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Examining the impact of motor symptoms on cognitive function in isolated dystonia

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List of abbreviations:

AES: Apathy Evaluation Scale
HADS: Hospital Anxiety and Depression Scale
MCST: Modified Card Sorting Test
NART PFSIQ: National Adult Reading Test Predicted Full Scale IQ
PIQ: Performance IQ
RMT: Recognition Memory Test
TEA: Test of Everyday Attention
TMT – A: Trail Making Test, part A
TMT – B: Trail Making Test, part B
VIQ: Verbal IQ
WAIS-III: Wechsler Adult Intelligence Scale – Third Edition

Tables, figures and supplemental digital content: 2 tables.

Abstract

Objectives: To investigate the impact of dystonia symptoms upon cognitive functioning, by comparing cognitive performance in focal and generalised dystonia subtypes, and examining the differential contribution of severity of symptoms and mood disorder.

Background: Studies investigating the non-motor syndrome in isolated dystonia have reported evidence of cognitive dysfunction. However, the cause of this cognitive impairment remains unclear. Several studies have suggested that poor cognitive performance reflects the distracting effects of the motor symptoms and/or mood disorder.

Methods: 25 cervical dystonia patients were compared with 13 generalised dystonia patients and 50 healthy controls on an extensive battery of cognitive and mood assessments.

Results: Cognitive performance was found to be independent of all clinical and mood variables. We found no significant differences in cognitive performance between the two dystonia groups. The whole dystonia group demonstrated significant impairment on only one measure of cognitive functioning, namely the Trail Making test. Two patients also showed impairment on one further measure, the Stroop test, and dystonia patients demonstrated more frequent impairment on the Hayling Sentence Completion Test.

Conclusions: This study suggests the presence of a subtle executive deficit in dystonia, not accounted for by dystonia subtype, severity of symptoms or medication burden.

Introduction

Isolated dystonia, formerly referred to as primary dystonia, is a movement disorder, characterised by sustained muscle contractions, leading to twisting and repetitive movements, and/or abnormal postures which occur in the absence of any structural or chemical abnormality (see Fahn, Marsden & Calne, 1987). Distribution of ensuing motor symptoms may be focal, affecting one region only; segmental or multi-focal, affecting at least two regions; or generalised, affecting the trunk and at least two other regions (Albanese et al., 2013). Underlying aetiology may be inherited, acquired or idiopathic (Albanese et al., 2013); with at least three causative genes identified and validated (including DYT1, DYT6, DYT25; Dauer et al., 2014)

In addition to these often disabling motor symptoms, several studies have reported abnormalities in cognition (Stamelou et al., 2012). However, there has been some inconsistency in the abnormalities reported, with several conflicting findings, and some studies reporting no impairment at all (Ostrem et al., 2011; Taylor et al., 1991; van Tricht et al., 2012). Thus, the evidence for cognitive impairment in dystonia remains controversial.

This may reflect the methods used to assess the cognitive profile. Some studies have suggested preserved cognition in dystonia on the basis of a brief assessment battery only (Taylor et al., 1991). A more comprehensive study by Scott et al. (2003) found intact performance on a range of standard measures of cognitive and executive functioning, but also selective impairment on one test of executive functioning from the CANTAB (Intra/Extra Dimensional Set-Shifting Task). Other investigations have also revealed scattered impairments, mostly on tests of executive functions. For example, Jahanashahi, Rowe and Fuller (2003) reported impairments in category fluency and dual tasking; Bugalho and colleagues (2008) reported an increased number of perseverations on the Wisconsin Card Sorting Test; and van Tricht et al. (2012) reported impairment in category fluency and the Trail Making Test – part B. A few studies have also reported impairment in visual and verbal memory (Balas et al., 2006; Romano et al., 2012).

It has been argued that any cognitive deficits observed may simply reflect other more basic factors, such as the distracting effects of motor symptoms (Stamelou et al., 2012).

In keeping with this, Allam and colleagues (2007) found that cognitive performance in nine patients with cranial dystonia improved following treatment with botulinum toxin. Yet, a larger, subsequent study found cognitive functioning in 20 patients with blepharospasm was independent of symptom severity or duration (Gonzalez Alemán, de Erausquin & Micheli, 2009). Thus, it remains unclear if the motor symptoms can fully account for the cognitive deficits noted.

