4% to an 83.3% lifetime risk.

Compared to CD, data is limited on the prevalence of psychiatric disturbances in patients with other focal dystonias. Laryngeal dystonia is associated with increased point prevalence but not lifetime risk of psychiatric comorbidity as compared to patients with vocal cord paralysis. By contrast, a more recent study failed to find differences in point prevalence of psychiatric diagnosis in patients with laryngeal dystonia as compared to healthy age-matched controls.

Patients with focal dominant hand dystonia did not show a difference in rates of primary psychiatric diagnoses, as compared to healthy controls, although the prevalence rate of obsessive compulsive disorder (OCD) was shown to be increased in one study. A subgroup of patients with focal hand dystonia employed as musicians demonstrated increased psychiatric illness, especially anxiety as compared to unaffected musician controls.

There is evidence of increased rates of obsessive compulsive symptoms and disorders in patients with various focal dystonias as compared to chronic illness case matched controls. Patients with blepharospasm were shown to have a significantly higher prevalence of mood...
disorders as compared to patients with hemifacial spasm. This is in contrast to an earlier larger study that did not associate higher rates of psychiatric disturbances with blepharospasm; however psychiatric diagnoses were based on questionnaires as opposed to the SCID in that study. Taken together, the available data suggest there is an increased risk of psychiatric illness in focal dystonias although the evidence is documented less consistently than for CD.

Rates of psychiatric illness are even less clear in non-focal dystonias. One study showed an increased prevalence of OCD in patients with myoclonus dystonia (MD) which is also linked to alcohol abuse disorders. Patients with autosomal dominant childhood-onset generalized isolated dystonia (DYT1) show a moderately increased risk for recurrent depression that becomes statistically significant when combined with the prevalence of recurrent depression in non-manifesting carriers of the mutation as compared to non-carriers. Prevalence of psychiatric illness in patients with other inherited dystonias is unclear given that most studies are limited to case or family phenomenological descriptions. Nevertheless, prevalence studies based on large samples of patients with various dystonias show increased comorbid psychiatric illness as compared to case matched or population controls.

**Psychopathology as a function of the disease process in dystonia**

Several lines of evidence suggest that mood and anxiety disorders are intrinsic to the neurobiology of dystonia, as opposed to coincidental conditions or emotional reactions to motor symptoms. Most convincing is the finding that psychiatric illness often precedes manifestations of the movement disorder, especially in CD. In 1998, Wenzel et al. demonstrated that mood disorders preceded CD in 53% of patients, and anxiety disorders preceded CD in 68% of patients. These findings were replicated by Moraru et al. and Lencer et al. Lencer et al. investigated 86 patients with focal dystonia, including 81% with CD and 19% with blepharospasm. In their sample, the mean age of onset of psychiatric illness was 24.3 years (+/− 11.4 years standard deviation (SD)) as compared to 42.5 years (+/− 14.4 SD) for the onset of motor symptoms. In virtually every case, the onset of a DSM-based psychiatric diagnosis preceded onset of the movement disorder. As such, the repeated finding of mood and anxiety disturbances prior to the onset of the movement disorder underscores that these emotional changes cannot simply be reactions to the difficulties encountered with dystonia. In addition, the 1:1 ratio of men to women with focal dystonia who meet psychiatric diagnoses is another indication that psychopathology is likely related to the pathophysiology of CD; in the general population, women usually show twice the rate of anxiety and major depression disorder diagnoses when compared to men.

One issue inherent to motor symptoms of dystonia is the high visibility of the physical signs of the disease. However, when compared with other visible or overt disorders, patients with dystonia still have higher rates of comorbid psychiatric syndromes. For instance, compared to patients with alopecia areata, a skin condition causing loss of hair including on the head and face, patients with CD demonstrate increased likelihood of any lifetime diagnosis of psychiatric disorder. This was especially true for lifetime anxiety disorders, including social phobia. Interestingly, a recent study investigating psychopathology in MD found that those with the DYT11 gene mutation had a higher likelihood of having anxiety symptoms, especially social anxiety, as compared to those with MD without the mutation. Both these lines of evidence suggest that the underlying brain pathophysiology of dystonia is linked to the development of psychiatric illnesses, especially anxiety.

Patients with dystonia also have personality attributes and emotional processing difficulties that differentiate them from healthy controls. In one study of patients with focal dystonia...
(mostly CD), the personality trait of openness was less common when compared to population controls, whereas traits of agreeableness and conscientiousness were significantly increased. In another study, musicians with hand dystonia were found to have increased perfectionism as compared to healthy musicians, but not musicians with chronic pain. These personality traits are seen as long-term predispositions that do not change significantly after late adolescence or early adulthood, and are therefore likely to be present prior to the onset of dystonia. Trait anxiety was also increased in patients with focal hand dystonia as compared to a healthy case control group.

