DYSTONIA
VIDEO DIAGNOSIS AND TREATMENT

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Our work ethic in movement disorders is “A video paints a thousand words; A patient paints a thousand videos.” The lectures will be very video-based. Nonetheless, due to time limitation of the course, it is impossible to provide details of every hyperkinetic movement disorder. We hope that our syllabi, as additional educational tools, will provide collections of practical approaches to these disorders.

Definition of dystonia
The following statement refers to the definition of dystonia, per the new classification of dystonia in 2013.

“Dystonia is a movement disorder characterized by sustained or intermittent muscle contraction causing abnormal, often repetitive, movements, postures, or both. Dystonic movements are typically patterned, twisting, and may be tremulous. Dystonia is often initiated and worsened by voluntary action and associated with overflow muscle activation”.

How can we differentiate dystonia from other phenomenologies?
When abnormal “posturing” is present, it may not be difficult to recognize dystonia. Nonetheless, abnormal “movements” may resemble other phenomenologies. Compared to dystonia, chorea generally has a flowing quality with *randomness*, unlike the *repetitive* twisting nature of dystonia. Myoclonic jerks are typically brief, correlating with their burst duration of less than 200 milliiseconds on electrophysiologic studies, whereas jerks in dystonia are slower (due to longer duration of the bursts) and are oftentimes associated with abnormal posturing. Tics can look repetitive, but are usually associated with a premonitory urge and suppressibility. Tics can easily occur at rest, whereas dystonia may not be appreciated in resting position, but more prominent with action. Dystonic tremor can be differentiated from other forms of tremor by its jerky quality and associated abnormal posturing, but this can sometimes be clinically problematic.

Major characteristics of dystonia
Note that not all features need be present. For example, patients may have abnormal posturing without abnormal (jerky or flowing) movements; some features such as geste antagoniste or null point may not be present in some patients.

1. **Abnormal posturing**. When present, this is one of the easiest features to recognize. However, this can be misdiagnosed, as some dystonia-mimics such as pseudodystonia (see detail below). Thus, caution has to be made especially when it is fixed and/or associated with prominent pain. Dystonic posturing may not be obvious at rest, and is usually more prominent with action such as when holding arms up.

2. **Dystonic tremor**. We do not view “tremor” in dystonia as a “true tremor” (which is typically a sinusoidal oscillatory movement around one axis). In fact dystonic tremor is typically jerky. Associated abnormal posturing can also provide an important clue. Dystonic tremor may have directionality, for example, jerky “tremor” in cervical dystonia is worse when a patient turns their head in one direction, diminished to very little-to-no tremor when the head is moved to some specific position or “null point”, typically in the direction opposite to the former. It is important to look for these features in order not to misdiagnose patients with essential tremor.

3**. Overflow movements**. These are characterized by unintentional movements of muscles. Sometimes overflow movements can be confused with chorea which occurs at rest in *random* fashion without requirement to activate any specific muscles. Pathophysiologically evidence of loss of surround inhibition has been demonstrated in several electrophysiologic studies.

4. **Mirror movements.** Mirror movements are not specific to dystonia. They can be found in parkinsonian disorders or present as congenital or genetic forms. In dystonia, when moving or performing a task with the contralateral unaffected (and usually, but not always, non-dominant) limb, mirror movements can be appreciated in the dystonic limb. This feature is very useful clinically to determine primary dystonic muscles

which are appropriate targets for botulinum toxin injections (BoNT), without contamination from compensatory movements. For example, when a patient develops “cramps” in the right hand when gripping a pen, it may be difficult to distinguish primary from compensatory movements. However, when an examiner asks the patient to write with his left hand, a mirror movement in the right hand or arm that emerges (such as wrist flexion) suggests the primary muscles involved and best targets for BoNT.

