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Non-motor symptoms in patients with adult-onset focal dystonia: Sensory and psychiatric disturbances☆

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ABSTRACT

Dystonia is characterized by the presence of involuntary muscle contractions that cause abnormal movements and posture. Adult onset focal dystonia include cervical dystonia, blepharospasm, arm dystonia and laryngeal dystonia. Besides motor manifestations, patients with focal dystonia frequently also display non-motor signs and symptoms. In this paper, we review the evidence of sensory and psychiatric disturbances in adult patients with focal dystonia. Clinical studies and neurophysiological investigations consistently show that the sensory system is involved in dystonia. Several studies have also demonstrated that neuropsychiatric disorders, particularly depression and anxiety, are more frequent in patients with focal dystonia, whereas data on obsessive compulsive disorders are more contrasting.

1. Introduction

Dystonia is characterized by sustained or intermittent muscle contractions that cause abnormal movements and postures. Focal dystonia i.e. that affecting a single body part is the most frequent form of dystonia in adult subjects. Basal ganglia structures and their connections with cortical areas have been implicated in the pathophysiology of dystonia [1]. Recent reports have shown that in addition to motor abnormalities, patients with dystonia also display non-motor symptoms and signs [2,3]. In this paper we review sensory and psychiatric disturbances, which are the most common non-motor features of patients with adult-onset focal dystonia.

2. Sensory disturbances in focal dystonia

Patients with focal dystonia often complain of various sensory symptoms that develop prior to or concomitantly with dystonia. In blepharospasm (BPS), ophthalmological symptoms, which include burning sensation, grittiness or dryness of the eyes and photophobia, are present in 40–60% of patients before or at the onset of BPS [4]. In keeping with this observation one case-control study reported a significant association between BPS and diseases of the anterior ocular segment, such as blepharitis and keratoconjunctivitis [5]. Moreover, relatives of patients with focal dystonia who develop BPS are more likely to have eye symptoms before the onset of BPS than relatives who develop focal dystonia other than BPS. About two/thirds of patients with cervical dystonia (CD) complain of pain in the cervical region; pain is also a frequent symptom in patients with upper limb dystonia, although to a lesser extent than in those with CD. Neurophysiological investigations on nociceptive pathways based on laser-evoked potentials have, however, provided controversial findings, possibly because results vary depending on the type of focal dystonia. In patients with focal hand dystonia, the N2–P2 amplitudes after stimulation of the dystonic arm are lower than the N2–P2 amplitudes recorded after stimulation of the unaffected side as well as lower than those in healthy subjects [3]. By contrast, the pain rating and N2–P2 laser-evoked potentials are normal in patients with CD and neck pain [6].

Proprioceptive afferent-related functions, and particularly "kinaesthesia and vibration-induced illusion of movement", are abnormal in patients with focal dystonia. This abnormality occurs in both affected and unaffected body regions [7–9] with similar results being reported in asymptomatic first-degree relatives [8]

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Table 1
Summary of findings on neurophysiological abnormalities in sensory functions in dystonia patients.

Reference number	Patients	Main diagnostic instrument	Main findings
[3]	WC patients	Laser-evoked potentials	N2–P2 amplitudes from the affected side lower than amplitude from the unaffected side and that found in healthy subjects
[6]	CD patients	Laser-evoked potentials	Normal N2–P2
[7]	AOPD patients	Vibration-induced illusion of movement	Abnormal in the affected and unaffected body parts
[8]	Asymptomatic first degree relatives of CD patients	Vibration-induced illusion of movement	Abnormal
[9]	FHD patients	Vibration-induced illusion of movement	Abnormal
[11]	BPS, FHD, CD patients	Spatial Discrimination threshold	Abnormal
[15]	BPS, LD, GD	Spatial Discrimination threshold	Abnormal
[12]	CD, FHD, LD and unaffected relatives	Temporal Discrimination Threshold	Abnormally higher in patients and in unaffected relatives
[14]	BPS, CD, WC, LD	Temporal Discrimination Threshold	Abnormally higher in affected and unaffected body parts
[13]	BPS, CD, LD and unaffected relatives	Temporal Discrimination Threshold	Abnormally higher in patients and in unaffected relatives
[17]	FHD, WC	Temporal Discrimination Threshold	Abnormally higher in affected and unaffected body parts
[16]	FHD	Temporal discrimination threshold	Abnormally higher.

CD: cervical dystonia; BPS: blepharospasm; LD: laryingeal dystonia, WC: writer's cramp; FHD: focal hand dystonia; GD: generalized dystonia; AOPD: adult onset primary dystonia.

