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The Non-Motor Manifestations of Dystonia: A Systematic Review

Daniel J. Kuyper[1], **Veronica Parra**[2], **Shanae Aerts**[2], **Michael S. Okun**[3], and **Benzi M. Kluger**[2]

[1]Department of Neurology, University of Colorado, Denver, Colorado

[2]Departments of Neurology and Psychiatry, University of Colorado, Denver, Colorado

[3]Departments of Neurology, Neurosurgery, Psychiatry and History, University of Florida, Gainesville, Florida

Abstract

Non-motor symptoms are increasingly recognized as important determinants of quality of life and disability in a wide range of movement disorders. There is a limited body of research suggesting that many of these symptoms are also commonly associated with primary and other genetic forms of dystonia. However, the significance, etiology, pathophysiology, and treatment of these symptoms remains poorly described. The following is a review of the literature which focuses primarily on the association of these types of dystonia with psychiatric disorders, cognition, sleep, pain, and autonomic symptoms. We will also discuss potential mechanisms and approaches to treatment for non-motor features of dystonia.

Keywords

dystonia; non-motor; depression; anxiety; cognition; pain; sleep

1. Introduction

Non-motor symptoms are increasingly recognized as an important determinant of quality of life (QOL) and disability in movement disorders. Non-motor symptoms include alterations of mood, cognition, sleep, autonomic function and/or pain which cannot be directly attributed as a secondary consequence of motor symptoms. These symptoms are described most commonly in Huntington's disease[1] and Parkinson's disease (PD).[2] but have also been reported in other movement disorders including dystonia.[3, 4]

The etiology of dystonia can be either primary or secondary. In primary dystonia, no abnormality is present other than the dystonia itself. Secondary dystonia is the result of neurodegenerative disease, metabolic disorders, or other acquired causes.[5] Dystonia-plus

Address correspondence and reprint requests to: Dr. Benzi M. Kluger, Mail Stop B185, 12631 East 17th Avenue, Aurora, CO 80045, Phone: (303) 724-2194, Fax: (303) 724-2212, benzi.kluger@ucdenver.edu.

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syndromes are inherited forms of secondary dystonia which are accompanied by other neurologic abnormalities. These, as well as other heterogeneities in dystonia populations, make for significant challenges in assessing non-motor symptoms across studies which may sample very different patient populations.

While psychological and other non-motor symptoms have been reported to occur in primary and other genetic forms of dystonia, their significance and causes are still debated. This paper will summarize the current literature on this topic, review the potential relationship to pathophysiological data, and finally suggest areas where further research is needed.

2. Methods

A search strategy was used to reference English language articles in Medline from 1966 to December 2009. A total of 1902 records were retrieved and the abstracts were reviewed. In the absence of an abstract the title was considered. Studies were included if the participants had primary dystonia or dystonia-plus syndromes, and if the focus was related to non-motor symptomatology. Reference lists of all initially included studies were searched for additional publications. Search terms were selected based on common non-motor features of other movement disorders (i.e. PD) and terms associated with mood disorders, the category of non-motor symptoms which has been studied most thoroughly in dystonia. The following search terms were used: dystonia, torticollis, dysphonia, blepharospasm, depression, bipolar, mood, anxiety, psychiatric, substance abuse, phobia, personality, deep brain stimulation, anticholinergic medications, neuroimaging, psychosis, hallucinations, memory, cognition, neuropsychology, sleep, fatigue, energy, pain, autonomic, sweating, blood pressure, orthostatic, constipation, urinary, urination, sexual, erectile.

3. Results

a. Mood (n=25 studies)

There are numerous reports in the literature indicating that patients with primary and other genetic forms of dystonia have higher than expected rates of depression and anxiety (see Table 1). The prevalence of depression and anxiety in patients with dystonia varies based on the study and on sample size, but cohorts analyzed in this paper indicate that 12–71% of patients with focal or generalized dystonia suffer from depression and anxiety over the course of a lifetime, with most studies falling in the range of about 25–50%. This percentage is similar to Parkinson disease, which also disturbs frontal-subcortical circuits.[6, 7] It is increased compared to those who are healthy [8–11] and those with other medical conditions. [12–14]

There is conflicting epidemiological evidence as to whether depression and anxiety are secondary to motor manifestations and subsequent psychosocial impairment, or a primary feature of the disease. On one hand, studies have reported a higher pre-morbid incidence of depression and anxiety in patients with dystonia[15] suggesting that, similar to PD, this may be an independent manifestation of dystonia. In addition, a study of manifesting and non-manifesting carriers of the DYT 1 gene showed that carriers (with or without symptoms) had a significantly higher rate and earlier onset of major depressive disorder than non-carrier controls.[10] While these studies may be prone to recall bias, they suggest that the underlying pathophysiology of dystonia may predispose patients to mood disorders. Striatofrontal circuits which help regulate mood and behavior have been shown to be disordered in dystonia patients based on functional imaging[16–18] and may act as a pathologic substrate. Functional imaging studies have shown that these nonmanifesting carriers have decreased D2 receptor binding in the basal ganglia and hypermetabolism in the putamen, anterior cingulate, and cerebellar hemispheres[19, 20]. Patients with GTP cyclohydrolase deficiency

(DYT 5 dystonia) may also have higher rates of depression than the general population, perhaps due to reduced conversion of tryptophan to serotonin.[21]

There is mixed evidence to suggest that depression and anxiety symptoms are associated with disease severity, with some studies showing correlation[7, 22, 23] and others no correlation.[9, 24] Of note, a two-year longitudinal follow up of patients with spasmodic torticollis showed that changes in the severity of the dystonia were closely linked to subsequent changes in mood, disability, and body concept.[25, 14] Other factors which have been correlated with higher depression scores include marital status (higher scores for separated/divorced patients) and body parts affected (higher scores for cervical dystonia versus spasmodic dysphonia or hemifacial spasm).[22] Self esteem, body concept, and QOL have also contributed to the variance of depression.[22] Finally, the degree of psychopathology may also be associated with triggering events. Scheidt et. al. reported that cervical dystonia patients were more likely to have psychopathology if symptoms were triggered by a stressful life event.[23]

Deep brain stimulation (DBS) of the internal globus pallidus, an emerging procedure for selected primary dystonias, deserves special attention for its effect on mood. While most studies suggest that DBS for dystonia results in mildly improved or unchanged measures of depression[26–29], worsened mood and suicide have also been reported[30, 31]. The majority of these patients had previous history of depression or other risk factors for suicide prior to surgery. Interestingly, most of the patients who committed suicide also had an excellent motoric response from stimulation, providing further evidence that severity of dystonia may not correlate with symptoms of low mood.

In dystonia, dysfunctional mood is one of the most important predictors of a patient's QOL.[25] We recently reported the results of a large retrospective case series of patients with dystonia who were given questionnaires assessing QOL, depression, anxiety, and other mood variables.[4] Both physical and mental aspects of QOL were strongly associated with depression and anxiety. Treatment of the motor symptoms of dystonia may or may not[32–34] lead to improvement in depression and health related QOL. Other factors besides motor symptoms – longstanding disability, pain, deformity, and lifestyle changes – may also contribute to depression and poor QOL.