5. **Task-specificity**. This feature is one of the unique features of dystonia. Task-specificity in dystonia can present as one of these patterns: 1. Dystonia occurs exclusively with a specific task but not others. 2. Dystonia is more prominent with a specific task but is still present to a lesser degree with other tasks 3. Dystonia begins with one specific task but over time spread to others. It is important to take a clinical history and careful examination to delineate these patterns. Here we provide some examples of affected tasks: speaking, eating and/or drinking in oromandibular dystonia; writing in writer’s cramp (may spread to other manual tasks later in some patients); playing musical instruments in musician’s dystonia, etc. When examined carefully, more details regarding task-specificity can be delineated in some patients. For example, specific letter(s) affected by writer’s cramp, or specific note(s)/repertoire/ascending vs. descending scales affected by some musicians may be specific triggers.

6**. Null point**. Null point is a position of the dystonic body part where dystonia (posturing and/or dystonic tremor) becomes minimal or remarkably less. This varies among patients even in the same form of dystonia. Examples include some specific head position or direction in cervical dystonia, or placing the arm in some specific position (e.g. internal rotation of an arm with hand on the back in some patient) in upper limb dystonia.

7. **Sensory tricks or geste antagoniste**. This phenomenon demonstrates one example of the role of the sensory system in pathophysiology of dystonia. A classic example of sensory tricks is touching a body region affected by dystonia or nearby *lightly*, leading to improvement in dystonia. This is not just simply pushing or applying pressure against the direction of dystonia, and is not necessarily located on the antagonist side, hence the term “antagoniste” may be misleading. Sensory tricks can be elicited in various interesting ways: 1. by the patient actually performing the tricks (exteroceptive geste) or 2. just imagination about the tricks (interoceptive). They can be effective in several fashions: 1. more commonly when the tricks are performed by a patient himself (closed-loop sensory feedback) 2. sometimes by the examiner (open-loop) 3. by the patient holding the examiner’s hand to touch the dystonic region (by this, open loop will be transformed to closed loop, reported as “closing-the-loop” sign). Table 1 demonstrates some examples of sensory tricks in dystonia.

Table 1. Geste antagoniste or sensory tricks in some forms of dystonia

Dystonia	Sensory tricks
Cervical dystonia	Touching upper or face on either right or left side
Blepharospasm	Touching upper or lower eyelid
Oromandibular dystonia	Putting candy in the mouth or placing syringe between teeth, either on the left or right side or the center
Spasmodic dysphonia	Singing or speaking with high-pitch voice ("Mickey-mouse voice")
Writer's cramp	Placing a pen between index and middle fingers, writing with a pen with large barrel or large nib
Truncal dystonia	Placing hand(s) in a pocket
Leg or foot dystonia	Running or walking backward; walking up- or downsteps or walking downsteps backward

Classification of dystonia

Classification of dystonia has evolved over time. The most recent classification was published in 2013. We will not discuss classification in greater detail, but will rather focus on the clinical approach. Reference is provided. Briefly, the new classification described dystonia mainly in 2 axes: Axis I Clinical characteristics and Axis II Etiology. Axis I can be further characterized based on age at onset, body distribution, temporal patter, and associated features. Axis II Etiology is further characterized whether 1) the dystonia has nervous system pathology and 2) the dystonia is inherited, acquired or idiopathic. While this new classification system may minimize lumping heterogeneous groups of dystonia together, hence “cleaner” for future

research, we view that learning from the old classification scheme is still useful. The most commonly used categories in the old classifications, “primary dystonia, dystonia-plus, heredodegenerative and secondary dystonia”, were transformed to “(inherited) isolated dystonia, (inherited) combined dystonia, inherited dystonia and acquired dystonia”, respectively, in the new classification.

How to approach patients with dystonia in the clinic

Pattern recognition remains important in dystonia, and in fact most movement disorders. However, we organize some general principles in order to help guide clinicians when encountering dystonia patients in clinic.