It is noted that no study to date has directly compared cognition across different dystonia subtypes. Should the cognitive deficits simply reflect the intrusiveness of motor symptoms, it may be hypothesised that more generalised and/or severe symptoms would be associated with greater cognitive impairment than that observed in patients with more focal or milder presentations.

Furthermore, although it is well recognised that the incidence of mood disorder is elevated in dystonia (Bugalho et al., 2008; Kleiner-Fisman et al., 2007; Ostrem et al., 2011; van Tricht et al., 2012), few studies have examined the relationship between cognitive performance and mood. Van Tricht et al. (2012) found that patients with isolated dystonia who also had a history of anxiety performed worse on a measure of working memory, and Jahanashahi et al. (2003) found that those with higher depression scores performed worse on a measure of executive functioning. This raises the possibility that any cognitive impairment may reflect the impact of mood disorder.

The aims of the present study were to: (1) compare cognition between dystonia patients and age-matched healthy controls; (2) determine if there are any differences in cognitive performance between generalised and cervical dystonia; (3) consider the impact of other relevant clinical factors, such as severity of symptoms and medication burden and (4) examine the relative contribution of mood.

Methods

Participants

Patients with a diagnosis of cervical or generalised dystonia who attended the Neuropsychology Department of the National Hospital for Neurology and Neurosurgery, Queen Square, London, were screened for eligibility. These patients had

been referred as part of a multi-disciplinary assessment for determining suitability for surgical treatments for dystonic symptoms. Exclusion criteria were: i) previous history of traumatic, neurological, psychiatric or systemic disorder; ii) history of alcohol/drug abuse; and iii) non-native English speaker. Application of these exclusion criteria resulted in five patients being excluded (*n* = 2, dystonia secondary to post-anoxic injury; *n* = 1, tardive dystonia; n = 1, history of alcoholism; *n* = 1, non-native English speaker). The remaining patients consisted of 25 cervical and 13 generalised dystonia. Over half of the generalised dystonia patients (69.2%, *n* = 9) had likely inherited forms (*n* = 7, DYT1; *n* = 1, DYT6; *n* = 1, autosomal dominant pattern of inheritance, but with no specific gene identified), with the four remaining generalised dystonia patients having a diagnosis of idiopathic isolated dystonia (negative for DYT1).

A total of 50 age-matched healthy controls were also recruited. These had no known history of traumatic, neurological, psychiatric or systemic disorder, no history of alcohol/drug abuse, and were native English speakers. The characteristics of the three participant groups are shown in Table 1.

-- Table 1 around here--

Severity of dystonia was independently rated by a Neurologist using the Burke-Fahn-Marsden Dystonia Rating Scale in the patient's optimal condition. A total of 33 (86.8 %) of the dystonia patients were taking medication at the time of testing (84.0 % of the cervical and 92.3 % of the generalised dystonia patients). These medications included anti-muscarinics (trihexyphenidyl [*n* = 11, 28.9 %], botulinum toxin [*n* = 18, 47.4 %], and tetrabenazine [*n* = 1, 2.6 %]); hypnotics (clonazepam [*n* = 7, 18.4 %], diazepam [*n* = 6, 15.8%], and chlorodiazepoxide [*n* = 1, 2.6 %]), relaxants (baclofen [*n* = 2, 5.3%]), and antidepressants (*n* = 7, 18.4%).

The research was done in accordance with the Helsinki declaration and the Institute of Neurology Joint Research Ethics Committee UCLH, NHS Trust Research and Development Directorate.

Cognitive assessment

All of the patient participants completed the following standardised neuropsychological assessments, assessing general intellectual functioning, memory abilities, attentional and executive functioning, speed of processing, and mood:

1. Global cognitive functioning

Current level of intellectual functioning was assessed using the Wechsler Adult Intelligence Scale – Third Edition (WAIS-III; Wechsler et al., 1997), pro-rated to generate scores for verbal (VIQ) and non-verbal intellectual abilities (PIQ). The National Adult Reading Test (NART; Nelson, 1982) was used in order to estimate premorbid level of intellectual functioning, by generating each patient's Predicted Full-Scale IQ (PFSIQ). The MMSE was administered as a screening test of global cognitive functioning (Folstein, Folstein & McHugh, 1975). Additional tests of naming (Graded Naming Test; McKenna & Warrington, 1983) and visuoperceptual skills (Silhouettes and/or Incomplete Letters from the Visual Object and Space Perception Battery; Warrington & James, 1991) were also administered to confirm the absence of a global cognitive disorder.