Several areas of future research may prove to be useful. Routine screening of patients with dystonia, or those who have genetic mutations predisposing to dystonia, for depression and anxiety would seem to be warranted. Development of a non-motor screening tool for patients with dystonia could make this process more efficient. Identifying those that are most at risk for mood dysfunction would be helpful to the clinicians caring for these patients. For instance, does the side of motor symptom onset make someone more likely to develop depression with their dystonia? Studies in healthy brain indicate that the right forebrain plays a large role in mood processing.[35] Also, patients with left-sided onset to their Parkinson motor symptoms may have more prominent mood and pain symptoms.[36] Lastly, studies utilizing more standardized scales of depression and anxiety would clarify the true incidence of mood disorders and make comparisons easier.

b. Other Psychiatric Disorders and Symptoms (n=10)

A small group of studies have looked specifically for obsessive-compulsive symptoms in dystonia (See Table 2). In one of the larger cohorts, 19.7% of patients with idiopathic focal dystonia met DSM-IV criteria for obsessive-compulsive disorder.[37] This percentage is slightly higher than other studies reviewed.[15, 38, 40] No significant differences in obsessive compulsive symptoms emerged in a study comparing DYT 1 carriers to a control population.[40] In contrast, symptomatic carriers of DYT 11, the gene for myoclonus-

dystonia, have a higher rate of obsessive compulsive symptoms compared to asymptomatic carriers and control populations.[38,41]

Alcohol abuse and dependence has been reported in DYT 11 mutation (myoclonus-dystonia), as well as idiopathic generalized and focal dystonia, albeit to a lesser extent. In DYT 11, a study of carriers versus non-carriers revealed no significant differences in alcohol dependence. However, some[38, 41], but not all[42], studies have shown that symptomatic carriers demonstrate more alcohol dependence than unaffected carriers. Given the typical sensitivity of the myoclonus to alcohol, the alcohol dependence seen in certain patients may be the result of alcohol's symptomatic effects rather than a manifestation of the gene itself.[38] Aside from the connection to DYT 11, alcohol abuse was found to be significantly higher than healthy controls in a small cohort of patients with primary generalized dystonia and spasmodic torticollis.[6]

Social phobia in dystonia is often co-morbid and associated with other anxiety symptoms. In one larger study of 116 patients with spasmodic torticollis, a 71% lifetime prevalence of social phobia was found by using the Social Phobia and Social Interaction Anxiety scales.[9] This prevalence correlated with body image, and a "maladaptive attitude" toward their illness, and not the objective severity of the dystonia.[9] Much like depression and other forms of anxiety, one can hypothesize that self esteem and body concept play an important role in the development of social phobia.

Screening for these conditions in patients with dystonia is of great importance. This is particularly true with the association of alcoholism in patients with DYT 11 dystonia. Physicians should consider counseling patients, specifically adolescents, about the risks of using alcohol to treat their symptoms. Further research verifying the possible association between different types of dystonia and alcoholism is needed. Also lacking from the literature are studies assessing the incidence of other psychiatric disorders (i.e. bipolar disorder) in dystonia patients.

c. Cognition (n=14)

Several studies of cognition have been performed in both idiopathic and genetic forms of dystonia (See Table 3). By using detailed neuropsychological testing, many of these studies have shown statistically significant (albeit, at times subtle) deficits in executive, attentional, or visuospatial function. From the available evidence, it is unclear how functionally significant these deficits are. The fact that certain findings, such as impaired sequence learning, are not consistently replicated suggests that the severity of these findings may be mild. There are several limitations of the current literature regarding cognition, including small sample sizes. Also notable is the variability of several factors, including age, education level, pre-morbid cognitive function, type of dystonia, and anti-dystonic medication burden at the time of the testing. The studies which accounted most thoroughly for these confounding factors showed either no difference between dystonia patients and controls, or only mild executive dysfunction including set-shifting deficits, verbal learning, category fluency, and performance of dual tasks. [43–46]

The etiology of these cognitive deficits is not entirely clear. One possible explanation is that anti-dystonic medications play a part, particularly if a patient is on an anticholinergic agent or on a benzodiazepine. While patients in several of these studies were on medications at the time of their testing, there has not been clear evidence that medications are directly causative. Chronic exposure to anticholinergic medications affected performance on a memory task in one study of adult patients with dystonia.[47] Another study showed that cognitive processes were only mildly impacted by anticholinergic medication, and this was

only in elderly patients.[48] Three of twenty three pediatric patients reported being forgetful in an early study using high-dose benzhexol therapy for dystonia.[49]

Another possibility is that concurrent mood disorders may lead to impairments in executive function. Depression causing a "pseudodementia" is well-established as a diagnostic consideration in patients with untreated low mood. Moreover, patients with OCD are known to have deficits in organizational strategies and executive dysfunction.[50] While disorders of mood have not been definitively linked to cognitive dysfunction in dystonia, one recent study showed a possible association between executive dysfunction in patients with idiopathic focal and segmental dystonia and obsessive compulsive symptoms.[45]

A third potential mechanism for cognitive impairment is the possibility that the disabling symptoms of dystonia, including pain, are impairing attentional processes. In a small sample of patients with primary cranial dystonia, sustained attention deficits were shown to improve following botulinum toxin injections, suggesting that dystonic activity may impair attentional processing.[51] Executive function also improved mildly but significantly in a group of generalized dystonia patients after undergoing GPi DBS surgery.[52]

While secondary effects of motor symptoms may be partly to blame, there is evidence to suggest that asymptomatic carriers of DYT 1, the most common form of genetic dystonia, also have mildly impaired cognition and abnormal functional imaging, particularly in motor and visual sequence learning.[21, 53] Functional imaging studies in this population have shown compensatory overactivation of the lateral cerebellum and right inferotemporal cortex with a lack of recruitment of prefrontal regions, which may be due to underlying frontostriatal dysfunction.[16]

Additional studies of cognition in dystonia which control for factors such as medication burden and mood symptoms are needed. Studying cognitive deficits in specific forms of dystonia without combining dystonia subtypes would also be helpful. In addition, it is unclear how medications for dystonia could potentially affect cognition in the long term. Anticholinergics, frequently used for symptomatic treatment of dystonia, can cause delirium in the short term and likely lead to cognitive impairment in the elderly and memory-impaired.[54, 55]

d. Sleep and Energy (n=13)

There are relatively few articles addressing sleep in patients with dystonia. Recent studies have focused on patient surveys in order to measure quality of sleep and symptoms of sleepiness. In patients with blepharospasm and cervical dystonia, quality of sleep was impaired in both groups using the Pittsburgh Sleep Quality Index.[56] Differences seen in the cervical dystonia group, however, were partly confounded by higher scores on the Beck Depression Inventory. Excessive daytime sleepiness, using the Epworth Sleepiness Scale (ESS), was not found to be significantly more frequent when compared to a group of control subjects. In contrast, another study specifically evaluating daytime sleepiness (again using the ESS) found that a significantly higher percentage of patients with cervical dystonia had scores > 11 when compared to patients with other focal movement disorders or to age matched controls.[57]