1. **Rule out pseudodystonia or dystonia-mimic.** Misdiagnosis of pseudodystonia as true dystonia can lead to loss of opportunity to obtain correct treatment and subsequent disability. Fixed dystonia and/or prominent pain are helpful clues that a patient may not have a true dystonia. Some important examples of pseudodystonia include congenital muscular torticollis, acute atlanto-axial rotatory subluxation (AARS) due to trauma or after inflammation of the adjacent tissue (Grisel’s syndrome), tetanus and psychogenic movement disorders.

2. **Rule out secondary dystonia from primary/idiopathic forms**. To simplify and avoid confusion about the terms used in multiple different classifications, primary/dystonia-plus are genetic dystonias with the conventional DYT designations (e.g. DYT1, 2, 3, etc.), whereas secondary dystonias are dystonias from other causes such as toxic, metabolic, structural, or infectious causes. In addition, we also include the forms of idiopathic focal dystonias (typically in adults), such as cervical dystonia, oromandibular dystonia as “primary”. It is probably impossible to generate the rules that can be applied to all cases. Knowing clinical features of each dystonia will help in pattern recognition (e.g. myoclonic jerks in the face, neck and proximal arms in a young patient, worse with action especially when writing, will make us think about DYT11 dystonia). Nevertheless, there are some important clues suggesting a secondary cause of dystonia as follows:

2.1 Body distribution

a) Hemidystonia suggests a contralateral basal ganglion lesion

b) Craniocervical onset in children or leg onset in adults. Primary dystonia in children especially the most common form, DYT1 and DYT5, typically has leg onset, and tends to generalize over time. When encountering children with cervical or oromandibular dystonia, one has to think about secondary causes which require further work-up such as metabolic screening. One exception is writer’s cramp can be a presentation of DYT1 dystonia in children. In addition, DYT6 dystonia (which tend to affect older children or adults) typically has craniocervical onset. In adults, idiopathic dystonia typically has craniocervical distribution, and this tend not to generalize. Examples include cervical dystonia, blepharospasm, oromandibular dystonia, etc. Therefore, when we encounter an adult with leg-onset dystonia, we have to first look carefully for secondary causes such as Parkinson’s disease. Again, there is always an exception to the rule: an idiopathic form of isolated foot dystonia in adults has been reported.

2.2 Time course

Presence of a preceding event such as trauma or infection may suggest secondary dystonia. However, it is important to note that dystonia can be delayed (months to years) after the events (delayed-onset dystonia). Conversely, acute temporal profile can also be seen in some forms of primary dystonia, for example, DYT12 or rapid-onset dystonia parkinsonism (RDP) where dystonia develops within minutes or days after an intercurrent illness.

2.3 Associated features

The presence of associated features such as focal neurologic findings, other neurologic findings such as neuropathy or deafness or other systemic features such as endocrine or hematologic abnormalities, as well as abnormal neuroimaging can be important clues for secondary causes.

The list of disorders that can present with secondary dystonia is exhaustive. Here we group them into 4 main categories:

1. Neurometabolic disorders such as glucose transporter 1 (GLUT1) deficiency syndrome and organic acidemias
2. Autosomal-recessive cerebellar ataxias (can present with dystonia and/or chorea in children)