2. Memory

Visual and verbal recognition memory were assessed using the Recognition Memory Tests (RMT; Warrington, 1984).

3. Attentional and executive functioning

Attentional and executive functioning was assessed using the Elevator Counting subtests from the Test of Everyday Attention (TEA; Robertson et al., 1994), part B of the Trail Making Test (TMT-B; Reitan & Wolfson, 1985), Modified Card Sorting Test (MCST; Nelson, 1976), Brixton Spatial Anticipation Test (Burgess & Shallice, 1997), Stroop (Trenerry et al., 1989), Hayling Sentence Completion Test (Burgess & Shallice, 1997) and phonemic verbal fluency (FAS; Spreen & Strauss, 1998).

4. Speed of processing

Speed of information processing was assessed using part A of the Trail-Making Test (TMT-A; Reitan & Wolfson, 1985) and the Symbol Search and Digit Symbol Coding subtests from the WAIS-III (Wechsler, 1997).

5. Mood

All patients were screened for mood disorder using the Hospital Anxiety and Depression Scale (HADS; Zigmond & Snaith, 1983) and the Apathy Evaluation Scale (AES; Marin, Biedrzycki & Fririniciogullari, 1991).

The healthy controls completed an abbreviated version of this full assessment, comprising the WAIS-III, NART, RMT, TMT-B, Stroop, Hayling Sentence Completion Test and TMT-A.

Statistical analysis

Means and standard deviations were calculated for each of the raw scores on the measures. Before analysis, all data underwent log transformation to achieve near-normal distributions. Frequency of impairment (scores of less than 5^{th} percentile) on each test was also calculated relative to published normative data.

Results

Patient participants

All patients scored at or above 27/30 on the MMSE and above the 5th percentile on the Graded Naming Test and the Silhouettes and/or Incomplete Letters tests of visual functioning.

Cervical vs generalised dystonia

As shown in Table 1, the generalised dystonia patients were significantly younger than the cervical dystonia patients [t (36) = -5.04, p < .001, r = .45], but there were no significant differences in NART PFSIQ. The generalised dystonia group also had a significantly younger age of disease onset than the cervical group [t (34) = -5.25, p < .001, r = .67], as well as greater severity of movement disorder [t (14) = 4.35, p < .001, r = .76] and disability [t (14) = 4.30, p < .001, r = .75].

Neuropsychological performance was compared between the two dystonia groups (Table 2). Mean test scores were compared using analyses of covariance (ANCOVA), with age as a covariate, and adjusted using Bonferroni correction.

--Table 2 around here--

As shown in Table 2, there were no significant differences in neuropsychological performance between the two dystonia groups. Further, chi-square tests revealed no significant associations between the type of dystonia and frequency of impairment on the neuropsychological assessments.

Dystonia vs healthy controls

The dystonia group was compared with healthy controls. There were no significant differences in mean age, NART, WAIS-III or memory. However, the dystonia group performed significantly worse on the TMT-B [t (54) = 4.05, p < .001, r = .43] and TMT-A [t (53) = 2.25, p < .05, r = .32]. TMT-A was related to performance on the TMT-B [F (1, 52) = 21.75, p < .001, r = .99]. However, there remained a significant difference in TMT-B after controlling for TMT-A [F (1, 52) = 9.62, p < .05, r = .81] between the dystonia group and healthy controls. Although there was no significant group difference

in mean age between the two dystonia patient groups, an ANCOVA was performed to consider if the differing age ranges may contribute to the significant group difference in TMT-B performance. This confirmed that age was not a significant factor. In addition, although a chi-square test revealed no significant association between participant type and frequency of impairment, it is notable that five of the dystonia patients (13.2 %) performed in the impaired range on TMT-B (< 10^{th} percentile), whereas none of the healthy controls did, and no participant did on TMT-A.