While there is mixed evidence that dystonia leads to sleepiness, several studies suggest that either sleep structure or quality is impaired. Specific polysomnographic abnormalities have been reported, including problems with sleep initiation and maintenance, abnormal or reduced REM sleep,[58–60] and changes in spindle activity.[58, 60, 61] In a study of ten patients with blepharospasm and oromandibular dystonia, impaired sleep efficiency and decreased REM sleep was found, both of which correlated with the severity of dystonia and EMG

abnormalities.[59] In contrast, a larger study of 24 patients with focal or generalized torsion dystonia (14 primary, 10 secondary) showed that sleep architecture and organization did not vary significantly from control patients.[62]

Much like other non-motor symptoms in dystonia, the etiology of sleep abnormalities may include primary effects of dystonia on sleep as well as secondary effects of pain and medications. Some of the patients in the aforementioned studies were on benzodiazepines, known to change sleep architecture and spindle activity.[57] Anticholinergic medications may also account for some of the sleepiness seen in patients with high ESS scores.[57] There is conflicting evidence as to whether the severity of dystonia is associated with the occurrence of sleep disorders. While impaired sleep efficiency, decreased REM sleep, and sleep quality have all been linked to severity of motor symptoms in focal or cervical dystonia, [59, 63] excessive daytime sleepiness was not correlated with scores on the Toronto Western Spasmodic Torticollis Rating Scale (TWSTRS) or its subscores in another study.[57] There is evidence that at least certain forms of dystonia, including blepharospasm and Meige's syndrome, may persist during sleep, although its frequency and severity is decreased.[64] Whether this may affect sleep quality is unknown. Restless-legs-like symptoms were found in six of thirty four patients with DYT 5 dystonia prior to initiation of levodopa in a detailed clinical evaluation.[65] Finally, Wetterberg (1978) found decreased amplitude of melatonin fluctuations in a patient with "hereditary dystonia"; however, this was not replicable in a larger series of 19 patients.[66]

Sleep impairment and its secondary symptoms are particularly burdensome for patients with dystonia. Studies using the Cervical Dystonia Impact Scale, a rating scale for measuring the health impact of cervical dystonia based on patient perceptions, [67] have shown that a large percentage of patients with dystonia report sleep affecting their QOL. Subjective ratings of both energy and tiredness are associated with QOL even when controlling for depression. In fact, the tired subscore of the Visual Analogue Mood Scale was found to be the most strongly correlated with overall QOL in our recent study.[4]

Additional research analyzing polysomnograms in patients off anti-dystonic medications would help clarify if changes in sleep structure are a primary or secondary effect in dystonia. Also, studies assessing whether treatment of motor symptoms alone improves objective sleep measures are needed. Finally, while fatigue plays a significant role in QOL in dystonia, no studies to date have assessed the symptom as a manifestation of dystonia.

e. Pain (n=12)

Pain is one of the most common and disabling complaints in many patients with dystonia. Studies suggest that the prevalence of pain in cervical dystonia ranges from 67–75% of patients.[68–70] In cervical dystonia, pain is often experienced in the head, neck, and down the ipsilateral arm on the side to which the head is rotated.[69] The sternocleidomastoid and trapezius are the most frequent muscles involved.[71] While it may seem obvious that dystonic muscles would be painful, not all patients with similar degrees of dystonia report equal amounts of pain. While degree of head deviation and subjective muscle tension may correlate with pain levels, somewhat surprisingly, the objective severity of neurologic signs have not.[69]

One potential reason that pain is so prevalent in dystonia is that the threshold for experiencing pain may be reduced. In a small study of nine patients with idiopathic cervical dystonia, pain-pressure thresholds were about two times lower in the dystonia group versus a group of age and gender matched controls.[72] Patients with dystonia may also have alterations in pain processing even in body parts without dystonic involvement. For example, in the same study, the non-affected masseter muscles of patients with idiopathic

cervical dystonia also showed reduced pain-pressure thresholds compared to the control group.[72] Another potential mechanism for excessive pain includes alterations in the somatosensory system that have been documented in patients with focal or generalized dystonia. These include changes in excitability on neurophysiological testing, abnormal representation in S1 of dystonic body parts, and changes in somatosensory cortical activity during movement.[73] Ongoing depression, common in this population, correlates with symptoms of pain. Lastly, sleep itself may mitigate against pain, as cervical spinal pain intensity and unpleasantness were reduced by about 50% overnight in one study of patients with idiopathic cervical dystonia.[74]

To our knowledge, no recent studies have evaluated any other pharmacologic agents to specifically treat either primary or secondary dystonic pain symptoms. Double-blind, randomized controlled trials assessing whether analgesic agents could lead to objective measures of additional decreased pain in dystonia patients are needed, particulary in patients refractory to botulinum toxin. Whether the type and location of dystonia correlates with pain levels is also not known.

f. Autonomic Symptoms (n=2)

Patients receiving botulinum toxin, especially type B, may experience autonomic symptoms including dry mouth, blurred vision, reduced sweating, constipation, and urinary retention.[75] Anticholinergic medications may also cause similar symptoms. Autonomic symptoms have rarely been reported outside of the context of these medical treatments or secondary dystonia (complex regional pain syndrome and brain injury). Tiple et al. (2008) found that patients with cervical dystonia had mild subclinical changes in some measures of heart rate variability and baroreflex sensitivity which were present before receiving botulinum toxin injections.[76] Aside from this, no reports of erectile, sexual, urinary, or bowel dysfunction were found. Future research should attempt to further clarify whether autonomic symptoms are seen outside of known side effects of treatment.

4. Conclusion

In addition to the more visually-apparent and well-defined motor symptoms of dystonia, there is emerging evidence for the presence of non-motor symptoms in primary and other genetic forms of dystonia. The available evidence can at times be conflicting, and the question remains: are these non-motor symptoms secondary to motor causes and medications, or do they reflect a primary defect in neuronal processing or neurochemistry? Given the fact that non-affected family members with dystonia biomarkers can be affected, and that symptoms can be seen prior to onset of motor symptoms, it seems likely that the primary effects of the disease are at least partly to blame. Although the pathophysiology and neuroanatomy of these effects has not been clearly elucidated, the underlying defects in dystonia may provide a substrate for non-motor symptoms to develop, particularly when combined with motor features of the disease and/or side effects of treatment.

