Phenotypic Characterization of DYT13 Primary Torsion Dystonia

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Abstract: We describe the phenotype of DYT13 primary torsion dystonia (PTD) in a family first examined in 1994. A complete neurological evaluation was performed on all available family members: 8 individuals were definitely affected by dystonia. The family was re-evaluated in March 2000: at that time, 3 more individuals had developed symptoms of dystonia. Inheritance of PTD was autosomal dominant, with affected individuals spanning three consecutive generations and male-to-male transmission. Age at onset ranged from 5 to 43 years. Onset occurred either in the cranio-cervical region or in upper limbs. Progression was mild, and the disease course was benign in most affected individuals: generalization occurred only in 2 cases. We did not find anticipation of age at onset or of disease severity through generations. Most subjects presented with jerky, myoclonic-like dystonic movements of the neck or shoulders. DYT13-PTD is an autosomal dominant disease, with incomplete penetrance (58%). Clinical presentation and age at onset were more variable than in DYT1-PTD, and the neck was involved in most of those affected. Moreover, the individuals with generalised dystonia were not severely disabled and were able to lead independent lives. To date, this is the only family with DYT13-PTD. © 2004 Movement Disorder Society

Key words: primary torsion dystonia; PTD; DYT13; family study; phenotype

Dystonia is a syndrome characterised by sustained involuntary muscle contractions, causing twisting and repetitive movements or abnormal postures.1,2 The current classification includes two major etiologic categories: primary (sporadic or familial) and symptomatic dystonia. Primary torsion dystonia (PTD) is a movement disorder in which dystonia is the sole abnormality attributable to the condition, in the absence of other neurological signs and without any known cause.3 The precise prevalence of familial cases is unknown; on the basis of the largest series of patients affected by dystonia, it accounts for less than 20%.4 Familial dystonia is a clinical and genetic heterogeneous entity with a wide range of phenotypic expressions; to date, one gene and several different loci have been linked to different presentations of PTD.

In 1994, we studied a large Italian family, with several members affected by PTD (Fig. 1). The phenotypic presentation of dystonia among the affected individuals was variable, the prevalent phenotype consisting in early onset, upper body segmental dystonia. This family underwent genetic analysis; linkage with the DYT1 locus on chromosome 9q34 was ruled out5; successively, the linkage with DYT6 and DYT7 was also excluded.6

Due to the large number of affected individuals, the family was considered suitable for a genome-wide search. This strategy allowed mapping a novel locus, DYT13, on chromosome 1p36, to a 22 cM region with high gene density.7 Until now, the linkage with the DYT13 region has been detected only in the family described. The phenotype of DYT13-PTD has not yet been reported in detail, so we present here a description of the clinical presentation of dystonia in the definitely affected members.

SUBJECTS AND METHODS

The family was studied for the first time in 1994. All family members were investigated for possible causes of secondary dystonia using a detailed questionnaire and received a complete on-site neurological examination.8 Each subject was videotaped during the assessment, and a senior neurologist viewed the videotapes. Examination included tasks designed to reveal minor signs of dystonia, or of other movement disorders. The final diagnosis (affected, not affected, or probably affected) was established with the agreement of all the examiners.

All family members were re-evaluated in March 2000, using the same methodology described above. During the last visit, the disability of the affected individuals was also assessed by means of a section of the dystonia rating scale designed to assess the residual function in daily routine tasks (speech, writing, eating, swallowing, hygiene, dressing, and walking). The score ranged from 0 to 4 (0–6 for walking).8 The family genotype was analysed by excluding linkage with DYT15; DYT6, and DYT7 loci in affected individuals.6 A genome-wide search allowed mapping a novel locus (DYT13) on chromosome 1p36.7

A videotape accompanies this article.

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RESULTS

Family Data and Clinical Features

This family included 45 members and 11 spouses. Ancestors and all family members originated from a small region on the pre-Apennine highlands. In 1994, we identified 8 definitely affected subjects (III:2; III:6; III:10; III:14; III:16; III:18; IV:1, and IV:3). All available individuals were re-evaluated approximately 6 years later (March 2000). At that time, 3 more individuals (III:11, III:20, and IV:9) had developed symptoms of dystonia. Two of them were unaffected in 1994; the third presented with mild symptoms, which at that time did not allow to diagnose a definite dystonia. The remaining 5 individuals, diagnosed as probably affected in 1994, did not present appreciable progression over 6 years. They still had minor clinical signs (jerks of the neck or of the arm or mild tremor), but no spasmodic movements or abnormal posture were evident, no abnormal directional or task-induced movements, and no sensory tricks. In conclusion, after the last visit in March 2000, 11 members were diagnosed as affected by dystonia. The history and clinical presentation in individuals with a definite diagnosis of dystonia is described below in some detail and is summarised in Table 1. The scores of the disability scale are analytically reported in Table 2.