Table 2. Examples of secondary dystonias with their specific treatment

Disorders	Specific treatment
Neurometabolic disorders	
Disorders of biogenic amine synthetic pathway	
Dopa-responsive dystonia (e.g. *GCH1, TH, SPR* mutations)	Levodopa
AADC deficiency (not DRD or DYT5)	Dopamine agonists; benefits to levodopa have been reported
Organic acidemia	
Glutaric aciduria type 1	Restriction of lysine; avoidance of triggers such as fever or acute illness
Methylmalonic acidemia	Low protein diet; avoidance of triggers such as fever or acute illness
Propionic acidemia	Low protein diet; avoidance of triggers such as fever or acute illness
AR ataxia with possible co-existing or even predominant dystonia	
Abetalipoproteinemia	Vitamin E, low fat diet
Ataxia with vitamin E deficiency	Vitamin E
Other disorders	
GLUT1 deficiency syndrome	Ketogenic diet
Cerebrotendinous xanthomatosis	Chenodeoxycholic acid
Biotin-thiamine responsive basal ganglia disease	Biotin along with thiamine
Niemann-Pick type C	N-butyl-deoxynojirimycin (Miglustat)
Heavy metal-related disorders	
Wilson's disease	Copper chelators including D-penicillamine, zinc sulfate, tetrathiomolybdate; restriction of high copper diet (such as shellfish, liver, chocolate, legumes, etc.); Liver transplant in severe cases
Manganese trasnsporter deficiency	Manganese chelation
Neurodegeneration with brain iron accumulation (NBIAs)	Trials on iron chelators such as deferiprone under way
Acquired causes	
Infectious (e.g. Toxoplasmosis)	Appropriate antibiotics
Autoimmune (e.g. LGI1 and NMDA encephalitis)	Immunosuppressive therapies including steroids and/or IVIG, or plasma exchange; search and remove teratoma in case of NMDA encephalitis
Paraneoplastic (e.g. anti-Ri)	Search and treat underlying malignancy; Immunosuppressive therapies including steroids and/or IVIG

3. Heavy metal-related disorders including Wilson's disease, manganese (Mn)-related disorders (secondary manganism from acquired hepatocerebral degeneration, ephedrone use, or Mn transporter deficiency from *SLC30A10* mutations), neurodegeneration with brain iron accumulation (NBIAs) and basal ganglia calcification

4. Acquired dystonia.

Table 2 demonstrates selected causes of secondary dystonia. It is crucial to recognize these mostly treatable disorders. One important "don't miss" diagnosis is Wilson's disease. One should always look for Kayser-Fleischer rings, and if still suspicious, refer for slit-lamp examination and check 24-hour urine copper.

3. **Once secondary causes have been excluded, identify whether dystonia is inherited isolated (primary) or combined (dystonia-plus)** (Table 3)

While these disorders can be recognized by their classic clinical phenotypes, clinicians must be aware that in the genomic era, phenotypic spectrum has been expanding and phenotypic variability contributes to clinical complexity.

In order to identify these disorders we would suggest these following steps:

3.1 Identify associated movement disorder phenomenology. This leads to diagnosis of dystonia-plus (or combined dystonia) as follows:

a) Parkinsonism: DYT3 (Lubag disease), DYT5 (dopa-responsive dystonia, DRD), DYT12 (rapid-onset dystonia parkinsonism, RDP). DYT16 is very rare, and will not be mentioned in further detail.

b) Myoclonus: DYT11 (myoclonus-dystonia syndrome)

Of note, DYT5 or DRD is a group of disorders worth mentioning here in further detail. DRD is an important "don't miss" diagnosis. The most common form of DRD is autosomal dominant due to deficiency of GTP cyclohydrolase I, a rate-limiting enzyme for synthesis of tetrahydrobiopterin which is an important cofactor for dopamine synthesis. Less commonly, there are also autosomal recessive forms of GTP cyclohydrolase I, and other enzymes such as tyrosine hydroxylase (TH) and sepiapterin reductase (SPR) deficiencies. Patients classically present in childhood with leg-onset dystonia and diurnal fluctuation, worse in the evening. However, atypical presentations such as dystonic cerebral palsy-like features, or upper limb-onset in children and adults have been reported. Therefore, it is crucial to give a levodopa trial in every pediatric and adult patients in whom the diagnosis of DRD cannot be completely excluded. Patients typically have dramatic response with low doses (200-400 mg/day or up to 10 mg/kg/day in children; up to 4 weeks), and have sustained long-term benefit without development of levodopa-induced dyskinesias (but rarely reported).

3.2 After excluding dystonia-plus, the genotype of primary dystonia can be clued by body regions involved at onset and progression.

a) Leg-onset with ascending progression to generalized dystonia is suggestive of DYT1 dystonia. Writer's cramp especially in children and young adults can also be a presentation in DYT1 dystonia. Speech is typically spared in DYT1 dystonia.

b) Craniocervical onset with speech involvement is suggestive of DYT6 dystonia.

c) DYT4 is rare and has been reported in an Australian family with whispering dysphonia and hobby-horse gait in some family members.