Further studies are clearly indicated. First, by investigating the specific cortical and subcortical networks involved in dystonia, the genesis of the disease and the development of non-motor symptoms might be better understood. Defining the neuroanatomy and pathways involved in these symptoms by using functional imaging studies may yield new treatment strategies. Using such studies to image non-manifesting carriers of dystonia genes may shed light on a “pre-motor” phase of dystonia, akin to what is described in PD. We also recommend a formal pre-surgical psychiatric evaluation for DBS candidates to screen specifically for mood disorders, given their prevalence in dystonia. This should include an assessment from a psychiatrist as well as a standardized measure of depression. Development of carefully-designed prevalence studies in all non-motor symptoms,

controlling for secondary effects of motor symptoms and side effects of medicine, are needed.

Much has been learned about the manifestations of dystonia, including both motor and non-motor symptoms, over the past two decades. We must understand that non-motor manifestations will likely widely vary among dystonia subtypes. Only when the entire phenotype of dystonia is fully understood will we be able to provide appropriate, comprehensive care and measurable improvements in QOL for these patients.

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References

1. Anderson KE, Marshall FJ. Behavioral symptoms associated with Huntington's disease. Adv Neurol. 2005; 96:197–208. [PubMed: 16383221]
2. Simuni T, Sethi K. Nonmotor manifestations of Parkinson's disease. Ann Neurol. 2008; 64 (Suppl 2):S65–80. [PubMed: 19127582]
3. Miller KM, Okun MS, Fernandez HF, et al. Depression symptoms in movement disorders: Comparing Parkinson's disease, dystonia, and essential tremor. Mov Disord. 2007; 22(5):666–672. [PubMed: 17266084]
4. Soeder A, Kluger BM, Okun MS, et al. Mood and energy determinants of quality of life in dystonia. J Neurol. 2009; 256(6):996–1001. [PubMed: 19277765]
5. Geyer HL, Bressman SB. The diagnosis of dystonia. Lancet Neurol. 2006; 5(9):780–790. [PubMed: 16914406]
6. 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(1):29–36. [PubMed: 14990756]
7. Naber D, Weinberger DR, Bullinger M, et al. Personality variables, neurological and psychopathological symptoms in patients suffering from spasmodic torticollis. Compr Psychiatry. 1988; 29(2):182–187. [PubMed: 3370969]
8. Cannito MP. Emotional considerations in spasmodic dysphonia: psychometric quantification. J Commun Disord. 1991; 24(5–6):313–329. [PubMed: 1809774]
9. Gundel H, Wolf A, Xidara V, et al. Social phobia in spasmodic torticollis. J Neurol Neurosurg Psychiatry. 2001; 71(4):499–504. [PubMed: 11561034]
10. Heiman GA, Ottman R, Saunders-Pullman RJ, et al. Increased risk for recurrent major depression in DYT1 dystonia mutation carriers. Neurology. 2004; 63(4):631–637. [PubMed: 15326234]
11. Murry T, Cannito MP, Woodson GE. Spasmodic dysphonia. Emotional status and botulinum toxin treatment. Arch Otolaryngol Head Neck Surg. 1994; 120(3):310–316. [PubMed: 8123241]
12. Jahanshahi M, Marsden CD. Personality in torticollis: a controlled study. Psychol Med. 1988; 18(2):375–387. [PubMed: 3399589]
13. Gundel H, Wolf A, Xidara V, et al. High psychiatric comorbidity in spasmodic torticollis: a controlled study. J Nerv Ment Dis. 2003; 191(7):465–473. [PubMed: 12891094]
14. Jahanshahi M, Marsden CD. A longitudinal follow-up study of depression, disability, and body concept in torticollis. Behav Neurol. 1990; 3:233–246.
15. Moraru E, Schnider P, Wimmer A, et al. Relation between depression and anxiety in dystonic patients: implications for clinical management. Depress Anxiety. 2002; 16(3):100–103. [PubMed: 12415533]
16. Carbon M, Ghilardi MF, Argyelan M, et al. Increased cerebellar activation during sequence learning in DYT1 carriers: an equiperformance study. Brain. 2008; 131(Pt 1):146–154. [PubMed: 17947338]

17. Ceballos-Baumann AO, Passingham RE, Warner T, et al. Overactive prefrontal and underactive motor cortical areas in idiopathic dystonia. Ann Neurol. 1995; 37(3):363–372. [PubMed: 7695236]
18. Ghilardi MF, Carbon M, Silvestri G, et al. Impaired sequence learning in carriers of the DYT1 dystonia mutation. Ann Neurol. 2003; 54(1):102–109. [PubMed: 12838525]
19. Asanuma K, Ma Y, Okulski J, et al. Decreased striatal D2 receptor binding in non-manifesting carriers of the DYT1 dystonia mutation. Neurology. 2005; 64:347–349. [PubMed: 15668438]
20. Carbon M, Su S, Dhawan V, et al. Regional metabolism in primary torsion dystonia. Neurology. 2004; 62:1384–1390. [PubMed: 15111678]
21. Van Hove JLK, Steyaert J, Matthijs G, et al. Expanded motor and psychiatric phenotype in autosomal dominant Segawa syndrome due to GTP cyclohydrolase deficiency. J Neurol Neurosurg Psychiatry. 2006; 77:18–23. [PubMed: 16361586]
22. Lewis L, Butler A, Jahanshahi M. Depression in focal, segmental and generalized dystonia. J Neurol. 2008; 255(11):1750–1755. [PubMed: 19156488]
23. Scheidt CE, Heinen F, Nickel T, et al. Spasmodic torticollis – a multicentre study on behavioural aspects IV: psychopathology. Behav Neurol. 1996; 9(97–103):97.
24. Grafman J, Cohen LG, Hallett M. Is focal hand dystonia associated with psychopathology? Mov Disord. 1991; 6(1):29–35. [PubMed: 2005919]
25. Jahanshahi, M. Behavioural and psychiatric manifestations in Dystonia. In: Anderson, K.; Weiner, W.; Lang, A., editors. Behavioural Neurology of Movement Disorders. 2. Lippincott, Williams & Wilkins; 2005. p. 291-319.
26. Halbig TD, Gruber D, Kopp UA, et al. Pallidal stimulation in dystonia: effects on cognition, mood, and quality of life. J Neurol Neurosurg Psychiatry. 2005; 76:1713–1716. [PubMed: 16291900]
27. Kupsch A, Benecke R, Muller J, et al. Pallidal Deep-Brain Stimulation in Primary Generalized or Segmental Dystonia. N Engl J Med. 2006; 355:1978–90. [PubMed: 17093249]
28. Valldeoriola F, Regidor I, Minguez-Castellanos A, et al. Efficacy and safety of pallidal stimulation in primary dystonia: results of the Spanish multicentric study. J Neurol Neurosurg Psychiatry. 2010; 81:65–69. [PubMed: 19744963]
29. Vidailhet M, Vercueil L, Houeto JL, et al. Bilateral, pallidal, deep-brain stimulation in primary generalized dystonia: a prospective 3 year follow-up study. Lancet Neurol. 2007; 6:223–29. [PubMed: 17303528]
30. Burkhard PR, Vingerhoets FJG, Berney A, et al. Suicide after successful deep brain stimulation for movement disorders. Neurology. 2004; 63:2170–2172. [PubMed: 15596774]
31. Foncke EMJ, Schuurman PR, Speelman JD. Suicide after deep brain stimulation of the internal globus pallidus for dystonia. Neurology. 2006; 66:142–3. [PubMed: 16401868]
32. Jahanshahi M, Marsden CD. Body concept, disability and depression in torticollis. Behav Neurol. 1990; 3:117–131.
33. Muller J, Kemmler G, Wissel J, et al. The impact of blepharospasm and cervical dystonia on health-related quality of life and depression. J Neurol. 2002; 249(7):842–846. [PubMed: 12140667]
34. Whurr R, Nye C, Lorch M. Meta-analysis of botulinum toxin treatment of spasmodic dysphonia: a review of 22 studies. Int J Lang Commun Disord. 1998; 33 (Suppl):327–329. [PubMed: 10343714]
35. Heller, W.; Koven, NS.; Miller, GA. Regional brain activity in anxiety and depression, cognition/emotion interaction, and emotion regulation. In: Hugdahl, K.; Davidson, RJ., editors. The Asymmetrical Brain. Cambridge: The MIT Press; 2003. p. 533-564.
36. McNamara P, Stavitsky K, Harris E, et al. Mood, side of motor symptom onset and pain complaints in Parkinson's disease. Int J Geriatr Psychiatry. 2010; 25(5):519–524. [PubMed: 19711336]
37. Cavallaro R, Galardi G, Cavallini MC, et al. Obsessive compulsive disorder among idiopathic focal dystonia patients: an epidemiological and family study. Biol Psychiatry. 2002; 52(4):356–361. [PubMed: 12208643]
38. Saunders-Pullman R, Shriberg J, Heiman G, et al. Myoclonus dystonia: possible association with obsessive-compulsive disorder and alcohol dependence. Neurology. 2002; 58(2):242–245. [PubMed: 11805251]