Affected Subjects

III:6.

A 67-year-old man is the index case. His personal history was uneventful until the age of 10, when cervical and head trauma were caused by a 6-metre fall (the patient reported the head trauma as “severe,” although he was not hospitalised). At the age of 15, he presented with abnormal movements of the head, described as rapid (clonic) rotational movements and lateral head tilt. The clinical picture was stable until the age of 46. After a high fever (over 42°C), cervical dystonia worsened without spreading to other body regions. Several years later, he developed right arm dystonia, which started with task-induced dystonic movement and rapidly progressed to dystonia at rest. Drug treatment did not produce clinical improvement. At age 54, he underwent surgical resection of the right sternocleidomastoid muscle without clinical benefit. During the first evaluation in 1994 (see Video, Segment 1), he had segmental dystonia, involving the cranial–cervical segment and the right upper limb. Symptoms consisted in involuntary jerks of the head and of the right shoulder, inducing a tremulous right rotational torticollis, pain and rigidity of the neck, and hyperlordosis. The patient had abnormal posture of the right wrist and dystonic movements of both arms (more severe on the right side). Because of upper limb dystonia, the patient was clumsy in performing tasks such as writing, drawing, or handling objects.
A 76-year-old woman suffered from fever-related seizures during infancy. Dystonic symptoms in the upper body (cranial–cervical and upper limbs) were noted since the age of 5. She had a head trauma and right arm fracture at age 18, without any consequence for the progression of dystonia. The patient and her relatives reported that she was fully symptomatic since the onset and that progression was noted only in terms of severity of symptoms. No spreading of dystonia to other body regions was observed. A pregnancy (ended in a caesarean delivery) and surgery for kidney stones did not influence dystonia. Different combinations of oral drugs and botulinum toxin treatment did not substantially improve dystonia. During the last visit, the patient presented segmental dystonia: moderate cranial–cervical involvement, and severe upper limb dystonia, which disabled the use of both upper limbs (see Video, Segment 2). She was unable to write, and needed help in the tasks of daily life requiring fine hand and finger movements.

### III:10.

A 68-year-old woman had an uneventful personal history until the age of 20, when she was cured with

<table>
<thead>
<tr>
<th>Subject</th>
<th>Age at onset (yr)</th>
<th>Presentation at onset</th>
<th>Age at last visit (yr)</th>
<th>Progression event-related</th>
<th>Presentation at last visit</th>
<th>Distribution at last visit</th>
<th>Disability (Overall score, Burke et al., 1985)</th>
<th>Response to therapy</th>
</tr>
</thead>
<tbody>
<tr>
<td>III:2</td>
<td>5</td>
<td>Cranial–cervical</td>
<td>71</td>
<td>No</td>
<td>Cranial–cervical</td>
<td>Segmental</td>
<td>Severe (10)</td>
<td>No</td>
</tr>
<tr>
<td>III:11</td>
<td>26</td>
<td>Cervical</td>
<td>63</td>
<td>Yes. After first pregnancy</td>
<td>Cranial–cervical</td>
<td>Segmental</td>
<td>Moderate (6)</td>
<td></td>
</tr>
<tr>
<td>III:14</td>
<td>5</td>
<td>Cervical</td>
<td>65</td>
<td>No</td>
<td>Cervical</td>
<td>Focal</td>
<td>Mild (0)</td>
<td></td>
</tr>
<tr>
<td>III:16</td>
<td>5</td>
<td>Upper limbs</td>
<td>59</td>
<td>No</td>
<td>Cranial–cervical</td>
<td>Segmental</td>
<td>Mild (2)</td>
<td>No (L-dopa 200 × 4)</td>
</tr>
<tr>
<td>III:18</td>
<td>20</td>
<td>Cervical</td>
<td>56</td>
<td>No</td>
<td>Cranial–cervical</td>
<td>Generalised</td>
<td>Moderate (6)</td>
<td></td>
</tr>
<tr>
<td>III:20</td>
<td>?</td>
<td>Cervical</td>
<td>53</td>
<td>No</td>
<td>Cranial–cervical</td>
<td>Segmental</td>
<td>Mild (1)</td>
<td></td>
</tr>
<tr>
<td>IV:1</td>
<td>43</td>
<td>Right upper limb</td>
<td>45</td>
<td>No</td>
<td>Right upper limb</td>
<td>Focal</td>
<td>Mild (1)</td>
<td></td>
</tr>
<tr>
<td>IV:3</td>
<td>14</td>
<td>Cranial–cervical</td>
<td>32</td>
<td>No</td>
<td>Cranial–cervical</td>
<td>Segmental</td>
<td>Mild (4)</td>
<td></td>
</tr>
<tr>
<td>IV:9</td>
<td>?</td>
<td>Upper limbs</td>
<td>41</td>
<td>No</td>
<td>Cranial–cervical</td>
<td>Segmental</td>
<td>Mild (1)</td>
<td></td>
</tr>
</tbody>
</table>

