REVIEW

Recent advances in understanding and managing dystonia

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Abstract

Within the field of movement disorders, the conceptual understanding of dystonia has continued to evolve. Clinical advances have included improvements in recognition of certain features of dystonia, such as tremor, and understanding of phenotypic spectrums in the genetic dystonias and dystonia terminology and classification. Progress has also been made in the understanding of underlying biological processes which characterize dystonia from discoveries using approaches such as neurophysiology, functional imaging, genetics, and animal models. Important advances include the role of the cerebellum in dystonia, the concept of dystonia as an aberrant brain network disorder, additional evidence supporting the concept of dystonia endophenotypes, and new insights into psychogenic dystonia. These discoveries have begun to shape treatment approaches as, in parallel, important new treatment modalities, including magnetic resonance imaging-guided focused ultrasound, have emerged and existing interventions such as deep brain stimulation have been further refined. In this review, these topics are explored and discussed.

Keywords

dystonia, cerebellum, deep-brain stimulation, stereotactic radiosurgery, functional magnetic resonance imaging

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Tremor in dystonia

A relatively recent development in dystonia has been increasing interest in and recognition of dystonic tremor. In support of this observation, the number of published articles concerning dystonic tremor has steadily increased. The most recent revised dystonia classification¹ specifically includes tremor as a potential feature of dystonia. However, defining tremor in dystonia has proven both difficult and controversial. The most recent tremor classification² uses dual axes of clinical features and etiology, similar to the revised dystonia classification. In the current classification, dystonic tremor can be diagnosed only when tremor is present in a body part also affected by dystonia. Tremor present in a body region unaffected by dystonia is defined as tremor associated with dystonia (TAWD). The current classification no longer retains the category “dystonia-gene associated tremor” found in the previous tremor classification³. It is worth noting that the current tremor classification, particularly as it relates to tremor in dystonia, remains somewhat controversial and not universally accepted. Some of the more recently discovered monogenic isolated dystonias, including *ANO3*⁴ and *GNAL*⁵, frequently manifest tremor. Dystonic tremor is clinically distinguishable by asymmetry, jerkiness, task and position specificity, and the frequent presence of null points where tremor diminishes or even disappears in certain positions of the affected body part. Recent large studies of adult idiopathic isolated focal and segmental dystonia have shown that tremor is common, most frequently involves the head followed by the upper limbs, and appears to be associated with the spread of dystonia to other body regions^{6–8}. Rest tremor, in dystonia, is not uncommon and usually involves the arm⁹, creating potential diagnostic confusion with Parkinson’s disease¹⁰. Under the current tremor classification, patients with pure tremor of the dystonic type are not considered to have dystonic tremor or TAWD, and an alternative designation, “indeterminate tremor”, has been proposed¹¹. Increasingly, movement disorder specialists recognize and diagnose pure dystonic tremor and distinguish it from essential tremor, although the clinical distinction may be difficult. Historically, there has been a tendency to over-diagnose essential tremor among patients with dystonic tremor, resulting in misclassification^{12,13}. The apparent coexistence of “essential tremor” and focal dystonia has long been recognized¹⁴ and continues to be described¹⁵, but it is more likely that these patients have dystonic tremor or TAWD rather than dual diagnosis of essential tremor.

Differentiation of dystonic tremor from essential tremor is clinically important because dystonic tremor behaves differently in its natural history and response to therapy and may have additional genetic implications. Pathophysiological differences between dystonic tremor and essential tremor may explain its differing clinical behavior. Electrophysiological tremor studies identify dystonic tremor as being more irregular and having varying duration and intensity of bursts of muscular activity¹⁶. Pathophysiological hallmarks of dystonia, including prolonged tactile temporal discrimination thresholds and reduced brainstem blink reflex inhibition, are found in dystonic tremor but not essential tremor^{17,18}. There is emerging evidence that dystonic tremor improves less than essential tremor with thalamic deep brain stimulation (DBS)¹⁹. Recently, phase-specific thalamic DBS has been shown to be more efficient than conventional

DBS for essential tremor, but the positive effects were smaller and inconsistent in dystonic tremor²⁰, suggesting fundamental differences in tremor networks between essential and dystonic tremor. Difficulties in achieving satisfactory control of dystonic upper limb tremor, particularly proximal components, and head tremor with thalamic DBS have led to interest in alternative targets, particularly the caudal zona incerta/posterior subthalamic area^{21,22}. Most recently, magnetic resonance imaging (MRI)-guided focused ultrasound (MRgFUS) thalamotomy has emerged as a promising less-invasive alternative to DBS for disabling dystonic tremor²³.

The role of the cerebellum in dystonia

In recent years, the traditional view of dystonia as being primarily a disorder of the basal ganglia has been broadened to recognize the role of the cerebellum in dystonia pathophysiology. There are many lines of evidence pointing to cerebellar involvement in dystonia. Dystonia has been recognized to occur in focal cerebellar lesions^{24,25} and in the setting of genetic degenerative cerebellar disease^{26–28}. Early attempts to ameliorate severe acquired dystonia included ablative surgery and chronic stimulation targeting the cerebellum. Cooper *et al.* reported chronic cerebellar cortical stimulation to be beneficial for athetosis (dystonia) and spasticity in cerebral palsy²⁹. Interestingly, the improvement in dystonia, unlike in spasticity, was delayed, analogous to progressive improvement in dystonia seen following pallidal DBS. Functional imaging studies, which have elucidated abnormal network activity in dystonia, have frequently demonstrated the cerebellum as an important node within pathological network activity^{30,31}. Diffusion tensor imaging studies have demonstrated abnormal integrity of cerebello-thalamic tracts in *DYT1* and *DYT6*³². Eyeblink auditory conditioning, a paradigm mediated by the olivo-cerebellar pathway, is abnormal in focal dystonia³³ but not in *DYT1* or *DYT6* dystonia³⁴, suggesting differential cerebellar involvement in different dystonia subtypes. The presence of pallido-cerebellar coupling, inversely correlated with severity of dystonic symptoms, has been demonstrated by using a combination of pallidal local field potentials and magnetoencephalography³⁵. In a murine pharmacological model of rapid-onset dystonia parkinsonism, chemical blockade of sodium pumps with ouabain in the basal ganglia induces parkinsonism without dystonia, whereas injections in the cerebellum induce ataxia and then dystonia, and the ensuing dystonia is preventable by lesioning the cerebellar–basal ganglia connections in the contralateral thalamic nucleus³⁶. In such mice rendered dystonic by cerebellar ouabain injection, striatal recordings disclose high-frequency discharge bursts, resembling those seen in human dystonia, which, along with accompanying dystonia, are abolished if the cerebellar–basal ganglia relay in the contralateral thalamus is lesioned³⁷. In the *DYT1* mouse, cerebellar synaptic maturation is impaired³⁸, and reduction of Torsin A production in healthy mice by injection of viral vectored short hairpin RNAs (shRNAs) produces dystonia for cerebellar but not basal ganglia injection³⁹, providing potential mechanisms for dysfunction in human *DYT1* dystonia.

Further evidence for a cerebellar contribution to dystonia has come from recent studies demonstrating improvement in dystonic symptoms in patients with cervical dystonia following

theta-burst transcranial magnetic stimulation (TMS) targeting the cerebellum^{40,41}. The cerebellum is also being revisited as a therapeutic target for DBS, and there is improvement in dystonia and spasticity in patients with cerebral palsy following DBS of the deep anterior cerebellum⁴².

Deep brain stimulation for the treatment of dystonia

DBS of globus pallidus internus (GPi) is well established for the treatment of isolated idiopathic or genetic (primary) generalized, segmental, and focal dystonias^{43–45}, and studies with longer follow-up have confirmed long-term benefit⁴⁶. Acquired combined (secondary) dystonia may also benefit from GPi DBS, but the clinical improvement is less and more variable^{47–49}. This distinction between superior benefit of “primary” versus “secondary” dystonia, though broadly true when dystonias were formerly classified in this way, is less relevant or accurate under the revised dystonia classification¹. For example, some acquired combined dystonias such as tardive dystonia improve to a similar degree as isolated idiopathic or genetic dystonia^{49,50}, and certain genetic combined dystonias such as X-linked parkinsonism dystonia (Lubag/*DYT3*)^{51,52} and *NBIA/PKAN* (*PANK2*) may respond very well to DBS^{53,54}. Conversely, some types of idiopathic isolated dystonia, particularly involving the face or larynx, may respond less or more variably⁵⁵. For these reasons, differing forms of dystonia respond differently to DBS in both the isolated and the combined groups, depending on the etiology and dystonia distribution, and dichotomizing outcomes with respect to older concepts of “primary” and “secondary” may be overly simplistic.

Many patients with acquired and combined dystonia have structural brain lesions visible on MRI, particularly involving the basal ganglia, which may help predict a poorer response to DBS⁴⁷. Predicting DBS outcome is more difficult in acquired combined dystonia because of the limited and variable benefit and the presence of combined features, including spasticity and cerebellar or sensory deficits, which are usually DBS resistant. A recent study evaluated the utility of somatosensory evoked potentials and central motor conduction time in pediatric dystonia prior to DBS and found abnormalities in these studies to be useful for predicting poorer outcome or treatment failure⁵⁶. Genetic testing may also provide important information in stratifying DBS outcome⁵⁷, as some genetic dystonias such as *DYT1* (Torsin A) and *DYT11* (*SCGE*) are highly DBS responsive^{48,58–60} whereas *DYT6* (*THAP1*) may show more modest or variable improvement^{61–63}.