The dystonia patients also performed significantly worse than healthy controls on the Stroop [t (44.71) = -2.11, $p < .05$, $r = .27$]. However, despite log transformation, the dystonia patients' scores remained significantly negatively skewed [$_z$skewness = -6.98], with insufficient homogeneity of variance [F (1, 70) = 10.73, $p < .05$]. Again, a chi-square test revealed no significant association between participant type and frequency of impairment, but four of the dystonia patients (10.5 %) performed in the impaired range (< 10^{th} percentile), whereas none of the healthy controls did. Two of these patients scored significantly below the group mean ($_z$Stroop: -4.67 and -2.68). The first of these patients had cervical dystonia and was taking botulinum toxin. The second had DYT1 generalised dystonia and was on antidepressant medication. When these two outliers were removed from the analysis, the group difference was no longer significant.

A chi-square test did reveal a significant association between participant type and frequency of impairment on the Hayling, with six of the dystonia patients (17.1 %) performing in the impaired range (< scaled score 4), whereas none of the healthy controls did [χ^2 (1) = 5.85, $p < .05$]. However, an ANOVA revealed no significant difference in mean scores.

In sum, nearly a third of all dystonia patients (n = 12, 31.6 %) performed in the impaired range on at least one of the TMT-B, Stroop and Hayling tests. One patient performed in the impaired range on all three, one patient was impaired on the Stroop and Hayling only, and the 10 remaining patients were impaired on only test (TMT-B: n = 4; Hayling: n = 4; Stroop: n = 2): Both of the patients with one than one impairment had a diagnosis of cervical dystonia, but the remaining patients had equally frequent diagnoses of cervical and generalised dystonia (both n = 5). Post-hoc analyses revealed no significant

group differences between those who were impaired on at least one test and those who were unimpaired in age, mood or severity of dystonia.

Contribution of disease variables

The role of age of disease onset, duration of illness, severity of movement disorder, or severity of disability was considered with the whole group. There were no significant correlations between neuropsychological performance and disease variables. Furthermore, when patients were separated into two groups according to severity of movement disorder, using a median split, no significant differences in neuropsychological performance was found.

There were no significant differences in neuropsychological performance between those using medications (n = 33) and those not (n = 5), after Bonferroni correction, Furthermore, there were no significant differences in those using medications thought to have greater cognitive side-effects (trihexyphenidyl, hypnotics: n = 15) and those who were not (n = 23).

Mood assessment

The dystonia patients disclosed high rates of mood disorder on the HADS and AES. 20 of the patients (52.6 %) scored above cut-off for anxiety, with a mean score of 7.53 (*SD* = 3.97). 11 of the patients (28.9 %) scored above cut-off for depression, with a mean score of 5.79 (*SD* = 3.75). 14 of the patients (36.8 %) scored above cut-off for apathy, with a mean score of 12.00 (*SD* = 8.02), and seven of these reached scored above cut-off for both depression and apathy. Depression and anxiety scores were highly intercorrelated (r = .63, p <.001), with a significant association between depression and apathy (r = .59, p < .001).

There were no significant differences in mood between the two dystonia groups. Mood was not significantly related to age of disease onset, duration of disease, severity of movement disorder or disability. When those endorsing high levels of mood disorder (scores > 11 for either anxiety or depression: n = 7) were compared with those endorsing only minimal levels (both scores < 8: n = 19), there were no significant group differences. Mood was also not associated with performance on any of the neuropsychological measures, and there was no significant association between level

of mood disorder (high/low) and frequency of impairment on neuropsychological assessments or severity of symptoms.

Discussion

Several studies have reported cognitive impairment in dystonia and have argued that this may simply reflect the distracting effects of the dystonia symptoms and/or mood disorder. We compared cognitive performance in patients with focal and generalised dystonia subtypes on a comprehensive range of neuropsychological assessments. We found no significant differences between cervical and generalised dystonia patients in mean performance or frequency of impairment. This is despite the fact that generalised dystonia patients have more severe and disabling motor symptoms than the cervical patients. This suggests that severity of motor symptoms has little or no impact upon cognitive performance.

Indeed, our correlational analyses revealed no significant associations between severity of symptoms and performance on any measure of cognitive functioning. Cognitive performance was also not associated with age of onset or duration of illness. There was no significant difference in cognitive performance between those using and not using any medication, or those using and not using medication with greater cognitive side-effect profiles. Although subgroup numbers precluded further analysis of any more fine-grained medication effects, the current findings suggest that cognitive performance is independent of these clinical variables.