### Table 2. Dystonia Disability Scale

<table>
<thead>
<tr>
<th>Subject</th>
<th>Speech (0–4)</th>
<th>Handwriting (0–4)</th>
<th>Feeding (0–4)</th>
<th>Eating/swallowing (0–4)</th>
<th>Hygiene (0–4)</th>
<th>Dressing (0–4)</th>
<th>Walking (0–6)</th>
<th>Total (0–30)</th>
</tr>
</thead>
<tbody>
<tr>
<td>III:2</td>
<td>1</td>
<td>3</td>
<td>2</td>
<td>0</td>
<td>2</td>
<td>2</td>
<td>0</td>
<td>10</td>
</tr>
<tr>
<td>III:6</td>
<td>0</td>
<td>1</td>
<td>1</td>
<td>0</td>
<td>1</td>
<td>1</td>
<td>0</td>
<td>4</td>
</tr>
<tr>
<td>III:10</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>0</td>
<td>6</td>
</tr>
<tr>
<td>III:11</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>III:14</td>
<td>1</td>
<td>2</td>
<td>1</td>
<td>0</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>7</td>
</tr>
<tr>
<td>III:16</td>
<td>0</td>
<td>1</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td>III:18</td>
<td>1</td>
<td>2</td>
<td>1</td>
<td>0</td>
<td>1</td>
<td>1</td>
<td>0</td>
<td>6</td>
</tr>
<tr>
<td>III:20</td>
<td>0</td>
<td>1</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>IV:1</td>
<td>0</td>
<td>1</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>IV:3</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>4</td>
</tr>
<tr>
<td>IV:9</td>
<td>0</td>
<td>1</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>Average</td>
<td>0.45</td>
<td>1.27</td>
<td>0.63</td>
<td>0.18</td>
<td>0.54</td>
<td>0.54</td>
<td>0.18</td>
<td>3.82</td>
</tr>
</tbody>
</table>

Scale from Burke et al.8

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penicillin for rheumatic fever. During childhood she stuttered. She had three pregnancies and a miscarriage. She reported the onset of jerky movements of the head when she was age 26, after the first pregnancy. Later, dystonia progressed to involve pharyngeal and laryngeal muscles; as a consequence, the patient had difficulties in swallowing and reported hypophonia and voice tremor.

During the last examination, she presented with segmental dystonia of the cranial and cervical muscles, larynx, and upper limbs (see Video, Segment 3). Dystonic movements of the neck consisted of backward jerks and gross irregular head tremor. She presented also tremor and dystonic posture of the hands but was able to write a trembling (but still understandable) calligraphy.

### III:11.

A 65-year-old housekeeper had an uneventful medical history. She was unaware of any involuntary movement. When examined in 1995 at the age of 60, she presented slight involuntary tilt of the head and tremor of both hands during the finger-to-nose test, but no dystonic posture or movement was evident. When re-evaluated in 2000, she presented torticollis and left-hand dystonia and was diagnosed as being definitely affected by segmental dystonia. The symptoms did not impair daily life activities.