A recognized limitation of GPi DBS is the unwanted side effect of slowness (bradykinesia/akinesia) and other Parkinson-like motor symptoms in a small proportion of patients^{58,64–66}. Although bradykinetic side effects of GPi DBS in dystonia may be reversible with adjustment of DBS electrical parameters, it is sometimes difficult to abolish side effects without compromising clinical benefit for dystonia. This limitation of GPi DBS has led to interest in alternative DBS targets in dystonia, and the most promising reported results have been for subthalamic nucleus (STN) stimulation, which has been shown to provide effective relief of isolated cervical, segmental,

and generalized dystonia^{67–69}. Although STN DBS does not induce bradykinesia, dyskinesia is a very frequent side effect but responds to DBS reprogramming⁶⁷. In acquired dystonia, STN provides a useful alternative in patients in whom the pallidum has been damaged precluding surgical targeting of GPi⁷⁰. The continued interest in and development of new DBS targets in dystonia are important because of therapeutic limitations of GPi DBS and potential improvements in side effect profiles and energy consumption allowing extended DBS device life span. Beyond targets, recent developments in adaptive DBS for Parkinson's disease⁷¹ herald similar potential in dystonia, provided that a suitable electrophysiological signal in dystonia for DBS modulation can be identified. Recently, low-frequency synchronized oscillations in the theta 3–7 Hz range identified in the basal ganglia thalamo-cortical circuits in dystonia correlating closely with dystonic movements appear to be a promising candidate as a physiological biomarker for adaptive DBS⁷². The identification of abnormal networks of brain activity in dystonia⁷³ raises the interesting possibility of customized approaches to dystonia DBS in the future where specific network nodes are targeted singly or multiply for neuromodulation, using adaptive stimulation to normalize brain network activity.

Stereotactic lesions for the treatment of dystonia

Stereotactic lesional interventions, having been almost abandoned after the advent of DBS, are experiencing a renaissance owing to the recent development of MRgFUS as well as renewed interest in stereotactic radiosurgery^{74,75}. These developments create potential for new and less-invasive stereotactic lesional treatment approaches for dystonia. MRgFUS has been successfully applied in the treatment of essential tremor by unilateral thalamotomy^{76,77} and Parkinson's disease by unilateral thalamotomy⁷⁸ and subthalamotomy⁷⁹. The first longer-term studies in essential tremor indicate that benefits remain stable over time⁸⁰. Currently, there is no evidence to support the use of MRgFUS stereotactic lesions for the treatment of dystonia, and its utility, at this stage, remains speculative.

Targeting the pallidum with MRgFUS, though currently unproven, may be a potential treatment option for dystonia in the future. In the past, bilateral surgical pallidotomy was found to be effective in generalized dystonia^{81,82} but was superseded by DBS. Recently, bilateral surgical pallidotomy has been revisited in cranio-cervical dystonia with good effect^{83,84}. For MRgFUS pallidotomy in dystonia, problems yet to be overcome include perfecting GPi lesions without causing optic tract injury and establishing the safety of bilateral lesions. Moreover, MRgFUS pallidotomy for dystonia, either unilateral or bilateral, remains investigational within clinical trials. For focal and unilateral forms of dystonia, MRgFUS thalamotomy may have a role. Surgical thalamotomy has been used successfully for focal task-specific hand dystonias^{85,86}, and emulating this procedure with MRgFUS may deliver similar benefits. To date, there are no published studies of MRgFUS in dystonia, but one clinical trial (ClinicalTrials.gov Identifier: NCT02252380) is evaluating MRgFUS for a range of movement disorders, including dystonia.

Dystonia pathophysiology: insights from neurophysiological studies

In the same way that conceptual shifts have challenged the traditional view of dystonia as a disorder of basal ganglia to include contributions from the cerebellum, the understanding of dystonia pathophysiology has evolved. The traditional view of dystonia as a disorder characterized by multi-level neural disinhibition^{87–90} has been refined to incorporate abnormal sensory processing^{91–93} and altered motor cortex plasticity⁹⁴. Although consistent patterns of neurophysiological abnormality exist in dystonia, it remains unclear the extent to which these abnormalities *cause* dystonia, create the conditions in which dystonia can develop (endophenotype), or represent a by-product of the dystonic movements (epiphenomenon). For example, neurophysiological abnormalities frequently can be identified in non-dystonic body parts or their homologous brain regions^{89,95,96}, can be present in non-manifesting dystonia gene carriers⁹⁷, and do not always correlate with dystonia severity or improvements after treatment. In acquired dystonia, some neurophysiological hallmarks of isolated idiopathic or genetic dystonia are lacking⁹⁸, suggesting that they are not a prerequisite for the development of dystonic movements. The presence of several different types of abnormality also raises questions as to which is the most important or fundamental. One of the most consistent sensory abnormalities in dystonia is impaired sensory temporal discrimination threshold (STDT)^{93,99,100}. Impaired STDT occurs with lesions involving the primary somatosensory and parietal cortex, thalamus, and striatum¹⁰¹ and in dystonia has been linked to defective inhibition within the somatosensory cortex^{102,103}. Impaired STDT not only discriminates between dystonia patients and healthy subjects⁹⁶ but also is present in non-manifesting *DYT1* gene carriers¹⁰⁴ and in asymptomatic first-degree relatives of dystonia patients in a frequency similar to that expected for a dominant gene with incomplete penetrance¹⁰⁵. Collectively, these data point to central timing defects (reflected in impaired STDT) playing an important part in dystonia endophenotypes and suggest that STDT provides a potential biomarker for dystonia susceptibility and dystonia gene carriage in unaffected relatives of patients with dystonia¹⁰⁶. An additional piece of evidence supporting a permissive or endophenotypic role for impaired STDT in dystonia is that STDT abnormalities are not reversed by effective therapies for dystonic symptoms such as DBS¹⁰⁷ or botulinum toxin¹⁰⁸. Of recent particular interest, the superior colliculus, a structure implicated in central timing circuits^{109,110} and dystonia¹¹¹, has been shown to exhibit abnormally reduced functional MRI activity correlated with impairments in STDT in patients with cervical dystonia¹¹².

Dystonia genetics: recent discoveries and highlights

Recently, a revised nomenclature for genetic dystonias has been proposed which replaces the numerical designation of each dystonia (*DYT1*, 2, 3, ...n) with a suffix denoting the gene responsible; for example, *DYT11* becomes *DYT-SCGE*¹¹³. These revisions offer a number of advantages but have not yet been universally adopted, so the traditional nomenclature is used in this review. Until quite recently, there were only two isolated dystonia genes identified: Torsin A (*DYT*) discovered in 1997¹¹⁴ and *THAP1* (*DYT6*) discovered in 2009¹¹⁵.

This list has expanded with the discovery of *GNAL* (*DYT25*)¹¹⁶, *ANO3* (*DYT24*)¹¹⁷, and *CIZ1* (*DYT23*)¹¹⁸. A major breakthrough has been the discovery of *TUBB4A* as the cause of *DYT4* “whispering dysphonia”¹¹⁹. *TUBB4A* mutations also cause hypomyelination with atrophy of the basal ganglia and cerebellum (H-ABC)¹²⁰, and intermediate phenotypes with features of both H-ABC and *DYT4* have been described¹²¹. *TUBB4A* mutations disrupt microtubular function¹²², and abnormal accumulation of microtubules in oligodendrocytes has been demonstrated in human and rodent models of *TUBB4A* hypomyelination¹²³. The wide phenotypic spectrum may be explained by the discovery that the specific *TUBB4A* mutation determines the extent of neuronal and oligodendrocytic involvement, such that neuronal involvement is present in *DYT4* whereas H-ABC is characterized by combined neuronal and oligodendrocytic involvement¹²⁴. The first two genes linked to recessively inherited isolated dystonia (*DYT2*) have been identified as *COL6A3*¹²⁵ and *HPCA*¹²⁶. However, the specificity of *COL6A3* mutations as a cause of dystonia has been questioned¹²⁷, and *HPCA* appears to be extremely rare in isolated dystonia cohorts¹²⁸.

The genetic understanding of combined dystonias has also expanded in recent years. Myoclonus dystonia (*DYT11*) is usually caused by *SGCE* mutations^{129,130} but has also been described with mutations of *KCTD17*¹³¹ and *CACNA1B*¹³². The paroxysmal dystonias and dyskinesias that have been genetically characterized include paroxysmal dystonic choreoathetosis *MR-1* (*DYT8*)¹³³, paroxysmal kinesogenic dyskinesia *PRRT2* (*DYT10*)¹³⁴, paroxysmal choreoathetosis/spasticity (*DYT9*), and paroxysmal exercise-induced dyskinesia (*DYT18*); the last two are allelic disorders and are due to mutations in the *SLC2A1* gene encoding glucose transporter 1 (*GLUT1*)^{135,136}.

Dystonia may coexist with spinocerebellar ataxia (SCA), parkinsonism, or hereditary spastic paraplegia (HSP). Dystonia in the setting of SCA is most frequently seen with SCA 2, 3, 1, and 6 and may be associated with longer repeat expansions^{26,137} whereas *SCA17* can rarely present with dystonia²⁷. Dystonia is also commonly seen in ataxia telangiectasia¹³⁸ and ataxia with oculomotor apraxia (AOA) type 2, senataxin gene^{139,140}, whereas in *AOA1* aprataxin gene, chorea is more common¹⁴¹ but dystonia has been reported¹⁴². *POLG* mutations with ataxia, neuropathy, or oculomotor palsy may also cause dystonia¹⁴³. Dystonia and parkinsonism occurs with gene mutations of *PRKRA* (*DYT16*)^{144,145}, *GCHI* (*DYT5a*)¹⁴⁶, *TH* (*DYT5b*)¹⁴⁷, *ATPIA3* (*DYT12*)¹⁴⁸, and *TAF1* (*DYT3*)¹⁴⁹. *GCHI*-related dystonia-parkinsonism may be more common than previously thought¹⁵⁰. *ATPIA3* has a wide phenotypic spectrum, including not only rapid-onset dystonia parkinsonism (*DYT12*) but also alternating hemiplegia of childhood¹⁵¹ and CAPOS (cerebellar ataxia, areflexia, pes cavus, optic atrophy, and sensorineural hearing loss) syndrome¹⁵² and familial generalized dystonia without parkinsonism¹⁵³. Dystonia may also be a prominent or presenting feature in predominantly parkinsonian genes, including *Parkin*¹⁵⁴ and *PINK1*¹⁵⁵. Dystonia has also been described in several genetic subtypes of HSP, including *SPG7*^{156–158}.