(Table 1). Impairment in reaching movements is not only present in patients with dystonia of the upper limb but also in those with cervical dystonia [10], which suggests that the proprioceptive function can be altered in body parts other than those affected by dystonia. This abnormality may be due to an error in the spatial representation of the hand location or to a failure in the integration of proprioceptive information with motor output.

Tactile afferent processing in dystonia has been extensively investigated by means of psychophysiological procedures (Table 1). The spatial discrimination threshold (defined as the shortest distance interval at which two stimuli applied to the same part of the body can be recognized as spatially separate) and the temporal discrimination threshold (defined as the minimum inter-stimulus interval at which participants recognize a pair of tactile stimuli as temporally separate) are abnormally higher in dystonic patients than in healthy subjects [11–14]. Altered temporal and spatial discrimination thresholds are also present in unaffected body regions [15], and have been observed in patients' unaffected relatives [12,13,15].

Further evidence of the involvement of the sensory system in dystonia comes from a number of studies that have investigated mechanisms of synaptic plasticity in cortical sensorimotor areas by means of transcranial magnetic stimulation. These neurophysiological studies have revealed impaired cortical somatosensory processing, which may be due to abnormal inhibitory interneuron activity, and abnormal sensory motor integration in patients with dystonia [16,17]. Using paired associative stimulation, which is a plasticity-inducing protocol that couples sensory input with primary motor cortex activation, Belvisi et al. [18], also reported abnormally increased TMS-motor-evoked potentials in target and non-target muscles.

3. Psychiatric disorders in focal dystonia

A current or lifetime diagnosis of a psychiatric illness may be found in up to 91.4% of patients with CD, as compared to 35% in the general population. Patients with CD have an increased lifetime risk of depression (from 15% to 53.4%) and of anxiety disorders (26.4%–83.3%) [19] (Table 2). In a case-control study, Fabbrini et al. [2] found that depressive disorders, diagnosed using the SCID-I interview, were significantly more frequent in CD patients than in age- and sex-matched healthy controls (26.9% vs 6%, $p < 0.01$); the BDI scores were also higher in CD patients than in controls (5.6 ± 4.7 vs 2.8 ± 2.2, $p < 0.01$). By contrast, Fabbrini et al. [2] found that the frequency of anxiety disorders did not differ between patients and controls. In another study, the prevalence rates of psychiatric diagnoses was evaluated in 86 patients with focal dystonia (70 with CD and 16 with BPS) and compared with those of a reference population based sample ($n = 3943$) [20]. The participants were also evaluated for personality traits by means of the Five Factor Personality Inventory. The results showed lifetime prevalence for any psychiatric or personality disorder of 70.9%. In contrast to the findings from the study by Fabbrini et al. [2] the likelihood of social phobia, agoraphobia and panic disorder was 4.5-fold higher in CD patients than in the reference population. Lencer et al. [20] also reported an increased prevalence rate for anxious personality disorders (32.6%) including increases in obsessive-compulsive (22.1%) and avoidant personality disorders (16.3%). In a single-center cross-sectional study on 103 consecutive patients with various forms of focal dystonia, 78 patients with hemifacial spasm (HFS) and 93 healthy control subjects, Lehn et al. [21] found that patients with focal dystonia had more obsessive compulsive, anxiety and depressive symptoms than either healthy subjects or patients with HFS.

Data on the frequency and type of psychiatric disturbances in BPS are more controversial than those in CD patients. In one case-control study that used a standardized psychiatric interview, the frequency of depressive disorders was higher in patients with BPS than in healthy controls but did not statistically differ from that in patients with HFS [2]. These results are in agreement with those that emerged from a previous study in which the frequency of depression in patients with BPS was similar to that observed in patients with HFS [22]. In a case control study, a diagnosis of OCD was found in only 1 out of 28 patients with BPS and the frequency of OCD did not differ between BPS patients and healthy controls [2]. A more recent study concluded that obsessive compulsive symptoms are more frequent in patients with focal dystonia (15 with CD, 15 with BPS and 15 with arm dystonia) than in patients with other forms of chronic disability [23], though the authors did not specifically examine the rate of obsessive compulsive symptoms separately for the three forms of dystonia.

Using the SCID-I in 47 patients with laryngeal dystonia and 27 patients with vocal fold paralysis, current psychiatric comorbidity was present in 41.7% of the laryngeal dystonia patients but in only 19.5% of patients with vocal fold paralysis [24]. In that study, the severity of voice impairment and the subjective assessment of "satisfaction with health" were significant predictors of psychiatric comorbidity. Similarly, Fabbrini et al. [2] found that psychiatric disturbances were present in 50% of their 16 patients with laryngeal dystonia, although no differences emerged between patients

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