### III:14.

A 61-year-old woman reported phobic symptoms starting in youth. She presented hand dystonia at the age of 6 and reported that, almost since the onset of the disease, she had a shaking tremor involving all the body. A mild occipital trauma was reported at age 7. She had 3 pregnancies; after the first one at the age of 26, she noted that the severity of dystonia had progressed. At the time of her last evaluation, she presented with dystonic dysphonia, dystonic posture of the head and upper limbs (more evident when speaking), and shaking tremor of the head, trunk, and legs (see Video, Segment 4). Axial and limb dystonic tremor was more evident when she was seated and was enhanced when speaking. Upper limb dystonia moderately impaired feeding, writing, and handling small utensils, but the overall disability was mild (see Table 2), i.e., she could conduct domestic activities.

### III:16.

A 59-year-old woman reported a nervous breakdown in her thirties. Several years ago, she was treated with increasing doses of levodopa (up to 200 mg q.i.d.) without any clinical improvement. She had two pregnancies (one ended in miscarriage), which are not reported to have influenced her dystonia. At the moment of the evaluation, she presented with involuntary movements of the upper and lower face (more evident when speaking), painful dystonic posture of the neck (right laterocollis), dystonic posture of both arms, involuntary movements of the fingers (evident when walking), and writer’s cramp. She also had marked scoliosis with hypertrophy of paravertebral muscles and hyperlordosis, with abnormal truncal posture when walking.

### III:18.

A 56-year-old man reported the onset of a mild cervical dystonia at the age of 20. Dystonia did not progress over the following 3 decades; in his fifties he experienced a mild worsening of symptoms, consisting in dystonic posture of right hand and involuntary movements of both hands and head. At the time of evaluation, he presented with scoliosis, tremulous dysphonia, dystonic tremor of hands, and involuntary movements of the lips and eyes (see Video, Segment 5). The subject also reported early morning painful contractures of both legs and rapid jerky movements of the neck; this latter symptom sometimes woke him up at night. Dystonia moderately affected writing and other daily chores, but he could work as a farm laborer engaged in a full-time physical job.

### III:20.

A 58-year-old woman was diagnosed as probably affected by cervical dystonia in 1994. When re-evaluated 6 years later, she was definitely affected and presented with dystonic posturing of the right arm while writing and dystonic jerks and posturing of the neck partially controlled by a sensory trick. Her writing was moderately clumsy and words were legible.

### IV:1.

A 45-year-old employed man had an uneventful personal history until the age of 40, when he noticed that writing had become painful and distressing; this forced him to change the way he held the pen and modified his handwriting style. At the time of evaluation, he presented with writer’s cramp, which did not excessively impair his handwriting. He also presented an abnormally high blink rate that he had noted since adolescence. In the 5 years after onset, symptoms of dystonia were reported as stable.

### IV:3.

A 32-year-old man was delivered pre-term with forceps and experienced normal psychomotor developmental stages. At the age of 14, he stuttered and had tic-like
movements of facial muscles. During the first evaluation in 1994, he presented with rapid tic-like movements in left upper and lower facial muscles, frequent irregular blinking, mild dysphagia with occasional choking (when drinking), voice tremor, stuttering and hypophonia, dystonic movements of the neck, and scoliosis (see Video, Segment 6). During writing, he presented abnormal posturing of the hands and jerky myoclonic-like movements of the neck, that forced the head to extend backward. When re-evaluated, 6 years later, no progression of dystonia was observed.

IV:9.

This 41-year-old man was unaffected in 1994. When re-evaluated 6 years later, he presented with marked irregular tremor and bilateral dystonic posturing of upper limbs and writer’s cramp. He is aware of a painful neck posturing of recent onset, but he is not aware of dystonia of the upper limb, which perhaps started a few years ago. During writing, he has some tic-like movement of the face.

DISCUSSION

This family affected by DYT13-PTD includes 11 affected subjects spanning three generations. The observation of the affected individuals during a 6-year interval (from 1994 until 2000) allowed us to depict the phenotype of DYT13-PTD in the family. Onset was variable in terms of age (ranging from 5 to over 43 years) but was homogeneous with regards to the presentation at onset. Dystonia invariably involved the upper body: the cranial–cervical region (in 8 patients; 73% of cases) or the upper limbs (in 3 patients; 27%). Progression was mild and the disease course relatively benign in all affected individuals. All the patients with long disease duration experienced a spread of symptoms to other body regions. Progression led in 7 cases (64%) to a segmental involvement, in 2 cases (18%) to generalization; in the remaining 2 other cases (18%) there was no progression and the disease remained focal. The time course of progression could not be established with accuracy because most patients were not completely aware of their symptoms. Crossed interviews of different family members allowed us to establish that progression was quite heterogeneous. Two subjects took notes of their disease progression, which clearly showed heterogeneity. In subject III:14, onset was during infancy, and symptoms since then consisted of tremor involving all the body and progressed almost imperceptibly into old age. Subject III:6 was affected by torticollis since age 15, but progression of dystonia only occurred after 30 years, with spread to the right shoulder and arm.