When we compared dystonia patients with healthy controls, we found that the dystonia patients on the whole performed less well on the Trail-Making Test. Two patients also showed impairment on a further measure, the Stroop test. In addition, patients demonstrated significantly more frequent impairment on the Hayling Sentence Completion Test. In total, nearly a third of all dystonia patients demonstrated impairment on at least one test of executive functioning in comparison with none of the healthy controls. This relative deficit in executive functioning is in keeping with several previous reports (van Tricht, Scott et al., 2003; Jahanashahi et al., 2003; Bugalho et al., 2008; Romano et al., 2012; Kleiner-Fisman et al., 2007). Importantly, this deficit does not appear to be explained by a more basic fluctuation in attentional abilities caused by distracting effects of dystonic symptom, as severity of symptoms was not related to performance on any measure of executive functioning.

However, it should be stated that poor performance on the Trail-Making Test has been found to be an unspecific marker of brain dysfunction (Chan et al., 2015; Demakis, 2004). It also remains unclear whether any strong conclusions can be drawn on the basis of impaired Stroop performance in two patients only. Thus, although this study found evidence of subtle cognitive symptoms, which may have significant implications for the patients and should be recognised as part of the syndrome, there was no indication of a pervasive or significant cognitive impairment. The subtlety of these cognitive symptoms may explain why several previous studies have reported preservation of cognitive functioning in dystonia (Ostrem et al., 2011; Taylor et al., 1991; Vidalihet et al., 2005).

It seems unlikely that the little evidence of cognitive impairment found in this patient sample is simply attributable to the number of participants. Our patient sample of 38 is larger than most previously published studies (Ostrem et al., 2011; Taylor et al., 1991; Scott et al., 2003; Jahanashahi et al., 2003; Balas et al., 2006; Kleiner-Fisman et al., 2007; Vidalihet et al., 2005). Studies with similar size limitations and those with larger samples (up to $n = 51$) have also reported scattered impairments on tests of executive functioning (van Tricht et al., 2012; Bugalho et al., 2008; Romano et al., 2012). However, these studies have not included a healthy control sample or used a comprehensive battery of cognitive assessments. Thus, the significance of their findings remains unclear.

Our investigation of the prevalence of mood disorder revealed that our patients demonstrated a high rate of anxiety and depression, with around half of all patients meeting criteria for mood disorder. These figures are very similar to those reported previously (van Tricht et al., 2012; Ostrem et al., 2011; Scott et al., 2003; Jahanashahi et al., 2003; Bugalho et al., 2008; Kleiner-Fisman et al., 2007; Kuyper et al., 2011). However, we found no significant relationship between mood and cognitive performance. Previously, a few studies have reported a correlation between mood symptoms and cognitive functioning (van Tricht et al., 2012; Jahanashahi et al., 2003). However, another large study did not (Bugalho et al., 2008) suggesting that the cognitive profile does not simply reflect mood.

Furthermore, mood symptoms were not associated with disease factors. This is in keeping with previous research, which has shown that the mood symptoms often precede onset of motor symptoms, perhaps explaining why dystonia was once thought of as a manifestation of a psychiatric disturbance (Kuyper et al., 2011). This raises the possibility that the mood disorder seen in dystonia may actually represent yet another clinical manifestation of the disease, rather than simply a reaction to its negative consequences (Fabbrini et al., 2012). Indeed, genetic analyses have also found higher rates of mood disorder in symptomatic and asymptomatic carriers of the DYT1 gene mutation when compared with healthy controls, with asymptomatic carriers demonstrating a four-fold increase in risk of developing depression (Heiman et al., 2004). Thus, there is growing evidence that the mood symptoms represent an important facet of the dystonia non-motor syndrome.

In sum, this study has shown that the poor performance on cognitive tests in dystonia is not simply a reflection of the distracting influence of motor symptoms and/or mood disorder. Rather, the non-motor syndrome of dystonia includes subtle cognitive symptoms and high rates of mood disorder. Both of which occur independently of disease severity or level of disability. Thus, it is argued that isolated dystonia is a tripartite disease, with motor, affective and subtle cognitive features.

References

Albanese A, Bhatia K, Bressman SB, et al. 2013. Phenomenology and classification of dystonia: A consensus update. *Mov Disord.* 28: 863 – 873.

Allam N, Frank JE, Pereira C, et al. 2007. Sustained attention in cranial dystonia patients treated with botulinum toxin. *Acta Neurol Scand.* 116: 196 – 200.

Balas M, Peretz C, Badarny S, et al. 2006. Neuropsychological profile of DYT1 Dystonia. *Mov Disord.* 21: 2073 – 2077.