4. **Once genetic primary dystonias have been excluded, we come to the diagnosis of idiopathic dystonia.** This group of dystonias (Table 4) is typically adult-onset, and has focal or segmental distribution. One may think that we have to perform extensive tests such as neuroimaging or genetic testing in order to proceed to this step. However, practically the disorders in this category are mainly identified by previous clinical knowledge that they are "idiopathic". Therefore, once classified disorders into this category, extensive investigations are not generally required.

However, thinking through our steps 1-3 is still important in order not to miss specific causes or existing genetic diagnosis. For example, in oromandibular dystonia, it is important to exclude secondary causes such as tardive etiology or chorea-acanthocytosis (Table 5). Another example is that some patients with craniosegmental dystonia, previously categorized as "idiopathic", have recently found to be due *CIZ1*, *ANO3* or *GNAL* mutations (designated as DYT23, DYT24, and DYT25, respectively). Nevertheless, genetic testing for these genes has not been performed routinely in clinical practice and has not had impact on patient management.

Table 3. Primary dystonia comprises of isolated ("primary dystonia") and combined ("dystonia-plus") dystonia. Only more common and important disorders are selected. Genes, typical clinical features and important clinical pearls are demonstrated.

DYT designation	Gene	Typical clinical features	Remarks
Isolated dystonia			
DYT1	*TOR1A*	• Leg-onset with ascending progression to generalized dystonia in children • Can also present with writer's cramp in children • Speech is typically spared	• The most common form of primary dystonia • Penetrance 30% • More common in Ashkenazi Jewish • Excellent response to DBS
DYT6	*THAP1*	• Craniocervical onset with prominent speech impairment	• The second most common form of primary dystonia after DYT1 • Penetrance 60% • Less response to DBS than DYT1
DYT4	*TUBB4A*	• "Whispering dysphonia" • Generalized or focal dystonia with prominent spasmodic dysphonia • Hobby-horse gait.	• Rare - reported in an Australian family • Allelic to hypomyelination with atrophy of basal ganglia and cerebellum (H-ABC)
Combined dystonia			
With parkinsonism			
DYT5 (Dopa-responsive dystonia or Segawa syndrome)	*GCH1, TH, SPR*	• Typically leg-onset with diurnal fluctuation • Phenotypic spectrum expanding - can be presented in adults with limb-onset dystonia; may mimic spastic paraparesis or dystonic cerebral palsy.	• "Don't miss" diagnosis • Give levodopa trial (200-400 mg/day or up to 10 mg/kg/day for 4 weeks) in any children or adults in whom DRD cannot be excluded • Sustained benefit, usually without levodopa-induced dyskinesia (rarely reported). • Oculogyria reported in DRD due to TH or SPR deficiency
DYT12 (Rapid-onset dystonia-parkinsonism or RDP)	*ATP1A3*	• Craniocervical onset with rostrocaudal gradient • Lower cranial involvement leading to risus sardonicus • Typically speech impairment. Expanding phenotypic spectrum (see the right column)	• Allelic to alternating hemiplegia of childhood (AHC) and CAPOS syndrome (cerebellar ataxia, pes cavus, optic atrophy, sensorineural hearing loss) • Phenotypes can be overlapping between these syndromes
DYT3 (X-linked dystonia-parkinsonism or Lubag disease)	*TAF1*	• Prominent craniocervical involvement • Meige syndrome with prominent jaw opening dystonia is common	• Founder effect in Filipino, in particular Island of Panay, Capiz province • Can develop levodopa-induced dyskinesia
With myoclonus			
DYT11 (Myoclonus-Dystonia syndrome)	*SGCE* (in about 15-30%), *KCTD17* (designated as DYT26)	• Myoclonic jerks may be more prominent than dystonia • Typically affected upper axial regions including face, neck and shoulders, giving "jello jiggling-like" feature • Myoclonus and dystonia typically more prominent when performing manual tasks such as writing or pouring water • Associated with psychiatric features including anxiety, OCD, depression • Alcohol-responsive	• Maternal imprinting • Also reported in uniparental (maternal) disomy in Russell-Silver syndrome • DYT15 also described as myoclonus-dystonia but gene has not been identified • Good response to GPi DBS (both dystonia and myoclonus improve)