Advances in genetic technology with next-generation sequencing allowing whole exome sequencing have made substantial

inroads in the field of dystonia genetics¹⁵⁹. Whole exome sequencing has been used successfully to identify the causative dystonia gene in almost 40% of a cohort of patients with early onset generalized dystonia¹⁶⁰. Focal dystonia cohorts, including spasmodic dysphonia (SD), have also been probed by using improved genetic techniques. SD is a focal laryngeal dystonia in which 10 to 15% of patients report a positive family history of dystonia^{161,162}. In cohorts of SD, identification of a known dystonia gene is rare, but isolated cases of *GNAL* mutations¹⁶³ or *THAPI* have been identified¹⁶⁴, leaving most of the familial cases unexplained. Early onset laryngeal dystonia with progression to generalized dystonia has been associated with *THAPI*¹⁶⁵; however, these patients differ clinically from those with conventional later-onset, sporadic, or familial SD, in whom generalized dystonia does not occur. Although the genes responsible for familial SD remain elusive in most cases, there is no doubt that familial clustering in SD may confer biological specificity, as demonstrated by a recent study which showed differences in brain morphology, determined by MRI, between familial and non-familial SD¹⁶⁶.

Psychogenic dystonia: a reappraisal in light of neurophysiological and imaging data

Psychogenic or functional dystonia is a recognizable subtype of dystonia, which can be diagnosed on the basis of positive clinical criteria^{167,168}. Additional features pointing to psychogenic dystonia include sudden onset, waxing/waning clinical course, variable and distractible motor phenomenology, fixed postures of distal limbs, and the frequent presence of chronic pain^{169–171}. In many cases of psychogenic dystonia, an initial triggering event such as minor trauma or illness is identified. Like organic dystonia, psychogenic dystonia can be severely disabling and result in fixed joint deformity, tendon contracture, and dependency¹⁷². Although many experts consider psychogenic dystonia to be caused primarily by underlying psychiatric or psychological disturbance (most commonly, conversion disorder), many patients with psychogenic dystonia have no identifiable psychiatric or psychological illness, and a proposed revision of the Fahn-Williams criteria¹⁶⁷ removes the need for psychiatric disorder to be identifiable¹⁷³. Moreover, there is significant pathophysiological overlap between organic and psychogenic dystonia. Shared abnormalities between the two conditions include cortical and spinal disinhibition^{174,175}, abnormal thalamic firing rates and sensory receptive fields¹⁷⁶, and impaired sensory temporal discrimination¹⁷⁷. Exceptions are TMS paired associative cortical plasticity, which is increased in organic dystonia but not in psychogenic dystonia¹⁷⁸, and the blink reflex recovery cycle, which is normal in psychogenic dystonia

and abnormally disinhibited in organic blepharospasm¹⁷⁹. Functional imaging studies, comparing patients with psychogenic dystonia with healthy subjects, demonstrate abnormal patterns of brain activation different from those seen in organic dystonia but with some shared similarities¹⁸⁰. TMS has been reported to be beneficial in treating functional movement disorders, including psychogenic dystonia¹⁸¹, and the probable mechanism of action is cognitive-behavioral adaptation rather than physiological cortical neuromodulation¹⁸².

The term psychogenic dystonia has been criticized as being potentially pejorative and over-emphasizing psychiatric mechanisms, and functional dystonia has been proposed as the preferred term¹⁸³, as it is more acceptable to patients and highlights an underlying disturbance of brain function rather than structure but leaves etiological mechanisms open for future elucidation. How can the demonstrated neurophysiological and imaging abnormalities be reconciled with a disorder that is widely considered to be psychiatric or psychological in origin? It is possible that the abnormalities can be explained by the presence of enduring patterns of dystonic movements, producing secondary brain adaptation (epiphenomenon). The other possibility is that some endophenotypic abnormalities that characterize organic dystonia patients and their asymptomatic relatives are shared by psychogenic dystonia sufferers and serve as a biological predisposing factor to both conditions and that environmental factors, including both physical and possibly psychological trauma, serve as a trigger.

Conclusions

Although the dystonias are collectively unified by the presence of involuntary movement patterns recognizable as dystonia, they present distinct challenges owing to their clinical, genetic, and pathophysiological diversity. As the understanding of differences between the dystonias improves, so too does the potential for more efficient and targeted therapy. In this review, topics in dystonia have been selected where there have been new discoveries and conceptual shifts, which will help drive therapeutic advances and benefits for dystonia patients in the future.

Competing interests

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References

1. Albanese A, Bhatia K, Bressman SB, *et al.*: **Phenomenology and classification of dystonia: a consensus update.** *Mov Disord.* 2013; 28(7): 863–73. [PubMed Abstract](#) | [Publisher Full Text](#) | [Free Full Text](#)
2. Bhatia KP, Bain P, Bajaj N, *et al.*: **Consensus Statement on the classification**

of tremors. from the task force on tremor of the International Parkinson and Movement Disorder Society. *Mov Disord.* 2018; 33(1): 75–87. [PubMed Abstract](#) | [Publisher Full Text](#)