Bugalho P, Corrêa B, Guimarães J, et al. 2008. Set-shifting and behavioural dysfunction in primary focal dystonia. *Mov Disord.* 23: 200 – 206.

Burgess PW, Shallice T. 1997. *The Hayling and Brixton Tests.* Bury St. Edmunds, U.K: Thames Valley Test Company.

Chan E., MacPherson SE, Robinson G, et al. 2015. Limitations of the trail making test part-B in assessing frontal executive dysfunction. *JINS.* 21: 169 – 174.

Demakis GJ. 2004. Frontal lobe damage and tests of executive processing: A meta-analysis of the category test, stroop test, and trail-making test. *J Clin Exp Neuropsychol.* 26: 441 – 450.

Dauer W. 2014. Inherited isolated dystonia: Clinical genetics and gene function. *Neurotherapeutics.* 11: 807 – 816.

Fabbrini G, Berardelli I, Moretti G, et al. 2010. Psychiatric disorders in adult-onset focal dystonia: A case-control study. *Mov Disord.* 25: 459 – 465.

Fahn S, Marsden CD, Calne DB. 1987. Classification and investigation of dystonia. In: Marsden CD, Fahn S, eds. *Movement Disorders*. Vol. 2. London: Butterworths; 332–58.

Folstein M, Folstein SE, McHugh PR. 1975. Mini-mental state: A practical method for grading the cognitive state of patients for the clinician. *J Psychiatr Res.* 12: 189 – 198.

Gonzalez Alemán G, de Erausquin GA, Micheli F. 2009. Cognitive disturbances in primary blepharospasm. *Mov Disord.* 24: 2112 – 2120.

Heiman GA, Ottman R, Saunders-Pullman RJ, et al. 2004. Increased risk for recurrent major depression in DYT1 dystonia mutation carriers. *Neurology.* 63: 631 – 637.

Jahanashahi M, Rowe J, Fuller R. 2003. Cognitive executive function in dystonia. *Mov Disord.* 18: 1470 – 1481.

Kleiner-Fisman G, Lin Liang GS, Moberg PJ, et al. 2007. Subthalamic nucleus deep brain stimulation for severe idiopathic dystonia: Impact on severity, neuropsychologica status, and quality of life. *J Neurosurg.* 107: 29 – 36.

Kuyper DJ, Parra V, Aerts S, et al. 2011. The non-motor manifestations of dystonia: A systematic review. *Mov Disord.* 26: 1206 – 1217.

Marin RS, Biedrzycki RC, Fririniciogullari S. 1991. Reliability and validity of the Apathy Evaluation Scale. *Psychiatry Res.* 38: 143 – 162.

McKenna P, Warrington EK. 1983. *The Graded Naming Test*. Windsor, Berks: NFER-Nelson.

Nelson H. 1976. A modified card sorting test sensitive to frontal lobe defects. *Cortex.* 12: 313 – 324.

Ostrem JL, Racine CA, Glass GA, et al. 2011. Subthalamic nucleus deep brain stimulation in primary cervical dystonia. *Neurology.* 76: 870 – 878.

Pavese N. 2013. Dystonia: Hopes for a better diagnosis and a treatment with long-lasting effect. *Brain.* 136: 692 – 695.

Reitan RM, Wolfson D. 1985. *The Halstead–Reitan neuropsychological test battery: Therapy and clinical interpretation*. Tucson, AZ: Neuropsychological Press.

Robertson IH, Ward T, Ridgeway V, et al. 1994. *The Test of Everyday Attention.* Bury St. Edmunds, UK: Thames Valley Test Company.

Romano R, Bertolino A, Gigante A, et al. 2012. Impaired cognitive functions in adult-onset primary cranial cervical dystonia. *Parkinsonism Relat Disor, 20,* 162 – 165.

Scott RG, Gregory R, Wilson J, et al. 2003. Executive cognitive deficits in primary dystonia. *Mov Disord.* 18: 539 – 550.

Stamelou M, Edwards MJ, Hallett M, et al. 2012. The non-motor syndrome of primary dystonia: Clinical and pathophysiological implications. *Brain.* 135: 1668 – 1681.

Spreen O, Strauss E. 1998. *A compendium of neuropsychological tests: Administration, norms and commentary* (2nd ed.). New York: Oxford University Press.