Table 4. Forms of idiopathic focal dystonia, listed from rostral to caudal body regions

Forms of idiopathic dystonia	Muscles involved	Clinical pearls
Blepharospasm	Orbicularis oculi	• Worse when exposing to bright light or reading books/newspaper • Improved when speaking, so patients tend to be talkative • Tonic form can cause to functional blindness • Phasic form may present with just increased eye blink rate without visible tonic muscular contraction • Sensory tricks - touching upper or lower eyelid
Meige syndrome	Upper and lower cranial muscles	
Oromandibular dystonia (idiopathic lower cranial dystonia)	• *Jaw deviation* - contralateral lateral pterygoid • *Jaw opening* - bilateral lateral pterygoids and submental complex • *Jaw closing* - bilateral masseters, temporalis, medial pterygoids • *Lingual protrusion* - genioglossus	• Patients may be misdiagnosed as TMJ arthritis or dental problems • May initially affected just one oral task such as speaking, eating or drinking, but can spread over time • Sensory tricks - putting syringe or tongue depressor *between* teeth. • Other causes of dystonia with predominant oromandibular involvement have to be excluded (see Table 5)
Embouchure dystonia	Complex perioral muscles including orbicularis oris and others	• A form of musician's dystonia affecting perioral muscles in brass and woodwind players
Spasmodic dysphonia (SD)	• *Adductor form (ADSD)* - thyroarytenoid • *Abductor form (ABSD)* - posterior cricoarytenoid.	• Adductor form is more common and has better response to BoNT • Can be better when shouting, singing or speaking with high-pitch voice • Alcohol responsive in about 60% • Caution that severe vocal essential tremor can also produce vocal breaks, resembling SD
Cervical dystonia	• *Torticollis* - contralateral sternocleidomastoid (SCM) and ipsilateral splenius capitis • *Laterocollis* - ipsilateral SCM • *Anterocollis* - anterior and middle scalenes, bilateral SCMs and prevertebral muscles including longus colli • *Retrocollis* - bilateral splenius capitis	• Sensory tricks - touching neck or upper neck area
Focal task-specific hand dystonia		• Other examples include typist dystonia, craft cramp, etc.
Writer's cramp	Common forms - wrist flexion, finger flexion or extension	• Sensory tricks - holding a pen between index and middle fingers, using a pen with large barrel or nib, writing on a wall • Mirror dystonia is valuable to determine primary dystonic muscles (not compensatory) to be treated with BoNT
Musician's dystonia such as in pianists, violinists, guitarists, drummers, trumpet players, etc.	Commonly affect high demand side e.g. right hand, especially 4th and 5th fingers, in pianists	
Yips	Usually wrist or forearm muscles	
Isolated truncal dystonia	• Truncal flexion - rectus abdominis • Truncal extension - paraspinal muscles	• One needs to rule out tardive dystonia especially in truncal extension dystonia.
Isolated foot dystonia	Most commonly foot inversion (tibialis posterior) +/- plantar flexion (gastrosoleus)	• One needs to rule out DRD and DYT1 in children, and DRD and PD in adults. • Sensory tricks - running, walking backward, imagining about walking backward when walking forward, walking up- or downsteps

Table 5. Differential diagnosis of dystonia with prominent lower cranial involvement including both primary and secondary dystonias