39. Wenzel T, Schnider P, Wimmer A, et al. Psychiatric comorbidity in patients with spasmodic torticollis. J Psychosom Res. 1998; 44(6):687–690. [PubMed: 9678750]
40. Heiman GA, Ottman R, Saunders-Pullman RJ, et al. Obsessive-compulsive disorder is not a clinical manifestation of the DYT1 dystonia gene. Am J Med Genet B Neuropsychiatr Genet. 2007; 144B(3):361–364. [PubMed: 17066475]
41. Hess CW, Raymond D, de Aguiar PC, et al. Myoclonus-dystonia, obsessive-compulsive disorder, and alcohol dependence in SGCE mutation carriers. Neurology. 2007; 68(7):522–524. [PubMed: 17296918]
42. Doheny DO, Brin MF, Morrison CE, et al. Phenotypic features of myoclonus-dystonia in three kindreds. Neurology. 2002; 59(8):1187–1196. [PubMed: 12391346]
43. Aleman GG, de Erausquin GA, Micheli F. Cognitive disturbances in primary blepharospasm. Mov Disord. 2009; 24(14):2112–2120. [PubMed: 19705473]
44. Balas M, Peretz C, Badarny S, et al. Neuropsychological profile of DYT1 dystonia. Mov Disord. 2006; 21(12):2073–2077. [PubMed: 17013905]
45. Bugalho P, Correa B, Guimaraes J, et al. Set-shifting and behavioral dysfunction in primary focal dystonia. Mov Disord. 2008; 23(2):200–206. [PubMed: 18044708]
46. Jahanshahi M, Rowe J, Fuller R. Cognitive executive function in dystonia. Mov Disord. 2003; 18(12):1470–1481. [PubMed: 14673884]
47. Fahn S, Burke R, Stern Y. Antimuscarinic drugs in the treatment of movement disorders. Prog Brain Res. 1990; 84:389–97. [PubMed: 2267310]
48. Taylor AE, Lang AE, Saint-Cyr JA, et al. Cognitive processes in idiopathic dystonia treated with high-dose anticholinergic therapy: implications for treatment strategies. Clin Neuropharmacol. 1991; 14(1):62–77. [PubMed: 2029694]
49. Marsden CD, Marion MH, Quinn N. The treatment of severe dystonia in children and adults. J Neurol Neurosurg Psychiatry. 1984; 47:1166–1173. [PubMed: 6502174]
50. Greisberg S, McKay D. Neuropsychology of obsessive-compulsive disorder: a review and treatment implications. Clin Psychol Rev. 2003; 23(1):95–117. [PubMed: 12559996]
51. Allam N, Frank JE, Pereira C, Tomaz C. Sustained attention in cranial dystonia patients treated with botulinum toxin. Acta Neurol Scand. 2007; 116(3):196–200. [PubMed: 17714334]
52. Pillon B, Ardouin C, Dujardin K, et al. Preservation of cognitive function in dystonia treated by pallidal stimulation. Neurology. 2006; 66(10):1556–1558. [PubMed: 16717218]
53. Ghilardi MF, Ghez C, Eidelberg D. Visuo-Spatial Learning May Be Impaired in Non-Manifesting Carriers of the DYT1 Dystonia Mutation. Neurology. 1999; 52(Supp l2):A516.
54. Lou JS, Kearns G, Benice T, et al. Levodopa improves physical fatigue in Parkinson's disease: a doubleblind, placebo-controlled, crossover study. Mov Disord. 2003; 18(10):1108–1114. [PubMed: 14534913]
55. Ancelin ML, Artero S, Portet F, et al. Non-degenerative mild cognitive impairment in elderly people and use of anticholinergic drugs: longitudinal cohort study. BMJ. 2006; 332(7539):455–459. [PubMed: 16452102]
56. Buysse DJ, Reynolds CF, Monk TH, et al. The Pittsburgh Sleep Quality Index: a new instrument for psychiatric practice and research. Psychiatry Res. 1989; 28(2):193–213. [PubMed: 2748771]
57. Trotti LM, Esper CD, Feustel PJ, Bliwise DL, Factor SA. Excessive daytime sleepiness in cervical dystonia. Parkinsonism Relat Disord. 2009; 15(10):784–786. [PubMed: 19447065]
58. Jankel WR, Allen RP, Niedermeyer E, Kalsher MJ. Polysomnographic findings in dystonia musculorum deformans. Sleep. 1983; 6(3):281–285. [PubMed: 6622883]
59. Sforza E, Montagna P, Defazio G, Lugaresi E. Sleep and cranial dystonia. Electroencephalogr Clin Neurophysiol. 1991; 79(3):166–169. [PubMed: 1714808]
60. Wein A, Golubev V. Polygraphic analysis of sleep in dystonia musculorum deformans. Waking Sleeping. 1979; 3(1):41–50. [PubMed: 227178]
61. Jankel WR, Niedermeyer E, Graf M, Kalsher M. Polysomnography of torsion dystonia. Arch Neurol. 1984; 41(10):1081–1083. [PubMed: 6477216]
62. Fish DR, Allen PJ, Sawyers D, Marsden CD. Sleep spindles in torsion dystonia. Arch Neurol. 1990; 47(2):216–218. [PubMed: 2302092]