Taylor AE, Lang AE, Saint-Cyr JA, et al. 1991. Cognitive processes in idiopathic dystonia treated with high-dose anticholinergic therapy: Implications for treatment strategies. *Clin Neuropharmacol. 14:* 62 – 77.

Trenerry MR, Crosson B, DeBoe J, et al. 1989. *Stroop neuropsychological screening test manual.* Odessa, Florida: Psychological Assessment Resources.

van Tricht MJ, Dreissen YEM, Cath D, et al. 2012. Cognition and psychopathology in myoclonus-dystonia. *J Neurol Neurosurg Psychiatry.* 83: 814 – 820.

Vidalihet M, Vercueil L, Houeto J-L, et al. 2005. Bilateral deep-brain stimulation of the globus pallidus in primary generalized dystonia. *N Engl J Med.* 352: 459 – 467.

Warrington EK. 1984. *Recognition Memory Test*. Windsor: NFER-Nelson.

Warrington EK, James M. 1991. *The visual object and space perception battery*. Bury St. Edmunds, UK: Thames Valley Test Company.

Wechsler D. 1997. *WAIS-III Manual.* San Antonio, TX: Psychological Corporation.

Zigmond AS, Snaith RP. 1983. The Hospital Anxiety and Depression Scale. *Acta Psychiatr Scand.* 67: 361 – 370.

Tables

Table 1: Characteristics of two isolated dystonia groups and healthy controls.

	Cervical dystonia	*Generalised dystonia*	*Healthy controls*
Gender			
Male	6	6	29
Female	19	7	21
Age (mean years ± SD)	57.84 ± 9.73	39.15 ±12.79	50.30 ± 12.49
Range	36 – 74	16 - 64	25 - 70
NART Predicted Full-Scale IQ (mean ± SD)	108.96 ± 12.20	103.85 ± 9.30	109.94 ± 7.96
Range	81 – 128	91 – 118	85 - 118
Age at disease onset (mean years ± SD)	42.33 ± 14.06	18.75 ± 9.25	-
Range	3 – 61	7 – 38	-
Duration of illness (mean ± SD)	14.75 ± 10.07	20.42 ± 8.67	-
Range	1 – 39	4 – 33	-
Burke-Fahn-Marsden Dystonia Rating Scale			
Movement	16.40 ± 9.66	38.42 ± 10.08	-
Range	2 – 36	25 – 50	-
Disability	3.00 ± 2.11	7.50 ± 1.87	-
Range	0 – 7	4 – 9	-

Table 2: Mean and standard deviations of the generalised and cervical dystonia patients on each of the measures.

		Generalised (Mean ± SD)	*Cervical (Mean ± SD)*	*Healthy Controls (Mean ± SD)*
Intellectual Functioning	WAIS-III			
	VIQ	97.85 ± 12.14	103.80 ± 14.34	106.08 ± 14.15
	PIQ	99.08 ± 19.22	107.16 ± 16.86	109.38 ± 15.66
Memory	RMT			
	Words	48.08 ± 2.75	45.65 ± 3.38	47.60 ± 4.87
	Faces	44.42 ± 4.52	41.09 ± 4.87	41.11 ± 4.87
Attentional	TEA			
	Elevator Counting	6.55± 0.69	6.92 ± 0.28	
	Elevator Counting with Distraction	6.64 ± 3.08	8.25 ± 2.66	
Executive	TMT-B (seconds)	89.92 ± 39.08	96.52 ± 42.30	59.53 ± 23.52
	MCST			
	Categories achieved	5.64 ± 1.21	5.57 ± 1.08	
	Errors	2.18 ± 2.79	5.10 ± 5.54	
	Brixton			
	Overall scaled score	6.83 ± 1.47	5.73 ± 1.61	
	Errors	13.14 ± 5.76	17.22 ± 4.89	
	Stroop	102.54 ± 16.12	96.92 ± 19.32	105.53 ±7.57
	Hayling	5.92 ± 1.08	5.26 ± 1.91	6.16 ± 1.07
	FAS	40.31± 9.88	44.80 ± 15.64	
Speed	TMT-A (seconds)	37.33 ± 16.18	35.38 ± 11.43	28.37 ± 8.11
	Symbol Search	35.50 ± 19.44	26.76 ± 7.02	
	Digit Symbol	55.25 ± 18.63	57.12 ± 14.65	