3. Deuschl G, Bain P, Brin M: **Consensus statement of the Movement Disorder**

- Society on Tremor. Ad Hoc Scientific Committee.** *Mov Disord.* 1998; **13** Suppl 3: 2–23.
[PubMed Abstract](#)
4. Stamelou M, Charlesworth G, Cordivari C, *et al.*: **The phenotypic spectrum of DYT24 due to ANO3 mutations.** *Mov Disord.* 2014; **29**(7): 928–34.
[PubMed Abstract](#) | [Publisher Full Text](#) | [Free Full Text](#)
 5. Carecchio M, Panteghini C, Reale C, *et al.*: **Novel GNAL mutation with intra-familial clinical heterogeneity: Expanding the phenotype.** *Parkinsonism Relat Disord.* 2016; **23**: 66–71.
[PubMed Abstract](#) | [Publisher Full Text](#)
 6. Erro R, Rubio-Agusti I, Saifee TA, *et al.*: **Rest and other types of tremor in adult-onset primary dystonia.** *J Neurol Neurosurg Psychiatry.* 2014; **85**(9): 965–8.
[PubMed Abstract](#) | [Publisher Full Text](#) | [Free Full Text](#)
 7. Svetel M, Pekmezovic T, Tomic A, *et al.*: **The spread of primary late-onset focal dystonia in a long-term follow up study.** *Clin Neurol Neurosurg.* 2015; **132**: 41–3.
[PubMed Abstract](#) | [Publisher Full Text](#)
 8. **F** Norris SA, Jinnah HA, Espay AJ, *et al.*: **Clinical and demographic characteristics related to onset site and spread of cervical dystonia.** *Mov Disord.* 2016; **31**(12): 1874–82.
[PubMed Abstract](#) | [Publisher Full Text](#) | [Free Full Text](#) | [F1000 Recommendation](#)
 9. Gigante AF, Berardelli A, Defazio G: **Rest tremor in idiopathic adult-onset dystonia.** *Eur J Neurol.* 2016; **23**(5): 935–9.
[PubMed Abstract](#) | [Publisher Full Text](#)
 10. Haggstrom L, Darveniza P, Tisch S: **Mild parkinsonian features in dystonia: Literature review, mechanisms and clinical perspectives.** *Parkinsonism Relat Disord.* 2017; **35**: 1–7.
[PubMed Abstract](#) | [Publisher Full Text](#)
 11. Quinn NP, Schneider SA, Schwingsenschuh P, *et al.*: **Tremor—some controversial aspects.** *Mov Disord.* 2011; **26**(1): 18–23.
[PubMed Abstract](#) | [Publisher Full Text](#)
 12. Schrag A, Münchau A, Bhatia KP, *et al.*: **Essential tremor: an overdiagnosed condition?** *J Neurol.* 2000; **247**(12): 955–9.
[PubMed Abstract](#) | [Publisher Full Text](#)
 13. Jain S, Lo SE, Louis ED: **Common misdiagnosis of a common neurological disorder: how are we misdiagnosing essential tremor?** *Arch Neurol.* 2006; **63**(8): 1100–4.
[PubMed Abstract](#) | [Publisher Full Text](#)
 14. Lou JS, Jankovic J: **Essential tremor: clinical correlates in 350 patients.** *Neurology.* 1991; **41**(2 (Pt 1)): 234–8.
[PubMed Abstract](#) | [Publisher Full Text](#)
 15. Poologaindran A, Ivanishvili Z, Morrison MD, *et al.*: **The effect of unilateral thalamic deep brain stimulation on the vocal dysfunction in a patient with spasmodic dysphonia: interrogating cerebellar and pallidal neural circuits.** *J Neurosurg.* 2018; **128**(2): 575–82.
[PubMed Abstract](#) | [Publisher Full Text](#)
 16. Jedynak CP, Bonnet AM, Agid Y: **Tremor and idiopathic dystonia.** *Mov Disord.* 1991; **6**(3): 230–6.
[PubMed Abstract](#) | [Publisher Full Text](#)
 17. **F** Tinazzi M, Fasano A, Di Matteo A, *et al.*: **Temporal discrimination in patients with dystonia and tremor and patients with essential tremor.** *Neurology.* 2013; **80**(1): 76–84.
[PubMed Abstract](#) | [Publisher Full Text](#) | [F1000 Recommendation](#)
 18. Nisticò R, Pirritano D, Salsone M, *et al.*: **Blink reflex recovery cycle in patients with dystonic tremor: a cross-sectional study.** *Neurology.* 2012; **78**(17): 1363–5.
[PubMed Abstract](#) | [Publisher Full Text](#)
 19. **F** Cury RG, Fraix V, Castrioto A, *et al.*: **Thalamic deep brain stimulation for tremor in Parkinson disease, essential tremor, and dystonia.** *Neurology.* 2017; **89**(13): 1416–23.
[PubMed Abstract](#) | [Publisher Full Text](#) | [F1000 Recommendation](#)
 20. **F** Cagnan H, Pedrosa D, Little S, *et al.*: **Stimulating at the right time: phase-specific deep brain stimulation.** *Brain.* 2017; **140**(1): 132–45.
[PubMed Abstract](#) | [Publisher Full Text](#) | [Free Full Text](#) | [F1000 Recommendation](#)
 21. Blomstedt P, Fytagoridis A, Tisch S: **Deep brain stimulation of the posterior subthalamic area in the treatment of tremor.** *Acta Neurochir (Wien).* 2009; **151**(1): 31–6.
[PubMed Abstract](#) | [Publisher Full Text](#)
 22. **F** Ramirez-Zamora A, Smith H, Kumar V, *et al.*: **Evolving Concepts in Posterior Subthalamic Area Deep Brain Stimulation for Treatment of Tremor: Surgical Neuroanatomy and Practical Considerations.** *Stereotact Funct Neurosurg.* 2016; **94**(5): 283–97.
[PubMed Abstract](#) | [Publisher Full Text](#) | [F1000 Recommendation](#)
 23. **F** Fasano A, Llinas M, Munhoz RP, *et al.*: **MRI-guided focused ultrasound thalamotomy in non-ET tremor syndromes.** *Neurology.* 2017; **89**(8): 771–5.
[PubMed Abstract](#) | [Publisher Full Text](#) | [F1000 Recommendation](#)
 24. Alarcón F, Tolosa E, Muñoz E: **Focal limb dystonia in a patient with a cerebellar mass.** *Arch Neurol.* 2001; **58**(7): 1125–7.
[PubMed Abstract](#) | [Publisher Full Text](#)
 25. LeDoux MS, Brady KA: **Secondary cervical dystonia associated with structural lesions of the central nervous system.** *Mov Disord.* 2003; **18**(1): 60–9.
[PubMed Abstract](#) | [Publisher Full Text](#)
 26. Sethi KD, Jankovic J: **Dystonia in spinocerebellar ataxia type 6.** *Mov Disord.* 2002; **17**(1): 150–3.
[PubMed Abstract](#) | [Publisher Full Text](#)
 27. Hagenah JM, Zühlke C, Hellenbroich Y, *et al.*: **Focal dystonia as a presenting sign of spinocerebellar ataxia 17.** *Mov Disord.* 2004; **19**(2): 217–20.
[PubMed Abstract](#) | [Publisher Full Text](#)
 28. Le Ber I, Clot F, Vercueil L, *et al.*: **Predominant dystonia with marked cerebellar atrophy: a rare phenotype in familial dystonia.** *Neurology.* 2006; **67**(10): 1769–73.
[PubMed Abstract](#) | [Publisher Full Text](#)
 29. Cooper IS, Riklan M, Amin I, *et al.*: **Chronic cerebellar stimulation in cerebral palsy.** *Neurology.* 1976; **26**(8): 744–53.
[PubMed Abstract](#) | [Publisher Full Text](#)
 30. Eidelberg D, Moeller JR, Antonini A, *et al.*: **Functional brain networks in DYT1 dystonia.** *Ann Neurol.* 1998; **44**(3): 303–12.
[PubMed Abstract](#) | [Publisher Full Text](#)
 31. Lehericy S, Tijssen MA, Vidailhet M, *et al.*: **The anatomical basis of dystonia: current view using neuroimaging.** *Mov Disord.* 2013; **28**(7): 944–57.
[PubMed Abstract](#) | [Publisher Full Text](#)
 32. Argyelan M, Carbon M, Niethammer M, *et al.*: **Cerebellothalamocortical connectivity regulates penetrance in dystonia.** *J Neurosci.* 2009; **29**(31): 9740–7.
[PubMed Abstract](#) | [Publisher Full Text](#) | [Free Full Text](#)
 33. Teo JT, van de Warrenburg BP, Schneider SA, *et al.*: **Neurophysiological evidence for cerebellar dysfunction in primary focal dystonia.** *J Neurol Neurosurg Psychiatry.* 2009; **80**(1): 80–3.
[PubMed Abstract](#) | [Publisher Full Text](#)
 34. Sadnicka A, Teo JT, Kojovic M, *et al.*: **All in the blink of an eye: new insight into cerebellar and brainstem function in DYT1 and DYT6 dystonia.** *Eur J Neurol.* 2015; **22**(5): 762–7.
[PubMed Abstract](#) | [Publisher Full Text](#)
 35. Neumann WJ, Jha A, Bock A, *et al.*: **Cortico-pallidal oscillatory connectivity in patients with dystonia.** *Brain.* 2015; **138**(Pt 7): 1894–906.
[PubMed Abstract](#) | [Publisher Full Text](#)
 36. Calderon DP, Fremont R, Kraenzlin F, *et al.*: **The neural substrates of rapid-onset Dystonia-Parkinsonism.** *Nat Neurosci.* 2011; **14**(3): 357–65.
[PubMed Abstract](#) | [Publisher Full Text](#) | [Free Full Text](#)
 37. Chen CH, Fremont R, Arteaga-Bracho EE, *et al.*: **Short latency cerebellar modulation of the basal ganglia.** *Nat Neurosci.* 2014; **17**(12): 1767–75.
[PubMed Abstract](#) | [Publisher Full Text](#) | [Free Full Text](#)
 38. Vanni V, Puglisi F, Bonsi P, *et al.*: **Cerebellar synaptogenesis is compromised in mouse models of DYT1 dystonia.** *Exp Neurol.* 2015; **271**: 457–67.
[PubMed Abstract](#) | [Publisher Full Text](#)
 39. **F** Fremont R, Tewari A, Angueyra C, *et al.*: **A role for cerebellum in the hereditary dystonia DYT1.** *eLife.* 2017; **6**: pii: e22775.
[PubMed Abstract](#) | [Publisher Full Text](#) | [Free Full Text](#) | [F1000 Recommendation](#)
 40. Koch G, Porcacchia P, Ponzo V, *et al.*: **Effects of two weeks of cerebellar theta burst stimulation in cervical dystonia patients.** *Brain Stimul.* 2014; **7**(4): 564–72.
[PubMed Abstract](#) | [Publisher Full Text](#)
 41. **F** Bradnam LV, McDonnell MN, Ridding MC: **Cerebellar Intermittent Theta-Burst Stimulation and Motor Control Training in Individuals with Cervical Dystonia.** *Brain Sci.* 2016; **6**(4): pii: E56.
[PubMed Abstract](#) | [Publisher Full Text](#) | [Free Full Text](#) | [F1000 Recommendation](#)
 42. Sokal P, Rudaš M, Harat M, *et al.*: **Deep anterior cerebellar stimulation reduces symptoms of secondary dystonia in patients with cerebral palsy treated due to spasticity.** *Clin Neurol Neurosurg.* 2015; **135**: 62–8.
[PubMed Abstract](#) | [Publisher Full Text](#)
 43. Vidailhet M, Vercueil L, Houeto J, *et al.*: **Bilateral deep-brain stimulation of the globus pallidus in primary generalized dystonia.** *N Engl J Med.* 2005; **352**(5): 459–67.
[PubMed Abstract](#) | [Publisher Full Text](#)
 44. Kupsch A, Benecke R, Müller J, *et al.*: **Pallidal deep-brain stimulation in primary generalized or segmental dystonia.** *N Engl J Med.* 2006; **355**(19): 1978–90.
[PubMed Abstract](#) | [Publisher Full Text](#)
 45. **F** Volkmann J, Mueller J, Deuschl G, *et al.*: **Pallidal neurostimulation in patients with medication-refractory cervical dystonia: a randomised, sham-controlled trial.** *Lancet Neurol.* 2014; **13**(9): 875–84.
[PubMed Abstract](#) | [Publisher Full Text](#) | [F1000 Recommendation](#)
 46. **F** Volkmann J, Wolters A, Kupsch A, *et al.*: **Pallidal deep brain stimulation in patients with primary generalised or segmental dystonia: 5-year follow-up of a randomised trial.** *Lancet Neurol.* 2012; **11**(12): 1029–38.
[PubMed Abstract](#) | [Publisher Full Text](#) | [F1000 Recommendation](#)
 47. Eltahawy HA, Saint-Cyr J, Giladi N, *et al.*: **Primary dystonia is more responsive than secondary dystonia to pallidal interventions: outcome after pallidotomy or pallidal deep brain stimulation.** *Neurosurgery.* 2004; **54**(3): 613–19; discussion 619–21.
[PubMed Abstract](#) | [Publisher Full Text](#)
 48. Andrews C, Aviles-Olmos I, Hariz M, *et al.*: **Which patients with dystonia benefit from deep brain stimulation? A metaregression of individual patient outcomes.** *J Neurol Neurosurg Psychiatry.* 2010; **81**(12): 1383–9.
[PubMed Abstract](#) | [Publisher Full Text](#)
 49. Vidailhet M, Jutras MF, Grabli D, *et al.*: **Deep brain stimulation for dystonia.** *J Neurol Neurosurg Psychiatry.* 2013; **84**(9): 1029–42.
[PubMed Abstract](#) | [Publisher Full Text](#)