Finally, patients with CD may have difficulty with visual and auditory emotional processing. Rinnerthaller et al. reported that patients with CD had difficulty identifying angry faces when compared to age-matched controls, while Nikolova et al. found deficits in the ability of patients with CD to identify auditory expressions of disgust. These separate lines of evidence suggest an interesting association between dystonia and longstanding emotional processing deficits however the exact interplay between these symptoms is not clear.

The close intertwining of physical and psychological symptoms in CD is also suggested by findings that subjectively experienced stress and self-consciousness, as well as physical factors such as walking, fatigue, and carrying objects all aggravate the motor symptoms of CD. This close association of motor symptoms to psychological changes or emotional states suggests a very close relationship of psychological and physical symptoms in CD.

Although psychiatric disturbances occur at an increased rate in patients with dystonia, the exact pathophysiology of these psychiatric symptoms is not known. Monoamine neurotransmitter systems implicated in mood disorders are not known to be affected in dystonia. Dopamine is a key neurotransmitter in basal ganglia motor function, as well as limbic functions, but changes in dopamine receptors are not evident in focal dystonias. However, reduced dopamine activity does cause some acquired and inherited dystonias, e.g., tardive dystonia due to antipsychotic drugs; dopa –responsive dystonia due to GTP-cyclohydrolase deficiency, and dystonia in Parkinson’s disease. Likewise, no changes in serotonergic receptors have been linked to the pathophysiology of dystonia. Investigations of dystonia along with its psychiatric comorbidities have been challenged by attempts to separate motor function from mood regulation in in vivo imaging studies. Post-mortem brain studies in dystonia are also limited.

Are psychiatric illnesses a response to dystonia?

The limited data and varied prevalence for psychiatric illnesses across different types of dystonia confound interpretations of the etiology of psychiatric disorders in patients with dystonia. This is best exemplified by evidence that different forms of dystonia have different prevalence rates for psychiatric diagnoses. For example, anxiety and depression are more common in CD, depression is most common in blepharospasm; OCD in MD, anxiety in hand dystonia and recurrent depression in DYT1 manifesting and non-manifesting mutation carriers as compared to non-mutation carrying family members. Variations in rates may be in part related to methodological differences, with some studies using DSM criteria and others using questionnaires to establish psychiatric diagnoses.

In studies on prevalence of psychiatric illness in dystonia, the choice of a comparison group presents another challenge; healthy controls may not be the most appropriate choice. When patients with dystonia are compared to those with other chronic illnesses, differences in psychiatric illness prevalence are not as pronounced. There may also be recall bias in studies of lifetime prevalence. Furthermore, pain is highly correlated with depression in patients with dystonia, but is often not adequately controlled for in studies looking at psychiatric morbidity. Therefore, study design limitations leave open the possibility that...
some psychiatric illnesses in patients with dystonia are related to extrinsic factors or are merely coincidental to dystonia.

There is also evidence that the presence and severity of psychiatric disorders are sensitive to the physical disability associated with dystonia. For example, Barahona et al. showed the incidence of psychopathology is greater in patients with an increased burden of illness. Evidence that the severity of depressive symptoms decreases with the successful use of botulinum toxin therapy for CD also supports the occurrence of secondary depression in dystonia. However, a similar association was not demonstrated in blepharospasm, despite a mean reduction of 42.2% in the global clinical impression score. Depression scores also decrease following deep brain stimulation, although the decrease is not clinically significant given that published surgical studies excluded patients who scored in the depressed range.

Reactive emotional responses can exacerbate depression scores in the context of the chronic, visible, painful and disabling nature of dystonic movements. Decreased self esteem was found to account for 56% of the variance in depression as measured by the Beck Depression Inventory in 329 patients with a wide range of dystonias. However it is unclear whether this relationship is due to negative self evaluation and perceived or real stigma, or whether it is a manifestation of negative cognitions that are part of depressive symptomatology. The timing of onset of these difficulties in relation to the onset of dystonia is also unknown. For example, it is conceivable, possibly because of emerging pathophysiology, that self-esteem difficulties arise prior to the onset of visible motor symptoms that further exacerbate self-esteem difficulties.