Such long delay between onset and the spread of symptoms is unusual among PTDs. There is consensus on the observation that most PTD cases, particularly those with early onset, progress within 5 years from onset.9,10 It is very uncommon that dystonia only progresses after decades. We reviewed the records of the PTD patients in the Gemelli Registry (Elia and colleagues, unpublished data). In a series of 360 sporadic PTD patients with a mean disease duration of 8.6 years (±8.5), 40% had a progression of dystonia: in 65% of them symptom spread occurred during the first 5 years, whereas 35% reported over a longer period (in none did dystonia progress after 10 years).

In 3 subjects, the progression of dystonia was related to specific events: in 2 of 6 affected women, pregnancy was related in time with onset (III:10) or progression (III:14). One of the patients (III:6) experienced symptom exacerbation after an acute fever. It is worth noting that several patients reported relevant traumatic events: none was related to disease progression. No correlation between the severity of the disease and age at onset was seen, and no anticipation occurred between generations.

At the last visit, the disability score was low in all the affected family members (even those with onset in infancy), and this finding is surprising when one considers the long disease duration. Compared with DYT1-PTD, the individuals with generalized dystonia were not severely disabled: they could lead normal daily lives (see Table 2).

One gene and four PTD loci have been identified (see Table 3). The clinical picture in the DYT13-PTD is noticeably different from the DYT1 phenotype, where dystonia presents in a limb, rarely affects the cranial–cervical region, and has a higher tendency to generalize, producing a much more disabling disease.11,12 The DYT6-phenotype is characterized by a greater number of body regions involved at onset and in the course of the disease, which tends to be more severe and to generalize more frequently.13 The phenotype in our family is also different from that described in PTD linked to the DYT7 gene, which is characterized by adult-onset and pure focal cervical dystonia without tendency to spread to other body regions.14

In several PTD families reported in the literature, linkage to the known PTD loci has been excluded; in some of these families, the phenotype shares relevant clinical features with DYT13 dystonia, and we may argue that they carry the same gene defect of this family. In two large non-Jewish families reported in 1996 by Bressman and coworkers (one previously described by Uitti and Maraganore15), the affected members presented with early or adult-onset dystonia confined to cervical
The prevalent phenotype of DYT13-PTD is an early onset segmental upper body dystonia with a benign course and frequent association of dystonic postures and slow movements with myoclonus-like jerks of neck and shoulders. The role of this new dystonia locus remains to be tested in other PTD families and in the general population, as it should be noted that most patients affected by cranial–cervical or upper limb (focal or segmental) dystonia have a sporadic occurrence, which may reflect the clinical expression of a gene with low penetrance such as the DYT13.

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Legends to the Video

Segment 1. Subject III:6, index case. The patient is sitting and talking; cervical dystonia, mild blepharospasm, mild breathing dysphonia, and right limb dystonia are evident. Neck dystonia is complex, with prevalent rotational right-oriented, antecollis and left head tilt. Sensory tricks (touching the nape with the left hand and pulling up and forward the shoulders) allow correction of head position for a very short time. The neck is asymmetric, as the right sternocleidomastoid muscle had been resected. When walking, the rotational rapid jerks of the head and antecollis are accentuated. The abnormal posture of right upper limb is evident: the dystonic posture of the right wrist (flexed) and slow abnormal movements of the hand are visible. Writing causes myoclonic jerks backward of the neck and an irregular tremor of the head. Bilateral writer’s cramp (more severe in the right hand) is illustrated.

Segment 2. Subject III:2, sister of the index case. The patient is sitting; cervical dystonia, moderate blepharospasm, mild breathing dysphonia, and upper limb dystonia (action-induced in the right limb; at rest in the left side) are evident. Dystonic posture and tremor of the neck are visible. Fine movements and finger taps of right upper limb are very clumsy as they induce dystonia in the hand and arm; she is unable to perform finger to nose test with her left hand. Performing tasks with both hands also induces abnormal orolingual movements. When walking, abnormal posture of the left upper limb is evident. Writing induces myoclonic jerks of the head. The patient cannot write with either hand.