50. Evidente VG, Lyons MK, Wheeler M, *et al.*: **First case of X-linked dystonia-parkinsonism ("Lubag") to demonstrate a response to bilateral pallidal stimulation.** *Mov Disord.* 2007; 22(12): 1790–3.
[PubMed Abstract](#) | [Publisher Full Text](#)
51. Martinez-Torres I, Limousin P, Tisch S, *et al.*: **Early and marked benefit with GPI DBS for Lubag syndrome presenting with rapidly progressive life-threatening dystonia.** *Mov Disord.* 2009; 24(11): 1710–2.
[PubMed Abstract](#) | [Publisher Full Text](#)
52. Castelnau P, Cif L, Valente EM, *et al.*: **Pallidal stimulation improves pantothenate kinase-associated neurodegeneration.** *Ann Neurol.* 2005; 57(5): 738–41.
[PubMed Abstract](#) | [Publisher Full Text](#)
53. **F** Timmermann L, Pauls KA, Wieland K, *et al.*: **Dystonia in neurodegeneration with brain iron accumulation: outcome of bilateral pallidal stimulation.** *Brain.* 2010; 133(Pt 3): 701–12.
[PubMed Abstract](#) | [Publisher Full Text](#) | [Free Full Text](#) | [F1000 Recommendation](#)
54. Limotai N, Go C, Oyama G, *et al.*: **Mixed results for GPI-DBS in the treatment of cranio-facial and cranio-cervical dystonia symptoms.** *J Neurol.* 2011; 258(11): 2069–74.
[PubMed Abstract](#) | [Publisher Full Text](#)
55. Gruber D, Trottenberg T, Kivi A, *et al.*: **Long-term effects of pallidal deep brain stimulation in tardive dystonia.** *Neurology.* 2009; 73(1): 53–8.
[PubMed Abstract](#) | [Publisher Full Text](#)
56. **F** McClelland VM, Fialho D, Flexney-Briscoe D, *et al.*: **Somatosensory Evoked Potentials and Central Motor Conduction Times in children with dystonia and their correlation with outcomes from Deep Brain Stimulation of the Globus pallidus internus.** *Clin Neurophysiol.* 2017; pii: S1388-2457(17)31164-1.
[PubMed Abstract](#) | [Publisher Full Text](#) | [Free Full Text](#) | [F1000 Recommendation](#)
57. Jinnah HA, Alterman R, Klein C, *et al.*: **Deep brain stimulation for dystonia: a novel perspective on the value of genetic testing.** *J Neural Transm (Vienna).* 2017; 124(4): 417–30.
[PubMed Abstract](#) | [Publisher Full Text](#) | [Free Full Text](#)
58. Tisch S, Zrinzo L, Limousin P, *et al.*: **Effect of electrode contact location on clinical efficacy of pallidal deep brain stimulation in primary generalised dystonia.** *J Neurol Neurosurg Psychiatry.* 2007; 78(12): 1314–9.
[PubMed Abstract](#) | [Publisher Full Text](#) | [Free Full Text](#)
59. Azoulay-Zyss J, Roze E, Welter ML, *et al.*: **Bilateral deep brain stimulation of the pallidum for myoclonus-dystonia due to ϵ -sarcoglycan mutations: a pilot study.** *Arch Neurol.* 2011; 68(1): 94–8.
[PubMed Abstract](#) | [Publisher Full Text](#)
60. Brüggemann N, Kühn A, Schneider SA, *et al.*: **Short- and long-term outcome of chronic pallidal neurostimulation in monogenic isolated dystonia.** *Neurology.* 2015; 84(9): 895–903.
[PubMed Abstract](#) | [Publisher Full Text](#)
61. Groen JL, Ritz K, Contarino MF, *et al.*: **DYT6 dystonia: mutation screening, phenotype, and response to deep brain stimulation.** *Mov Disord.* 2010; 25(14): 2420–7.
[PubMed Abstract](#) | [Publisher Full Text](#)
62. Panov F, Tagliati M, Ozelius LJ, *et al.*: **Pallidal deep brain stimulation for DYT6 dystonia.** *J Neurol Neurosurg Psychiatry.* 2012; 83(2): 182–7.
[PubMed Abstract](#) | [Publisher Full Text](#)
63. Krause P, Brüggemann N, Völzmann S, *et al.*: **Long-term effect on dystonia after pallidal deep brain stimulation (DBS) in three members of a family with a THAP1 mutation.** *J Neurol.* 2015; 262(12): 2739–44.
[PubMed Abstract](#) | [Publisher Full Text](#)
64. Schrader C, Capelle HH, Kinfe TM, *et al.*: **GPI-DBS may induce a hypokinetic gait disorder with freezing of gait in patients with dystonia.** *Neurology.* 2011; 77(5): 483–8.
[PubMed Abstract](#) | [Publisher Full Text](#)
65. Blahak C, Capelle HH, Baezner H, *et al.*: **Micrographia induced by pallidal DBS for segmental dystonia: a subtle sign of hypokinesia?** *J Neural Transm (Vienna).* 2011; 118(4): 549–53.
[PubMed Abstract](#) | [Publisher Full Text](#)
66. Huebl J, Brücke C, Schneider GH, *et al.*: **Bradykinesia induced by frequency-specific pallidal stimulation in patients with cervical and segmental dystonia.** *Parkinsonism Relat Disord.* 2015; 21(7): 800–3.
[PubMed Abstract](#) | [Publisher Full Text](#)
67. **F** Ostrem JL, Racine CA, Glass GA, *et al.*: **Subthalamic nucleus deep brain stimulation in primary cervical dystonia.** *Neurology.* 2011; 76(10): 870–8.
[PubMed Abstract](#) | [Publisher Full Text](#) | [F1000 Recommendation](#)
68. **F** Cao C, Pan Y, Li D, *et al.*: **Subthalamus deep brain stimulation for primary dystonia patients: a long-term follow-up study.** *Mov Disord.* 2013; 28(13): 1877–82.
[PubMed Abstract](#) | [Publisher Full Text](#) | [F1000 Recommendation](#)
69. **F** Ostrem JL, San Luciano M, Dodenhoff KA, *et al.*: **Subthalamic nucleus deep brain stimulation in isolated dystonia: A 3-year follow-up study.** *Neurology.* 2017; 88(1): 25–35.
[PubMed Abstract](#) | [Publisher Full Text](#) | [F1000 Recommendation](#)
70. Chakraborti S, Hasegawa H, Lumsden DE, *et al.*: **Bilateral subthalamic nucleus deep brain stimulation for refractory total body dystonia secondary to metabolic autopathology in a 4-year-old boy with infantile methylmalonic acidemia: case report.** *J Neurosurg Pediatr.* 2013; 12(4): 374–9.
[PubMed Abstract](#) | [Publisher Full Text](#)
71. Little S, Pogossyan A, Neal S, *et al.*: **Adaptive deep brain stimulation in advanced Parkinson disease.** *Ann Neurol.* 2013; 74(3): 449–57.
[PubMed Abstract](#) | [Publisher Full Text](#) | [Free Full Text](#)
72. **F** Neumann WJ, Horn A, Ewert S, *et al.*: **A localized pallidal physiomaer in cervical dystonia.** *Ann Neurol.* 2017; 82(6): 912–24.
[PubMed Abstract](#) | [Publisher Full Text](#) | [F1000 Recommendation](#)
73. **F** Jinnah HA, Neychev V, Hess EJ: **The Anatomical Basis for Dystonia: The Motor Network Model.** *Tremor Other Hyperkinet Mov (N Y).* 2017; 7: 506.
[PubMed Abstract](#) | [Publisher Full Text](#) | [Free Full Text](#) | [F1000 Recommendation](#)
74. **F** Krack P, Martinez-Fernandez R, Del Alamo M, *et al.*: **Current applications and limitations of surgical treatments for movement disorders.** *Mov Disord.* 2017; 32(1): 36–52.
[PubMed Abstract](#) | [Publisher Full Text](#) | [F1000 Recommendation](#)
75. **F** Higuchi Y, Matsuda S, Serizawa T: **Gamma knife radiosurgery in movement disorders: Indications and limitations.** *Mov Disord.* 2017; 32(1): 28–35.
[PubMed Abstract](#) | [Publisher Full Text](#) | [F1000 Recommendation](#)
76. **F** Elias WJ, Huss D, Voss T, *et al.*: **A pilot study of focused ultrasound thalamotomy for essential tremor.** *N Engl J Med.* 2013; 369(7): 640–8.
[PubMed Abstract](#) | [Publisher Full Text](#) | [F1000 Recommendation](#)
77. **F** Elias WJ, Lipsman N, Ondo WG, *et al.*: **A Randomized Trial of Focused Ultrasound Thalamotomy for Essential Tremor.** *N Engl J Med.* 2016; 375(8): 730–9.
[PubMed Abstract](#) | [Publisher Full Text](#) | [F1000 Recommendation](#)
78. **F** Bond AE, Shah BB, Huss DS, *et al.*: **Safety and Efficacy of Focused Ultrasound Thalamotomy for Patients With Medication-Refractory, Tremor-Dominant Parkinson Disease: A Randomized Clinical Trial.** *JAMA Neurol.* 2017; 74(12): 1412–8.
[PubMed Abstract](#) | [Publisher Full Text](#) | [Free Full Text](#) | [F1000 Recommendation](#)
79. **F** Martínez-Fernández R, Rodríguez-Rojas R, Del Álamo M, *et al.*: **Focused ultrasound subthalamotomy in patients with asymmetric Parkinson's disease: a pilot study.** *Lancet Neurol.* 2018; 17(1): 54–63.
[PubMed Abstract](#) | [Publisher Full Text](#) | [F1000 Recommendation](#)
80. **F** Chang JW, Park CK, Lipsman N, *et al.*: **A prospective trial of magnetic resonance-guided focused ultrasound thalamotomy for essential tremor: Results at the 2-year follow-up.** *Ann Neurol.* 2018; 83(1): 107–14.
[PubMed Abstract](#) | [Publisher Full Text](#) | [F1000 Recommendation](#)
81. Lozano AM, Kumar R, Gross RE, *et al.*: **Globus pallidus internus pallidotomy for generalized dystonia.** *Mov Disord.* 1997; 12(6): 865–70.
[PubMed Abstract](#) | [Publisher Full Text](#)
82. Ondo WG, Desaloms JM, Jankovic J, *et al.*: **Pallidotomy for generalized dystonia.** *Mov Disord.* 1998; 13(4): 693–8.
[PubMed Abstract](#) | [Publisher Full Text](#)
83. Horisawa S, Goto S, Takeda N, *et al.*: **Bilateral Pallidotomy for Cervical Dystonia After Failed Selective Peripheral Denervation.** *World Neurosurg.* 2016; 89: 728.e1–4.
[PubMed Abstract](#) | [Publisher Full Text](#)
84. Minkin K, Gabrovski K, Dimova P, *et al.*: **Bilateral pallidotomy for Meige syndrome.** *Acta Neurochir (Wien).* 2017; 159(7): 1359–63.
[PubMed Abstract](#) | [Publisher Full Text](#)
85. Taira T, Hori T: **Stereotactic ventro-oralis thalamotomy for task-specific focal hand dystonia (writer's cramp).** *Stereotact Funct Neurosurg.* 2003; 80(1–4): 88–91.
[PubMed Abstract](#) | [Publisher Full Text](#)
86. Horisawa S, Taira T, Goto S, *et al.*: **Long-term improvement of musician's dystonia after stereotactic ventro-oral thalamotomy.** *Ann Neurol.* 2013; 74(5): 648–54.
[PubMed Abstract](#) | [Publisher Full Text](#)
87. Nakashima K, Rothwell JC, Day BL, *et al.*: **Reciprocal inhibition between forearm muscles in patients with writer's cramp and other occupational cramps, symptomatic hemidystonia and hemiparesis due to stroke.** *Brain.* 1989; 112(Pt 3): 681–97.
[PubMed Abstract](#) | [Publisher Full Text](#)
88. Nakashima K, Rothwell JC, Thompson PD, *et al.*: **The blink reflex in patients with idiopathic torsion dystonia.** *Arch Neurol.* 1990; 47(4): 413–6.
[PubMed Abstract](#) | [Publisher Full Text](#)
89. Ridding MC, Sheean G, Rothwell JC, *et al.*: **Changes in the balance between motor cortical excitation and inhibition in focal, task specific dystonia.** *J Neurol Neurosurg Psychiatry.* 1995; 59(5): 493–8.
[PubMed Abstract](#) | [Publisher Full Text](#) | [Free Full Text](#)
90. Hallett M: **Neurophysiology of dystonia: The role of inhibition.** *Neurobiol Dis.* 2011; 42(2): 177–84.
[PubMed Abstract](#) | [Publisher Full Text](#) | [Free Full Text](#)
91. Abbruzzese G, Marchese R, Buccolieri A, *et al.*: **Abnormalities of sensorimotor integration in focal dystonia: a transcranial magnetic stimulation study.** *Brain.* 2001; 124(Pt 3): 537–45.
[PubMed Abstract](#) | [Publisher Full Text](#)