Differential diagnosis of dystonia with prominent lower cranial involvement
➢ DYT3 dystonia (Lubag disease)
➢ DYT12 dystonia (Rapid-onset dystonia parkinsonism, RDP)
➢ Wilson's disease
➢ Chorea-acanthocytosis
➢ Pantothenate kinase-associated neurodegeneration (PKAN)
➢ Lesch-Nyhan syndrome

Treatment of dystonia

Treatment of dystonia can be classified into specific and symptomatic therapies. Please refer to provided references for further detail on this topic. We would like to reiterate here that it is important to correctly recognize pseudodystonia and secondary dystonia since specific treatments are available for most of these disorders. Another "don't miss" diagnosis is dopa-responsive dystonia (DRD or DYT5) for which levodopa plays a role as specific therapy (see above).

For symptomatic therapies, three treatment modalities include 1. Pharmacological treatment 2. Botulinum toxin injections (BoNT) and 3. Deep brain stimulation (DBS). Intrathecal baclofen has become less popular among movement disorder practice only due to hardware problems including infection and malfunction, and advances in DBS.

BoNT is generally a treatment of choice in focal or segmental dystonia where specific muscle group(s) can be targeted. However, in some cases with generalized dystonia, it is still useful to target muscles focally such as hand muscles for rehabilitation or hygienic purpose. In contrast, we do not usually employ BoNT in some forms of dystonia such as embouchure dystonia (as the activated muscles are complex and, in our experience, it is not effective) or lingual dystonia (as BoNT poses very high risk for dysphagia; although this has been reported by some, we do not perform in our clinical practice).

Indications of DBS in dystonia have been expanding. Well-known indications include DYT1, non-DYT1 generalized dystonia, DYT6 (although the response is usually less robust than in DYT1 patients), DYT11 and tardive dystonia. The relatively new indications reported in small studies requiring further confirmation include DYT3 dystonia, cervical dystonia, and some forms of secondary dystonias such as cerebral palsy and pantothenate kinase-associated neurodegeneration (PKAN). The usual target for dystonia is globus pallidus interna (GPi). In DYT11, bilateral DBS at ventral intermediate nucleus (Vim) of thalamus has been reported to improve myoclonus but not dystonia, whereas GPi DBS improved both components, therefore being a target of choice. There has been more evidence to suggest early consideration of GPi DBS in DYT1 generalized dystonia patients in clinical practice to prevent potentially irreversible disability. One of the challenges in DBS for dystonia is that DBS programming in dystonia may take days, weeks or several months to take effect after appropriate setting, as opposed to immediate effect for tremor or bradykinesia in Parkinson's disease.

For pharmacological treatment, three main medications include anticholinergics (trihexyphenidyl being used most commonly), baclofen and benzodiazepines (clonazepam being used most commonly). Among these, anticholinergics have been studied and employed most commonly in clinical practice. As a general principle, medications should be started at a low dose, and titrated up slowly (usually every 2-3 days in children, or up to a week in elderly). Slow taper should be entertained prior discontinuation to prevent withdrawal symptoms (e.g. seizure in case of baclofen and benzodiazepines). The doses and side effects of conventional medications are demonstrated in Table 6.

Paroxysmal dyskinesias are beyond the scope of our lecture, and will be discussed in dedicated AAN session.

Table 6. Three conventional medications for pharmacological treatment of dystonia

Pharmacological treatment of dystonia			
	Trihexyphenidyl	**Baclofen**	**Clonazepam**
Usual dose range (mg/day)	4-30	10-30	0.5-4
Side effects	• *Central*: sedation, memory impairment, psychosis, chorea • *Autonomic*: blurred vision, urinary retention, constipation, dry mouth	Drowsiness, dizziness, nausea, fatigue	Sedation, depression, nocturnal drooling, behavioral disinhibition
Caution	Contraindicated in angle-closure glaucoma	Abrupt discontinuation can trigger baclofen withdrawal syndrome (psychosis, seizure)	FDA recommends *CYP2D6* genotyping when using the dose ≥ 50 mg/day

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