Therefore, despite evidence of higher rates of psychiatric difficulties and evidence for long term personality traits and emotional processing deficits in patients with dystonia, possibly even prior to the onset of their movement disorder, it is difficult to draw a clear line that dichotomizes the population between those with intrinsic and those with reactive psychopathology. The interpretation of data is constrained by the mixing of dystonia types, incomplete evaluations that often do not include the assessment of pain, and the selection of appropriate control groups. There is likely also an element of emotional reactivity of patients with dystonia that complicates the interpretation of data currently available.

The influence of psychiatric disturbances on current assessment tools for dystonia

There is an ongoing interplay between emotions and movements in patients with dystonia, whether the individual is psychiatrically healthy and experiences mood fluctuations or has a more persistent and disturbed emotional state such as with a depressive or anxiety disorder. Psychiatric illnesses certainly have a major impact on quality of life (QoL) in patients with dystonia as they do in the general population. The QoL studies in dystonia have been limited by use of self-report measures to identify psychiatric illness and measure dystonia severity. Despite this, subjects with dystonia consistently demonstrate lower QoL as compared to healthy controls and patients with other chronic illnesses. Most notable in some studies is the finding that depression and anxiety not only affect mental health QoL but also have a larger effect on physical QoL than dystonia severity. Accordingly, psychiatric illness in patients with dystonia has a significant impact on patient QoL.

In order to better understand and integrate the multiple dimensions of dystonia and evaluate the efficacy of dystonia treatments, research is needed that evaluates the validity and psychometric properties of existing psychiatric symptom rating scales. Research should focus on developing tools to evaluate the severity and extent of dystonia and account for the

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impact of the psychiatric state on motor status at the time of assessment. Otherwise, it is not clear the extent to which the dystonia itself contributes to the presentation versus the additional influence of the psychological state, especially given the high prevalence of mood and anxiety disorders in patients with dystonia and the known impact of emotional states on dystonia symptoms.

Currently, dystonia rating scales typically evaluate various aspects of motor dysfunction; some also assess pain. However, to date, no scales include measures of psychiatric status as part of the overall motor assessment. A multidimensional scale to assess dystonia that includes a psychiatric component with validated questions regarding mood and anxiety would be useful. Ideally, such a scale, akin to that developed for Parkinson’s disease (the Movement Disorder Society Revised Unified Parkinson Disorder Rating Scale) would assess objective motor symptoms and subjective mood states, with both linked to a QoL measure and validated psychiatric symptom rating scales.

How might psychiatric co-morbidities influence treatment of the movement disorder?

Psychiatric co-morbidities in patients with dystonia are significant and could influence assessment of dystonia treatment effects. Currently, dystonia treatment studies often exclude patients with these comorbidities or patients who are taking antidepressant medications. Yet, benzodiazepines are often used to treat dystonia because of their muscle relaxation properties but their known anxiolytic effect has not been described in patients with dystonia. In fact, to date, there are no published treatment trials of psychiatric illness in the context of dystonia.

Prior to the current era of dystonia being understood as a purely physical illness, psychotherapeutic approaches were used to alleviate motor symptomatology. These treatments typically involved long-term psychotherapy to address underlying psychological conflicts (see Patterson et al. for review) and, understandably, met with limited success. However, recent psychotherapeutic approaches are more symptom based, time-limited, and have established efficacy in treating mood and anxiety disorders.

For example, cognitive behavioral therapy (CBT) can be used to target anxious thoughts, emotions, and the accompanying muscle tension, leading to the potential for improved outcomes of psychiatric and motor symptoms. Already, one case report describes the efficacy of CBT in alleviating symptoms of CD. However caution must be exercised in interpreting individual case reports as the motor symptoms of dystonia can remit spontaneously in a minority of cases, and controlled, adequately sampled studies are essential. There is also a need to examine the effects of psychiatric treatment on both motor symptoms as well as mental and physical aspects of QoL. Such multidimensional approaches are necessary to improve the objective and subjective well being of patients with dystonia.

Conclusions

Psychiatric disorders appear to be related to the underlying disease processes of many of the dystonia syndromes. In addition, a reactive element exacerbates psychiatric distress and may be the result of the visible and painful nature of the motor symptoms. The subjective aspect of illness as manifest through psychiatric measures of distress has profound effects on patient rated QoL. The recognition of psychiatric aspects of dystonia and the inclusion of psychiatric assessments in future clinical and research assessments of patients with dystonia will lead to a greater understanding of brain function and improved treatments.

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Abbreviations

CD  cervical dystonia
SCID  Structured Clinical Interview for DSM
DSM  Diagnostic and Statistical Manual for Mental Disorders
OCD  obsessive compulsive disorder
MD  myoclonus dystonia
QoL  quality of life
CBT  cognitive behavioral therapy
DYT  inherited dystonia
SD  standard deviation

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