63. Avanzino L, Martino D, Marchese R, et al. Quality of sleep in primary focal dystonia: a case-control study. Eur J Neurol. 2010; 17(4):576–581. [PubMed: 20039936]
64. Silvestri R, De Domenico P, Di Rosa AE, Bramanti P, Serra S, Di Perri R. The effect of nocturnal physiological sleep on various movement disorders. Mov Disord. 1990; 5(1):8–14. [PubMed: 2296264]
65. Trender-Gerhard I, Sweeney MG, Schwingenschuh P, et al. Autosomal-dominant GTPCH1-deficient DRD: clinical characteristics and long-term outcome of 34 patients. J Neurol Neurosurg Psychiatry. 2009; 80:839–845. [PubMed: 19332422]
66. Menkes JH, Wetterberg L, Ross SB, Yuwiler A. Catecholaminergic activity in idiopathic torsion dystonia. Neurology. 1987; 37(5):779–783. [PubMed: 3574676]
67. Cano SJ, Warner TT, Linacre JM, et al. Capturing the true burden of dystonia on patients: the Cervical Dystonia Impact Profile (CDIP-58). Neurology. 2004; 63(9):1629–1633. [PubMed: 15534247]
68. Jankovic J, Leder S, Warner D, Schwartz K. Cervical dystonia: clinical findings and associated movement disorders. Neurology. 1991; 41(7):1088–1091. [PubMed: 2067638]
69. Kutvonen O, Dastidar P, Nurmikko T. Pain in spasmodic torticollis. Pain. 1997; 69(3):279–286. [PubMed: 9085302]
70. Lowenstein DH, Aminoff MJ. The clinical course of spasmodic torticollis. Neurology. 1988; 38(4): 530–532. [PubMed: 3352905]
71. Duane, DD. Spasmodic torticollis. In: Jankovic, J.; Tolosa, E., editors. Advances in Neurology. New York: Raven Press; 1988. p. 135-150.
72. Lobbezoo F, Tanguay R, Thon MT, Lavigne GJ. Pain perception in idiopathic cervical dystonia (spasmodic torticollis). Pain. 1996; 67(2–3):483–491. [PubMed: 8951945]
73. Tinazzi M, Rosso T, Fiaschi A. Role of the somatosensory system in primary dystonia. Mov Disord. 2003; 18(6):605–622. [PubMed: 12784263]
74. Lobbezoo F, Thu Thon M, Remillard G, et al. Relationship between sleep, neck muscle activity, and pain in cervical dystonia. Can J Neurol Sci. 1996; 23(4):285–290. [PubMed: 8951207]
75. Dressler D, Benecke R. Autonomic side effects of botulinum toxin type B treatment of cervical dystonia and hyperhidrosis. Eur Neurol. 2003; 49(1):34–38. [PubMed: 12464716]
76. Tiple D, Strano S, Colosimo C, et al. Autonomic cardiovascular function and baroreflex sensitivity in patients with cervical dystonia receiving treatment with botulinum toxin type A. J Neurol. 2008; 255(6):843–847. [PubMed: 18458860]
77. Aronson AE, Brown JR, Litin EM, et al. Spastic dysphonia. I. Voice, neurologic, and psychiatric aspects. Journal of Speech and Hearing Disorders. 33:203–218. [PubMed: 4385966]
78. Van Hoof JJ, Horstink MW, Berger HJ, et al. Spasmodic torticollis: the problem of pathophysiology and assessment. J Neurol. 1987; 234(5):322–327. [PubMed: 3612203]
79. Harrington RC, Wieck A, Marks IM, et al. Writer's cramp: not associated with anxiety. Mov Disord. 1988; 3(3):195–200. [PubMed: 3193960]
80. Jahanshahi M, Marsden CD. Depression in torticollis: a controlled study. Psychol Med. 1988; 18(4):925–933. [PubMed: 3270835]
81. Jahanshahi M, Marsden CD. Conversion "V" profiles in torticollis. Behavioural Neurology. 1989; 2:219–225.
82. Meares R. Obsessionality, the Sandler-Hazari scale and spasmodic torticollis. Br J Med Psychol. 1971; 44(2):181–182. [PubMed: 5088448]
83. Bindman E, Tibbetts RW. Writer's cramp – a rational approach to treatment? The British Journal of Psychiatry. 1977; 131:143–148. [PubMed: 912215]
84. Bihari K, Hill JL, Murphy DL. Obsessive-compulsive characteristics in patients with idiopathic spasmodic torticollis. Psychiatry Res. 1992; 42:267–272. [PubMed: 1496058]
85. Broocks A, Thiel A, Angerstein D, et al. Higher prevalence of obsessive-compulsive symptoms in patients with blepharospasm than in patients with hemifacial spasm. Am J Psychiatry. 1998; 155:555–557. [PubMed: 9546005]
86. Kubota Y, Murai T, Okada T, et al. Obsessive-compulsive characteristics in patients with writer's cramp. J Neurol Neurosurg Psychiatry. 2001; 71:413–414. [PubMed: 11534517]

87. Eldridge R, Harlan A, Cooper IS, et al. Superior intelligence in recessively inherited torsion dystonia. Lancet. 1970; 1:65–67. [PubMed: 4188627]

88. Hinse P, Leplow B, Humbert T, et al. Impairment of visuospatial function in idiopathic spasmodic torticollis. J Neurol. 1996; 243(1):29–33. [PubMed: 8869384]

89. Scott R, Gregory R, Wilson J, et al. Executive cognitive deficits in primary dystonia. Mov Disord. 2003; 18(5):539–550. [PubMed: 12722168]