92. Molloy FM, Carr TD, Zeuner KE, *et al.*: **Abnormalities of spatial discrimination in focal and generalized dystonia.** *Brain.* 2003; 126(Pt 10): 2175–82.
[PubMed Abstract](#) | [Publisher Full Text](#)
93. Fiorio M, Tinazzi M, Bertolasi L, *et al.*: **Temporal processing of visuotactile and tactile stimuli in writer's cramp.** *Ann Neurol.* 2003; 53(5): 630–5.
[PubMed Abstract](#) | [Publisher Full Text](#)
94. **F** Quartarone A, Bagnato S, Rizzo V, *et al.*: **Abnormal associative plasticity of the human motor cortex in writer's cramp.** *Brain.* 2003; 126(Pt 12): 2586–96.
[PubMed Abstract](#) | [Publisher Full Text](#) | [F1000 Recommendation](#)
95. Panizza M, Lelli S, Nilsson J, *et al.*: **H-reflex recovery curve and reciprocal inhibition of H-reflex in different kinds of dystonia.** *Neurology.* 1990; 40(5): 824–8.
[PubMed Abstract](#) | [Publisher Full Text](#)
96. Meunier S, Garnero L, Ducorps A, *et al.*: **Human brain mapping in dystonia reveals both endophenotypic traits and adaptive reorganization.** *Ann Neurol.* 2001; 50(4): 521–7.
[PubMed Abstract](#) | [Publisher Full Text](#)
97. Edwards MJ, Huang YZ, Wood NW, *et al.*: **Different patterns of electrophysiological deficits in manifesting and non-manifesting carriers of the DYT1 gene mutation.** *Brain.* 2003; 126(Pt 9): 2074–80.
[PubMed Abstract](#) | [Publisher Full Text](#)
98. Kojovic M, Pareés I, Kassaveti P, *et al.*: **Secondary and primary dystonia: pathophysiological differences.** *Brain.* 2013; 136(Pt 7): 2038–49.
[PubMed Abstract](#) | [Publisher Full Text](#)
99. Bara-Jimenez W, Shelton P, Sanger TD, *et al.*: **Sensory discrimination capabilities in patients with focal hand dystonia.** *Ann Neurol.* 2000; 47(3): 377–80.
[PubMed Abstract](#) | [Publisher Full Text](#)
100. Scontrini A, Conte A, Defazio G, *et al.*: **Somatosensory temporal discrimination in patients with primary focal dystonia.** *J Neurol Neurosurg Psychiatry.* 2009; 80(12): 1315–9.
[PubMed Abstract](#) | [Publisher Full Text](#)
101. Lacruz F, Artieda J, Pastor MA, *et al.*: **The anatomical basis of somesthetic temporal discrimination in humans.** *J Neurol Neurosurg Psychiatry.* 1991; 54(12): 1077–81.
[PubMed Abstract](#) | [Publisher Full Text](#) | [Free Full Text](#)
102. **F** Rocchi L, Casula E, Tocco P, *et al.*: **Somatosensory Temporal Discrimination Threshold Involves Inhibitory Mechanisms in the Primary Somatosensory Area.** *J Neurosci.* 2016; 36(2): 325–35.
[PubMed Abstract](#) | [Publisher Full Text](#) | [F1000 Recommendation](#)
103. **F** Antelmi E, Erro R, Rocchi L, *et al.*: **Neurophysiological correlates of abnormal somatosensory temporal discrimination in dystonia.** *Mov Disord.* 2017; 32(1): 141–8.
[PubMed Abstract](#) | [Publisher Full Text](#) | [F1000 Recommendation](#)
104. Fiorio M, Garbarin M, Valente EM, *et al.*: **Defective temporal processing of sensory stimuli in DYT1 mutation carriers: a new endophenotype of dystonia?** *Brain.* 2007; 130(Pt 1): 134–42.
[PubMed Abstract](#) | [Publisher Full Text](#)
105. Kimmich O, Bradley D, Whelan R, *et al.*: **Sporadic adult onset primary torsion dystonia is a genetic disorder by the temporal discrimination test.** *Brain.* 2011; 134(Pt 9): 2656–63.
[PubMed Abstract](#) | [Publisher Full Text](#)
106. Conte A, McGovern EM, Narasimham S, *et al.*: **Temporal Discrimination: Mechanisms and Relevance to Adult-Onset Dystonia.** *Front Neurol.* 2017; 8: 625.
[PubMed Abstract](#) | [Publisher Full Text](#) | [Free Full Text](#)
107. Sadnicka A, Kimmich O, Pisarek C, *et al.*: **Pallidal stimulation for cervical dystonia does not correct abnormal temporal discrimination.** *Mov Disord.* 2013; 28(13): 1874–7.
[PubMed Abstract](#) | [Publisher Full Text](#)
108. Scontrini A, Conte A, Fabbrini G, *et al.*: **Somatosensory temporal discrimination tested in patients receiving botulinum toxin injection for cervical dystonia.** *Mov Disord.* 2011; 26(4): 742–6.
[PubMed Abstract](#) | [Publisher Full Text](#)
109. Dhamala M, Assisi CG, Jirsa VK, *et al.*: **Multisensory integration for timing engages different brain networks.** *Neuroimage.* 2007; 34(2): 764–73.
[PubMed Abstract](#) | [Publisher Full Text](#) | [Free Full Text](#)
110. Toda K, Lusk NA, Watson GDR, *et al.*: **Nigrotectal Stimulation Stops Interval Timing in Mice.** *Curr Biol.* 2017; 27(24): 3763–3770.e3.
[PubMed Abstract](#) | [Publisher Full Text](#)
111. Marras C, Lang A, van de Warrenburg BP, *et al.*: **Nomenclature of genetic movement disorders: Recommendations of the international Parkinson and movement disorder society task force.** *Mov Disord.* 2016; 31(4): 436–57.
[PubMed Abstract](#) | [Publisher Full Text](#)
112. Holmes AL, Forcelli PA, Desjardins JT, *et al.*: **Superior colliculus mediates cervical dystonia evoked by inhibition of the substantia nigra pars reticulata.** *J Neurosci.* 2012; 32(38): 13326–32.
[PubMed Abstract](#) | [Publisher Full Text](#) | [Free Full Text](#)
113. McGovern EM, Killian O, Narasimham S, *et al.*: **Disrupted superior collicular activity may reveal cervical dystonia disease pathomechanisms.** *Sci Rep.* 2017; 7(1): 16753.
[PubMed Abstract](#) | [Publisher Full Text](#) | [Free Full Text](#)
114. Ozelius LJ, Hewett JW, Page CE, *et al.*: **The early-onset torsion dystonia gene (DYT1) encodes an ATP-binding protein.** *Nat Genet.* 1997; 17(1): 40–8.
[PubMed Abstract](#) | [Publisher Full Text](#)
115. **F** Fuchs T, Gavarini S, Saunders-Pullman R, *et al.*: **Mutations in the THAP1 gene are responsible for DYT6 primary torsion dystonia.** *Nat Genet.* 2009; 41(3): 286–8.
[PubMed Abstract](#) | [Publisher Full Text](#) | [F1000 Recommendation](#)
116. **F** Fuchs T, Saunders-Pullman R, Masuho I, *et al.*: **Mutations in GNAL cause primary torsion dystonia.** *Nat Genet.* 2013; 45(1): 88–92.
[PubMed Abstract](#) | [Publisher Full Text](#) | [Free Full Text](#) | [F1000 Recommendation](#)
117. **F** Charlesworth G, Plagnol V, Holmström KM, *et al.*: **Mutations in ANO3 cause dominant craniocervical dystonia: ion channel implicated in pathogenesis.** *Am J Hum Genet.* 2012; 91(6): 1041–50.
[PubMed Abstract](#) | [Publisher Full Text](#) | [Free Full Text](#) | [F1000 Recommendation](#)
118. Xiao J, Ulitti RJ, Zhao Y, *et al.*: **Mutations in CIZ1 cause adult onset primary cervical dystonia.** *Ann Neurol.* 2012; 71(4): 458–69.
[PubMed Abstract](#) | [Publisher Full Text](#) | [Free Full Text](#)
119. Lohmann K, Wilcox RA, Winkler S, *et al.*: **Whispering dysphonia (DYT4 dystonia) is caused by a mutation in the TUBB4 gene.** *Ann Neurol.* 2013; 73(4): 537–45.
[PubMed Abstract](#) | [Publisher Full Text](#)
120. Simons C, Wolf NI, McNeil N, *et al.*: **A de novo mutation in the β -tubulin gene TUBB4A results in the leukoencephalopathy hypomyelination with atrophy of the basal ganglia and cerebellum.** *Am J Hum Genet.* 2013; 92(5): 767–73.
[PubMed Abstract](#) | [Publisher Full Text](#) | [Free Full Text](#)
121. Erro R, Hersheson J, Ganos C, *et al.*: **H-ABC syndrome and DYT4: Variable expressivity or pleiotropy of TUBB4 mutations?** *Mov Disord.* 2015; 30(6): 828–33.
[PubMed Abstract](#) | [Publisher Full Text](#)
122. **F** Watanabe N, Itakaoka M, Seki Y, *et al.*: **Dystonia-4 (DYT4)-associated TUBB4A mutants exhibit disorganized microtubule networks and inhibit neuronal process growth.** *Biochem Biophys Res Commun.* 2018; 495(1): 346–52.
[PubMed Abstract](#) | [Publisher Full Text](#) | [F1000 Recommendation](#)
123. **F** Duncan ID, Bugiani M, Radcliff AB, *et al.*: **A mutation in the Tubb4a gene leads to microtubule accumulation with hypomyelination and demyelination.** *Ann Neurol.* 2017; 81(5): 690–702.
[PubMed Abstract](#) | [Publisher Full Text](#) | [Free Full Text](#) | [F1000 Recommendation](#)
124. **F** Curiel J, Rodríguez Bey G, Takanohashi A, *et al.*: **TUBB4A mutations result in specific neuronal and oligodendrocytic defects that closely match clinically distinct phenotypes.** *Hum Mol Genet.* 2017; 26(22): 4506–18.
[PubMed Abstract](#) | [Publisher Full Text](#) | [F1000 Recommendation](#)
125. Zech M, Lam DD, Francescato L, *et al.*: **Recessive mutations in the α 3 (VI) collagen gene COL6A3 cause early-onset isolated dystonia.** *Am J Hum Genet.* 2015; 96(6): 883–93.
[PubMed Abstract](#) | [Publisher Full Text](#) | [Free Full Text](#)
126. Charlesworth G, Angelova PR, Bartolomé-Robledo F, *et al.*: **Mutations in HPCA cause autosomal-recessive primary isolated dystonia.** *Am J Hum Genet.* 2015; 96(4): 657–65.
[PubMed Abstract](#) | [Publisher Full Text](#) | [Free Full Text](#)
127. Lohmann K, Schlicht F, Svetel M, *et al.*: **The role of mutations in COL6A3 in isolated dystonia.** *J Neurol.* 2016; 263(4): 730–4.
[PubMed Abstract](#) | [Publisher Full Text](#)
128. Carecchio M, Reale C, Invernizzi F, *et al.*: **DYT2 screening in early-onset isolated dystonia.** *Eur J Paediatr Neurol.* 2017; 21(2): 269–71.
[PubMed Abstract](#) | [Publisher Full Text](#)
129. **F** Zimprich A, Grabowski M, Asmus F, *et al.*: **Mutations in the gene encoding epsilon-sarcoglycan cause myoclonus-dystonia syndrome.** *Nat Genet.* 2001; 29(1): 66–9.
[PubMed Abstract](#) | [Publisher Full Text](#) | [F1000 Recommendation](#)
130. Asmus F, Zimprich A, Tezenas Du Montcel S, *et al.*: **Myoclonus-dystonia syndrome: epsilon-sarcoglycan mutations and phenotype.** *Ann Neurol.* 2002; 52(4): 489–92.
[PubMed Abstract](#) | [Publisher Full Text](#)
131. Mencacci NE, Rubio-Agusti I, Zdebik A, *et al.*: **A missense mutation in KCTD17 causes autosomal dominant myoclonus-dystonia.** *Am J Hum Genet.* 2015; 96(6): 938–47.
[PubMed Abstract](#) | [Publisher Full Text](#) | [Free Full Text](#)
132. Groen JL, Andrade A, Ritz K, *et al.*: **CACNA1B mutation is linked to unique myoclonus-dystonia syndrome.** *Hum Mol Genet.* 2015; 24(4): 987–93.
[PubMed Abstract](#) | [Publisher Full Text](#) | [Free Full Text](#)
133. Rainier S, Thomas D, Tokarz D, *et al.*: **Myofibrillogenesis regulator 1 gene mutations cause paroxysmal dystonic choreoathetosis.** *Arch Neurol.* 2004; 61(7): 1025–9.
[PubMed Abstract](#) | [Publisher Full Text](#)
134. **F** Wang JL, Cao L, Li XH, *et al.*: **Identification of PRRT2 as the causative gene of paroxysmal kinesigenic dyskinesias.** *Brain.* 2011; 134(Pt 12): 3493–501.
[PubMed Abstract](#) | [Publisher Full Text](#) | [Free Full Text](#) | [F1000 Recommendation](#)
135. **F** Suls A, Dedeken P, Goffin K, *et al.*: **Paroxysmal exercise-induced dyskinesia and epilepsy is due to mutations in SLC2A1, encoding the glucose transporter**