Segment 3. Subject III:10, sister of the index case. The patient is sitting: neck is in a sustained posture of right laterocollis. When she turns her head right, she presents dystonic tremor of the neck. Speaking reveals tremulous voice and dysphonia. Writing induces jerks of the neck and pulls the head forward.

Segment 4. Subject III:14, cousin of the index case. Sitting: the patient has a severe tremor of all the body segments, most pronounced in the trunk, neck, and lower limbs. When the patient speaks, the dystonic tremor of the neck accentuates, and a rotational right-oriented torticollis becomes evident; the patient tries to use a geste antagoniste of the right hand to correct the position of the head. Fine movements of the upper limbs are clumsy. Tremor affects mostly upper body while legs are possi-

### TABLE 3. Features of PTD linked to the known loci

<table>
<thead>
<tr>
<th>Locus</th>
<th>Age at onset</th>
<th>Distribution of dystonia at onset</th>
<th>Prevalent phenotype</th>
<th>Generalization</th>
<th>Severity</th>
<th>Progression</th>
<th>Transmission</th>
<th>Penetrance</th>
</tr>
</thead>
<tbody>
<tr>
<td>DYT 13 (1p36)</td>
<td>Variable (5–43)</td>
<td>Cranial–cervical or upper limb</td>
<td>Segmental, upper body</td>
<td>Infrequent</td>
<td>Mild</td>
<td>Slow</td>
<td>AD</td>
<td>58%</td>
</tr>
<tr>
<td>DYT 1 (9q34)</td>
<td>Childhood–adolescence</td>
<td>Limb (frequently lower)</td>
<td>Generalised, limb involvement, spared cranioocular</td>
<td>Severe</td>
<td>Moderate</td>
<td>Rapid</td>
<td>AD</td>
<td>30–40%</td>
</tr>
<tr>
<td>DYT 6 (8q21–22)</td>
<td>Variable (Average: 18.9)</td>
<td>Variable</td>
<td>Segmental, upper body</td>
<td>High</td>
<td>Severe</td>
<td>Rapid</td>
<td>AD</td>
<td>30%</td>
</tr>
<tr>
<td>DYT7 (18)</td>
<td>Adult (28–70)</td>
<td>Cervical</td>
<td>Focal, cranioocular</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>&lt; 40%</td>
<td></td>
</tr>
</tbody>
</table>

PTD, primary torsion dystonia; AD, autosomal dominant.
bly involved only with transmitted jerks when sitting, and the patient is able to walk, her gait being largely normal. During writing, the neck and shoulders are pulled backward by a massive myoclonus-like jerk.

**Segment 5.** Subject III:18, cousin of the index case. He presents with tremulous spasmodic dysphonia; while speaking, upper limbs dystonic tremor and involuntary movements of the lips and eyes (excessive blinking) are evident. When writing, he presents perioral dyskinesias and some jerky movements of neck and upper limbs.

**Segment 6.** Subject IV:3, son of the index case. When sitting, he presents with upper and lower face dystonia and excessive and prolonged blinking. When speaking, voice tremor and stuttering are evident and he presents with perioral dyskinesias as well as dystonic movements of the neck. Writing discloses myoclonic jerks of the neck and shoulder muscles.

**REFERENCES**


**Parkinson’s Disease Patients With Bilateral Subthalamic Deep Brain Stimulation Gain Weight**

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Abstract: Weight, body mass index (BMI) and energy expenditure/energy intake (EE/EI) was studied in 19 Parkinson’s disease (PD) patients after subthalamic deep brain stimulation (STN-DBS) versus 14 nonoperated ones. Operated patients had a significant weight gain (WG, + 9.7 ± 7 kg) and BMI increase (+ 4.7 kg/m²). The fat mass was higher after STN-DBS. Resting EE (REE; off/ON stimulation) was significantly decreased in STN-DBS patients, while their daily energy expenditure (DEI) was not significantly different. A significant correlation was found among WG, BMI increase, and pre-operative levodopa-equivalent daily dose, their reduction after STN-DBS, and the differential REE related to stimulation and the REE in the off/ON stimulation condition. In conclusion, STN-DBS in PD induces a significant WG associated with a

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