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Table 1

Depression/anxiety studies in dystonia

Author, Year	Study Type	Sample Size	Findings	Comments
Aronson, 1968	Case control	31 spasmodic dysphonia 50000 controls (gen. outpt medical population) 18 psychogenic aphonia	No statistically significant difference between the 3 groups on MMPI.	
Van Hoof, 1987	Retrospective Case Control	17 spasmodic torticollis Healthy controls (Unspecified)	No difference in personality inventory. 2 of 17 spasmodic torticollis patients had depression.	
Harrington, 1988	Retrospective Case Control	22 writer's cramp 22 healthy controls	No difference in anxiety indices. 3 subjects had symptoms of generalized anxiety.	
Naber, 1988	Case Control	32 spasmodic torticollis 32 controls with Parkinson disease	MMPI scores, specifically hypochondriasis, depression, and hysteria, were elevated in 50% of pts.	MMPI scores correlated with severity of neurologic symptoms and were similar to PD controls.
Jahanshahi, 1988b	Case control	100 spasmodic torticollis 49 controls (cervical spondylosis)	No difference in MMPI, anxiety or obsessive symptoms.	7 ST patients with prior psychiatric histories were excluded.
Jahanshahi, 1989	Case series	61 spasmodic torticollis	36% had normal MMPI profiles, conversion "V" profiles were seen in 9%.	58.5% had MMPI pattern consistent with mild depression
Jahanshahi, 1990a	2 year Longitudinal cohort	67 spasmodic torticollis	25% of patients depressed at both time points.	Depression improved in patients with successful botox treatment.
Jahanshahi, 1990b and Jahanshahi, 1988a	Retrospective case control	85 spasmodic torticollis 49 controls (cervical spondylosis)	ST patients had higher prevalence (54%) and severity of depression, disability and negative body concept.	Body image, neuroticism, pain and disability correlated with depression.
Grafman, 1991	Case series	20 focal hand dystonia	4/20 had mild depression, 30% with elevated anxiety inventory scores.	MMPI and psychiatric histories were unremarkable and did not correlate with dystonia severity.
Cannito, 1991	Retrospective case control	18 spasmodic dysphonia 18 healthy controls	SD had higher rates of clinical depression and anxiety (both 39%).	
Jahanshahi, 1992	Longitudinal cohort	26 spasmodic torticollis	Improved depression and disability after botox injections in 22 pts whose torticollis improved.	Body concept also improved but not significantly
Murry, 1994	Case control	32 spasmodic dysphonia 28 healthy controls	SD had higher ratings of depression, state and trait anxiety.	Improvements noted in depression and anxiety following botox treatment.
Scheidt, 1996 I–IV	Retrospective case control	256 spasmodic torticollis HC (Unspecified)	27% of ST patients had psychopathology including 23% with clinical depression.	Depression correlated with severity.
Wenzel, 1998	Case series	44 spasmodic torticollis	High lifetime prevalence of psychiatric disorders (66%) especially anxiety disorders (34%), including panic disorder (20%) and MDD (25%).	43% of patients reported psychopathology preceded motor symptoms.
Gundel, 2001	Case control	116 spasmodic torticollis 483 healthy controls	Higher lifetime prevalence of MDD (46%) and anxiety d/o, especially social phobia (71%)	Psychopathology did not correlate with dystonia severity. Social phobia correlated with body image.

Author, Year	Study Type	Sample Size	Findings	Comments
Moraru, 2002	Case series	40 spasmodic torticollis	40% with anxiety, 37.5% with major depressive disorder.	Criteria for 1 lifetime psychiatric dx fulfilled prior to onset of ST in 42.5%
Muller, 2002	Longitudinal cohort	131 spasmodic torticollis 89 blepharospasm	47% depression in ST pts, 37% in BL pts. Health related QOL significantly worse in all domains compared to controls.	Botox improved clinical symptoms but minimal improvement in health related QOL.
Gundel, 2003	Retrospective case control	48 spasmodic torticollis 48 controls (alopecia areata)	Higher prevalence of psychiatric diagnosis (77%) including anxiety (69%) and mood (19%) disorders.	Social phobia (54%) was the most common anxiety disorder
Heiman, 2004	Case control	96 manifesting carriers of DYT1 60 non-manifesting carriers of DYT1 65 noncarriers	Risk for recurrent major depressive disorder increased in both NMC (RR 4.95) and MC (RR 3.62) compared with noncarriers	Mutation carriers also had earlier onset depression than noncarriers
Lauterbach, 2004	Retrospective case control	28 primary generalized dystonia and spasmodic torticollis 1:128 matching with healthy controls	Higher prevalence of MDD (25%), BMD (7%), phobias (39%), GAD (25%) and alcohol abuse (11%) than in HC.	53% of dystonia patients were on GABA agonists. Phobias and GAD frequently preceded motor symptoms.
Lewis, 2008	Case series	329 focal and generalized dystonia	30% reported moderate to severe depression. Disfigurement, negative body concept, low self-esteem, and QOL were important contributors to depression.	

BL – blepharospasm; BMD – bipolar mood disorder; FHD – focal hand dystonia; GAD – generalized anxiety disorder; HC – healthy controls; MC – manifesting carriers; MDD – major depressive disorder; MMPI – Minnesota Multiphasic Personality Inventory; NMC – nonmanifesting carriers; PA – psychogenic aphonia; PD – Parkinson disease; PG – primary generalized dystonia; QOL – quality of life; SD – spasmodic dysphonia; ST – spasmodic torticollis; WC – writer's cramp

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Table 2

Obsessive compulsive symptoms

Author, Year	Study Type	Sample Size	Findings	Comments
Meares, 1971	Case control	32 spasmodic torticollis Healthy controls (unspecified N)	ST had higher than expected obsessional personality traits but not symptoms.	Obsession correlated with neuroticism.
Bindman, 1977	Case series	10 writer's cramp	9 of 10 WC had obsessive personalities.	
Mathews, 1978	Case series	29 spasmodic torticollis	Neuroticism, obsessional symptoms, intropunitive hostility unchanged from general population.	23/29 with "adverse social effects" and 9/21 with mod-severe marital discord
Bihari, 1992	Retrospective case control	21 blepharospasm 19 healthy controls	BL patients had higher scores on obsessive compulsive inventory.	Did not assess for clinical OCD.
Broocks, 1998	Case series	13 blepharospasm 13 hemifacial spasm	Significantly more obsessive-compulsive symptoms in BL group than HFS group.	
Kubota, 2001	Retrospective case control	12 writer's cramp 12 disease control (including CTS) 12 healthy controls	WC had significantly higher obsessive compulsive symptoms score than either control group.	There were no differences between diseased and healthy controls.
Cavallaro, 2002	Case series	76 idiopathic focal dystonia	19.7% satisfied DSM-IV criteria for OCD. Morbidity risk for first degree family members of OCD pts was 13.8%, significantly higher than general population.	
Heiman, 2007	Case Control	96 manifesting carriers of DYT1 60 non-manifesting carriers of DYT1 65 healthy controls	No difference in OCD or obsessive-compulsive symptoms between controls and carriers.	1st study examining OCD specifically in DYT1 carriers
Saunders- Pullman, 2002	Case control	16 manifesting carriers of DYT 11 11 non-manifesting carriers of DYT 11 28 non carriers	Rate of OCD higher in carriers (5/27) than noncarriers (0/28) and greater in symptomatic (4/16) than nonsymptomatic (1/11).	
Hess, 2007	Retrospective Case Control	20 manifesting carriers of DYT11 10 non-manifesting carriers of DYT11 34 healthy controls	Increased rate of OCD, EtOH dependence among MC group, not NMC group.	

BL-blepharospasm; CTS-carpal tunnel syndrome; HC- healthy controls; HFS – hemifacial spasm; IFD – idiopathic focal dystonia; MC – manifesting carriers; NMC – nonmanifesting carriers; OCD-obsessive compulsive disorder; QOL – quality of life; ST- spasmodic torticollis; WC-writer's cramp

Table 3

Studies of cognition in dystonia.