- GLUT11**. *Brain*. 2008; **131**(Pt 7): 1831–44.
[PubMed Abstract](#) | [Publisher Full Text](#) | [Free Full Text](#) | [F1000 Recommendation](#)
136. Weber YG, Kamm C, Suls A, *et al.*: **Paroxysmal choreoathetosis/spasticity (DYT9) is caused by a GLUT1 defect**. *Neurology*. 2011; **77**(10): 959–64.
[PubMed Abstract](#) | [Publisher Full Text](#)
 137. **F** Kuo PH, Gan SR, Wang J, *et al.*: **Dystonia and ataxia progression in spinocerebellar ataxias**. *Parkinsonism Relat Disord*. 2017; **45**: 75–80.
[PubMed Abstract](#) | [Publisher Full Text](#) | [F1000 Recommendation](#)
 138. Méneret A, Ahmar-Beaugendre Y, Rieunier G, *et al.*: **The pleiotropic movement disorders phenotype of adult ataxia-telangiectasia**. *Neurology*. 2014; **83**(12): 1087–95.
[PubMed Abstract](#) | [Publisher Full Text](#)
 139. Le Ber I, Bouslam N, Rivaud-Péchoix S, *et al.*: **Frequency and phenotypic spectrum of ataxia with oculomotor apraxia 2: a clinical and genetic study in 18 patients**. *Brain*. 2004; **127**(Pt 4): 759–67.
[PubMed Abstract](#) | [Publisher Full Text](#)
 140. Anheim M, Monga B, Fleury M, *et al.*: **Ataxia with oculomotor apraxia type 2: clinical, biological and genotype/phenotype correlation study of a cohort of 90 patients**. *Brain*. 2009; **132**(Pt 10): 2688–98.
[PubMed Abstract](#) | [Publisher Full Text](#)
 141. Le Ber I, Moreira MC, Rivaud-Péchoix S, *et al.*: **Cerebellar ataxia with oculomotor apraxia type 1: clinical and genetic studies**. *Brain*. 2003; **126**(Pt 12): 2761–72.
[PubMed Abstract](#) | [Publisher Full Text](#)
 142. Sekijima Y, Hashimoto T, Onodera O, *et al.*: **Severe generalized dystonia as a presentation of a patient with aprataxin gene mutation**. *Mov Disord*. 2003; **18**(10): 1198–200.
[PubMed Abstract](#) | [Publisher Full Text](#)
 143. Synofzik M, Strülings K, Godau J, *et al.*: **Characterizing POLG ataxia: clinics, electrophysiology and imaging**. *Cerebellum*. 2012; **11**(4): 1002–11.
[PubMed Abstract](#) | [Publisher Full Text](#)
 144. Camargos S, Scholz S, Simón-Sánchez J, *et al.*: **DYT16, a novel young-onset dystonia-parkinsonism disorder: identification of a segregating mutation in the stress-response protein PRKRA**. *Lancet Neurol*. 2008; **7**(3): 207–15.
[PubMed Abstract](#) | [Publisher Full Text](#)
 145. Zech M, Castrop F, Schormair B, *et al.*: **DYT16 revisited: exome sequencing identifies PRKRA mutations in a European dystonia family**. *Mov Disord*. 2014; **29**(12): 1504–10.
[PubMed Abstract](#) | [Publisher Full Text](#)
 146. Furukawa Y, Shimadzu M, Rajput AH, *et al.*: **GTP-cyclohydrolase I gene mutations in hereditary progressive aml dopa-responsive dystonia**. *Ann Neurol*. 1996; **39**(5): 609–17.
[PubMed Abstract](#) | [Publisher Full Text](#)
 147. Clot F, Grabli D, Cazeneuve C, *et al.*: **Exhaustive analysis of BH4 and dopamine biosynthesis genes in patients with Dopa-responsive dystonia**. *Brain*. 2009; **132**(Pt 7): 1753–63.
[PubMed Abstract](#) | [Publisher Full Text](#)
 148. Brashear A, Dobyns WB, de Carvalho Aguiar P, *et al.*: **The phenotypic spectrum of rapid-onset dystonia-parkinsonism (RDP) and mutations in the ATP1A3 gene**. *Brain*. 2007; **130**(Pt 3): 828–35.
[PubMed Abstract](#) | [Publisher Full Text](#)
 149. Makino S, Kaji R, Ando S, *et al.*: **Reduced neuron-specific expression of the TAF1 gene is associated with X-linked dystonia-parkinsonism**. *Am J Hum Genet*. 2007; **80**(3): 393–406.
[PubMed Abstract](#) | [Publisher Full Text](#) | [Free Full Text](#)
 150. **F** Dobričić V, Tomić A, Branković V, *et al.*: **GCH1 mutations are common in Serbian patients with dystonia-parkinsonism: Challenging previously reported prevalence rates of DOPA-responsive dystonia**. *Parkinsonism Relat Disord*. 2017; **45**: 81–4.
[PubMed Abstract](#) | [Publisher Full Text](#) | [F1000 Recommendation](#)
 151. Rosewich H, Ohlenbusch A, Hupke P, *et al.*: **The expanding clinical and genetic spectrum of ATP1A3-related disorders**. *Neurology*. 2014; **82**(11): 945–55.
[PubMed Abstract](#) | [Publisher Full Text](#)
 152. Sweney MT, Newcomb TM, Swoboda KJ: **The expanding spectrum of neurological phenotypes in children with ATP1A3 mutations, Alternating Hemiplegia of Childhood, Rapid-onset Dystonia-Parkinsonism, CAPOS and beyond**. *Pediatr Neurol*. 2015; **52**(1): 56–64.
[PubMed Abstract](#) | [Publisher Full Text](#) | [Free Full Text](#)
 153. Wilcox R, Brænnø I, Brüggemann N, *et al.*: **Genome sequencing identifies a novel mutation in ATP1A3 in a family with dystonia in females only**. *J Neurol*. 2015; **262**(1): 187–93.
[PubMed Abstract](#) | [Publisher Full Text](#)
 154. Wiley J, Lynch T, Lincoln S, *et al.*: **Parkinson's disease in Ireland: clinical presentation and genetic heterogeneity in patients with parkin mutations**. *Mov Disord*. 2004; **19**(6): 677–81.
[PubMed Abstract](#) | [Publisher Full Text](#)
 155. Rohé CF, Montagna P, Breedveld G, *et al.*: **Homozygous PINK1 C-terminus mutation causing early-onset parkinsonism**. *Ann Neurol*. 2004; **56**(3): 427–31.
[PubMed Abstract](#) | [Publisher Full Text](#)
 156. van Gassen KL, van der Heijden CD, de Bot ST, *et al.*: **Genotype-phenotype correlations in spastic paraplegia type 7: a study in a large Dutch cohort**. *Brain*. 2012; **135**(Pt 10): 2994–3004.
[PubMed Abstract](#) | [Publisher Full Text](#)
 157. Caballero Oteyza A, Battaloğlu E, Ocek L, *et al.*: **Motor protein mutations cause a new form of hereditary spastic paraplegia**. *Neurology*. 2014; **82**(22): 2007–16.
[PubMed Abstract](#) | [Publisher Full Text](#) | [Free Full Text](#)
 158. **F** Hirst J, Madeo M, Smets K, *et al.*: **Complicated spastic paraplegia in patients with AP5Z1 mutations (SPG48)**. *Neurol Genet*. 2016; **2**(5): e98.
[PubMed Abstract](#) | [Publisher Full Text](#) | [Free Full Text](#) | [F1000 Recommendation](#)
 159. Domingo A, Erro R, Lohmann K: **Novel Dystonia Genes: Clues on Disease Mechanisms and the Complexities of High-Throughput Sequencing**. *Mov Disord*. 2016; **31**(4): 471–7.
[PubMed Abstract](#) | [Publisher Full Text](#)
 160. **F** Zech M, Boesch S, Jochim A, *et al.*: **Clinical exome sequencing in early-onset generalized dystonia and large-scale resequencing follow-up**. *Mov Disord*. 2017; **32**(4): 549–59.
[PubMed Abstract](#) | [Publisher Full Text](#) | [F1000 Recommendation](#)
 161. Blitzer A, Brin MF, Stewart CF: **Botulinum toxin management of spasmodic dysphonia (laryngeal dystonia): a 12-year experience in more than 900 patients**. *Laryngoscope*. 1998; **108**(10): 1435–41.
[PubMed Abstract](#) | [Publisher Full Text](#)
 162. Payne S, Tisch S, Cole I, *et al.*: **The clinical spectrum of laryngeal dystonia includes dystonic cough: observations of a large series**. *Mov Disord*. 2014; **29**(6): 729–35.
[PubMed Abstract](#) | [Publisher Full Text](#)
 163. **F** Putzel GG, Fuchs T, Battistella G, *et al.*: **GNAL mutation in isolated laryngeal dystonia**. *Mov Disord*. 2016; **31**(5): 750–5.
[PubMed Abstract](#) | [Publisher Full Text](#) | [Free Full Text](#) | [F1000 Recommendation](#)
 164. **F** de Gusmão CM, Fuchs T, Moses A, *et al.*: **Dystonia-Causing Mutations as a Contribution to the Etiology of Spasmodic Dysphonia**. *Otolaryngol Head Neck Surg*. 2016; **155**(4): 624–8.
[PubMed Abstract](#) | [Publisher Full Text](#) | [Free Full Text](#) | [F1000 Recommendation](#)
 165. Djarmati A, Schneider SA, Lohmann K, *et al.*: **Mutations in THAP1 (DYT6) and generalised dystonia with prominent spasmodic dysphonia: a genetic screening study**. *Lancet Neurol*. 2009; **8**(5): 447–52.
[PubMed Abstract](#) | [Publisher Full Text](#)
 166. **F** Bianchi S, Battistella G, Huddleston H, *et al.*: **Phenotype- and genotype-specific structural alterations in spasmodic dysphonia**. *Mov Disord*. 2017; **32**(4): 560–8.
[PubMed Abstract](#) | [Publisher Full Text](#) | [Free Full Text](#) | [F1000 Recommendation](#)
 167. Fahn S, Williams DT: **Psychogenic dystonia**. *Adv Neurol*. 1988; **50**: 431–55.
[PubMed Abstract](#)
 168. Shill H, Gerber P: **Evaluation of clinical diagnostic criteria for psychogenic movement disorders**. *Mov Disord*. 2006; **21**(8): 1163–8.
[PubMed Abstract](#) | [Publisher Full Text](#)
 169. Lang AE: **Psychogenic dystonia: a review of 18 cases**. *Can J Neurol Sci*. 1995; **22**(2): 136–43.
[PubMed Abstract](#) | [Publisher Full Text](#)
 170. Schrag A, Trimble M, Quinn N, *et al.*: **The syndrome of fixed dystonia: an evaluation of 103 patients**. *Brain*. 2004; **127**(Pt 10): 2360–72.
[PubMed Abstract](#) | [Publisher Full Text](#)
 171. Hallett M: **Functional (psychogenic) movement disorders - Clinical presentations**. *Parkinsonism Relat Disord*. 2016; **22** Suppl 1: S149–52.
[PubMed Abstract](#) | [Publisher Full Text](#) | [Free Full Text](#)
 172. Ziegler JS, von Stauffenberg M, Vlaho S, *et al.*: **Dystonia with secondary contractures: a psychogenic movement disorder mimicking its neurological counterpart**. *J Child Neurol*. 2008; **23**(11): 1316–8.
[PubMed Abstract](#) | [Publisher Full Text](#)
 173. Gupta A, Lang AE: **Psychogenic movement disorders**. *Curr Opin Neurol*. 2009; **22**(4): 430–6.
[PubMed Abstract](#) | [Publisher Full Text](#)
 174. Espay AJ, Morgante F, Purzner J, *et al.*: **Cortical and spinal abnormalities in psychogenic dystonia**. *Ann Neurol*. 2006; **59**(5): 825–34.
[PubMed Abstract](#) | [Publisher Full Text](#)
 175. Avanzino L, Martino D, van de Warrenburg BP, *et al.*: **Cortical excitability is abnormal in patients with the "fixed dystonia" syndrome**. *Mov Disord*. 2008; **23**(5): 646–52.
[PubMed Abstract](#) | [Publisher Full Text](#)
 176. Kobayashi K, Lang AE, Hallett M, *et al.*: **Thalamic neuronal and EMG activity in psychogenic dystonia compared with organic dystonia**. *Mov Disord*. 2011; **26**(7): 1348–52.
[PubMed Abstract](#) | [Publisher Full Text](#) | [Free Full Text](#)
 177. **F** Morgante F, Tinazzi M, Squintani G, *et al.*: **Abnormal tactile temporal discrimination in psychogenic dystonia**. *Neurology*. 2011; **77**(12): 1191–7.
[PubMed Abstract](#) | [Publisher Full Text](#) | [F1000 Recommendation](#)
 178. **F** Quartarone A, Rizzo V, Terranova C, *et al.*: **Abnormal sensorimotor plasticity in organic but not in psychogenic dystonia**. *Brain*. 2009; **132**(Pt 10): 2871–7.
[PubMed Abstract](#) | [Publisher Full Text](#) | [Free Full Text](#) | [F1000 Recommendation](#)

179. Schwingenschuh P, Katschnig P, Edwards MJ, *et al.*: **The blink reflex recovery cycle differs between essential and presumed psychogenic blepharospasm.** *Neurology*. 2011; **76**(7): 610–4.
[PubMed Abstract](#) | [Publisher Full Text](#) | [Free Full Text](#) | [F1000 Recommendation](#)
180. Schrag AE, Mehta AR, Bhatia KP, *et al.*: **The functional neuroimaging correlates of psychogenic versus organic dystonia.** *Brain*. 2013; **136**(Pt 3): 770–81.
[PubMed Abstract](#) | [Publisher Full Text](#) | [Free Full Text](#)
181. Garcin B, Roze E, Mesrati F, *et al.*: **Transcranial magnetic stimulation as an efficient treatment for psychogenic movement disorders.** *J Neurol Neurosurg Psychiatry*. 2013; **84**(9): 1043–6.
[PubMed Abstract](#) | [Publisher Full Text](#)
182. Garcin B, Mesrati F, Hubsch C, *et al.*: **Impact of Transcranial Magnetic Stimulation on Functional Movement Disorders: Cortical Modulation or a Behavioral Effect?** *Front Neurol*. 2017; **8**: 338.
[PubMed Abstract](#) | [Publisher Full Text](#) | [Free Full Text](#) | [F1000 Recommendation](#)
183. Edwards MJ, Bhatia KP: **Functional (psychogenic) movement disorders: merging mind and brain.** *Lancet Neurol*. 2012; **11**(3): 250–60.
[PubMed Abstract](#) | [Publisher Full Text](#)

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