Author, Year	Study Type	Sample Size	Findings	Neuro-psychologic al tests	Comments
Eldridge, 1970	Case control	14 autosomal recessive dystonia 10 siblings 24 controls	Stastitically significant increase in IQ scores for patients affected with autosomal recessive dystonia	IQ test	
Taylor, 1991	Case control	20 idiopathic focal dystonia 20 healthy controls	Only explicit memory, speed of information processing affected by high dose anticholinergics	NART, WAIS-R, LP, VR, DRT, TT, BSRT, CALT, BC, Item 99 from LNNB, SCWT, VFT, WCST	Vulnerability to meds highly age dependent
Hinse, 1996	Case control	15 spasmodic torticollis 15 normal controls	ST pts performed significantly worse on spatial tasks requiring mental manipulation of personal space	MW, HRDT, CBTT, VST	No significant difference in spatial perception
Ghilardi, 1999	Case control	4 non-manifesting carriers of DYT 1 5 healthy controls	NMC pts had significantly decreased scores for motor and visual sequence learning than HC group	ME, MSL, VSL	
Ghilardi, 2003	Case control	12 non-manifesting carriers of DYT 1(no hx of psychiatric disease) 12 healthy controls	Sequence learning impaired in carriers with preserved motor performance	CCW, RAN, SEQ	Overactivation of left PMC, right SMA in NMC patients during sequence learning (PET scan). May be compensating for striatal dysfunction
Jahanshahi, 2003	Case control	10 idiopathic focal dystonia + idiopathic generalized dystonia 12 healthy controls	Significant difference in category fluency and performing dual tasks. Otherwise, preserved executive fxn compared to controls	NART, WFT, WCST, SCWT, MDT, SORNS, RNG, VVCAL, PVSAT, DTP	Only 1/10 pts on meds (4 mg Artane/day), dystonia group had nonsignificant increase in self reported depression
Scott, 2003	Case series	14 primary dystonia (7 men, 7 women) prior to undergoing GPi deep brain stimulation surgery	Baseline impairment with extradimensional set-shifting (prior to DBS surgery), part of CANTAB battery	CANTAB, NART, Raven, SDMT, Stroop, TM, BNT, JLO, SCOLP, RMT, AMIPB, DS, CF	Not clear if this impairment is functionally significant, or if it improves with GPi surgery. Study not controlled for mood, pain, meds
Balas, 2006	Case control	20 manifesting carriers of DYT1 8 non-manifesting carriers of DYT1 28 matched controls	Symptomatic pts performed better on semantic verbal fluency test, worse on verbal learning test	Raven, RAVLT, RCF, PVF, SVF, TMA/B, Stroop, CANTAB, WAIS-III, JLO, PP	No difference between nonsymptomatic carriers and controls. Statistically accounted for meds, anxiety levels
Pillon, 2006	Longitudinal cohort	22 primary generalized dystonia undergoing DBS surgery	No pre-surgical cognitive decline in executive function. GPi DBS mildly but significantly improved executive fxn.	Raven, WAIS-R, GBT, WCST, VFT, TMA/B	Improvement either related to DBS or reduction in anticholinergic drugs. 20/22 pts on meds prior to surgery
Allam, 2007	Case control	9 primary cranial dystonia (blepharospasm) 9 healthy controls	Sustained attention deficits prior to botox injections; following injections, no significant difference in sustained attention compared to controls	RAVLT, TPT, DSub, DSY, SCWT	Executive dysfxn may be related to disrupting effects of symptoms

Author, Year	Study Type	Sample Size	Findings	Neuro-psychologic al tests	Comments
Bugalho, 2008	Case control	45 idiopathic focal/segmental dystonia 27 healthy controls	More set-shifting deficits in dystonia group, also had significantly more obsessive compulsive symptoms	WCST, SCWT, BAT, BVRT	No pts on anticholinergic medication
Carbon, 2008	Case control	6 non-manifesting carriers of DYT1 6 healthy controls	NMC pts performed at control levels during sequence learning	TSEQ, CCW	NMC pts overactivated lateral cerebellum, R inferotemporal cortex, underactivated prefrontal regions
Aleman, 2009	Case control	20 blepharospasm 17 healthy controls	BL pts showed impairment of complex movement planning, motor dexterity, visuospatial working memory, and tactile object recognition	WAIS-III, FDT, Raven, LT, LOW I/II, SL, WCST, PP, OMT, DR, TD, Tap	Groups matched for severity of depression and education level

AC- anticholinergic; BC-Block Counting Item from Stanford-Binet Intelligence Test; AMIPB- Adult Memory and Information Processing Battery; BAT- Block Assembly Test of WAIS; BL-blepharospasm; BNT- Boston Naming Test; BSRT- Buschke Selective Reminding Test; BVRT- Benton Visual Retention Test; CALT- Conditional Associative Learning Test; CANTAB- Cambridge Neuropsychological Test Automated Battery; CBTT- Corsi's Block Tapping Test; CCW- matched motor baseline task; CF- Medical College of Georgia Complex Figures; CLTR- Consistent Long-Term Memory; DR- Digital Recognition; DRT-Delayed Recognition Span Test; DS- Digit span; DSub- Digit Subtest of Wechsler Memory Scale-R; DSY- Digit Symbol subtest of the Wechsler Intelligence Scale-R; DTP- dual task performance; FDT- Five Digits Test; GBT- Grober and Buschke test; HC- healthy controls; HRDT- Hebb's Recurring Digits Test; IFD-idiopathic focal dystonia; IGD-idiopathic generalized dystonia; HC-healthy controls; JLO-judgment of line orientation; LNNB-Luria-Nebraska neuropsychological battery; LOW I/II- List of Words I and II; LP- Logical Passages; LT- Luria task; MC-manifesting carriers; MDT- missing digit test; ME- motor execution; MSW- motor sequence learning; MW- Mehrfachwahl-Worschatztest; NART- National Adult Reading Test; NMC-non-manifesting carriers; OMT- Oral Making Trails; PET-positron emission tomography; PMC- premotor cortex; PP- Purdue pegboard; PVF- phonemic verbal fluency; PVSAT- Paced Visual Serial Addition Test; RAN – reaction time/motor performance; Raven- Raven's Matrices; RAVLT- Rey auditory verbal learning test; RCF- Rey complex figure; RMT- Recognition Memory Test; RNG- random number generation; SCOLP- Speed and Capacity of Language Processing test; SCWT-Stroop Colour-Word Test; SDMT- Simple Digit Modalities Test; SEQ – motor learning task; SL- Spatial Location; SMA- supplementary motor area; SORNS-Self-Ordered Random Number Sequences; SVF- semantic verbal fluency; Tap- Tapping Test; TD- Tactile Denomination; TMA/B- Trail-making A and B; TPT- Toulouse-Pieron Test; TSEQ – trial-and-error-guided motor sequence learning task; TT-Tower of Toronto Test; VFT-Verbal Fluency Test; VR-Visual Reproduction; VVCAL- Visual-Visual Conditional Associative Learning; VSL- visual sequence learning; VST- Visuospatial testing; WAIS-R – Wechsler Adult Intelligence Scale-revised; WAIS-III- Wechsler Adult Intelligence Scale-III; WCST-Wisconsin Card Sorting Test; WFT-word fluency test;