Tics and Tourette Syndrome

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TIC PHENOMENOLOGY

- Tics are sudden, rapid, recurrent, nonrhythmic motor movements or vocalizations (phonic productions).

Categories and Types

- Tics are classified into two larger categories (motor and phonic), with each being subdivided into a simple and complex grouping

- Simple : Brief, rapid, abrupt jerklike, nonrhythmic movements that involve only a single muscle or localized group (eye blink, head jerk, shoulder shrug)

Complex :

- involve either a cluster of simple actions or a more coordinated pattern of movements. Complex motor tics can be nonpurposeful (facial or body contortions) or appear purposeful but actually serve no purpose (touching, hitting, smelling, jumping, bending, imitating observed movements [echopraxia], and making obscene gestures [copropraxia]).
- They may have a dystonic quality (oculogyric movements, sustained mouth opening, body posturing, torticollis)
- or have a tonic character (prolonged tensing of abdominal muscles, immobility, staring), labeled by some as blocking tics

- In approximately 4% to 5% of patients, self-injurious (“malignant”) tics can cause myelopathies, ocular damage, or body injuries.

- Simple vocal tics include various sounds and noises (grunts, barks, hoots, hollers, moans, groans, sniffs, and throat clearing)
- Complex vocalizations involve linguistically meaningful vocalizations and utterances; the repetition of words, syllables, or phrases; echolalia (repeating other people's words); palilalia (repeating one's own words); or coprolalia (obscene words or profanity). Although coprolalia is commonly associated with Tourette syndrome,
- Vocal alterations can also include pauses and hesitations in speech, word interjections, changes in tone/pitch, and prolongations of words.

- some vocalizations can be secondary to a nasal, pharyngeal, chest, or abdominal motor tic. For example, a rapid contraction of the chest or abdomen can lead to the expulsion of air and production of a simple vocalization

- uncommon tics have included anterior-posterior movements of the external ear, sign language tics, palatal movements, air swallowing, vomiting, and retching.

Characteristics

- including precipitating factors, a waxing and waning pattern, admixture of new and old tics, a premonitory urge that resolves when the tic is done, reduction when engrossed, and variable severity.
- They can range from infrequent and unnoticed to very frequent, intense, intrusive, and even self-injurious.
- Tics are exacerbated by stress, anxiety, excitement, anger, fatigue, elevated temperatures, or infections These conditions, however, do not account for more prolonged changes in tic severity
- Tics are reduced when the individual is concentrating on a physical or mental task or sleeping.
- Although most parents and patients report that tics do not occur while sleeping, polysomnograms have identified their presence in all phases of sleep

- About 90% of adults[13] and 37% of children[14] report a premonitory urge/sensation just before a motor or phonic tic. Vaguely defined as an urge, mounting tension, pressure, itch, or feeling, it is generally localized to the region of the tic and resolves when the tic is permitted to occur
- Tic disorders are more common in males than in females (ratio of 3:1 to 4:1) and usually begin between the ages of 4 and 8. Motor tics usually precede vocal tics
- maximum severity of tics tends to occur between 8 and 12 years of age
- that one-third of tics disappear, one-third improve, and one-third continue to fluctuate.

- Assumptions that adult tic severity can be predicted by childhood tic severity, childhood fine motor skills, and reduced childhood MRI caudate volumes require additional confirmation.
- symptom worsening has occurred in adults after prolonged periods of clinical remission
- Adult-onset tic disorders (formally, other specified tic disorder with onset after age 18 years) have been reported and often include severe symptoms, greater social morbidity, and poorer response to medications compared to childhood-onset tic disorders

- Neurologic examination and neuroimaging studies are typically normal.
- "Soft" neurologic findings may include coordination issues, synkinesis (involuntary muscular movements accompanying voluntary movements), and motor restlessness, especially in individuals with ADHD.

DIAGNOSIS

- The diagnosis of a tic disorder is based on historical features and observation of the tics; there is no definitive diagnostic laboratory test. Tics must be differentiated from drug-induced movements (akathisia, dystonia, parkinsonism), obsessivecompulsive behaviors, hyperactivity, antisocial behaviors, and stereotypies

- compulsions are complex activities that are performed to prevent or relieve anxiety, are executed in a rigid pattern, and may be done in response to an obsession
- Motor stereotypies typically have an earlier onset, fixed pattern, rhythmic quality, prolonged duration, and lack of a premonitory urge and stop abruptly with distraction
- repetitive sniffing, throat clearing, and coughing tics are often mistakenly attributed to allergies, sinusitis, or pulmonary issues; eye blinking tics are mistakenly thought to stem from ophthalmic problems; and ocular tics are confused with opsoclonus.

- Psychogenic disorders that present with ticlike movements can arise in childhood but are more common in adults; they are also more common in females than in males

(DSM-5)

u Provisional tic disorder designates an individual whose tics (motor or vocal) have been present for less than 1 year since first tic onset, and onset is before age 18 years. The disturbance cannot be attributable to the psychological effects of a substance or other medical conditions. For example, tics can result as a direct consequence of a variety of neurodegenerative disorders (eg, neuroacanthocytosis, Huntington disease, neurodegeneration with brain iron accumulation), neurocutaneous syndromes, and Creutzfeldt-Jakob disease.[3,28] Tics have also been reported in association with infections, Sydenham chorea, toxins (carbon monoxide), stroke, head and peripheral trauma, and surgery. Drugs reported to induce tics include cocaine, lamotrigine, and neuroleptics.[29] Significant data exist refuting the concept that stimulant medications are precipitating agents for tics.[30]

u Chronic motor or vocal tic disorder indicates the presence of either motor or vocal tics, but not both, for longer than 1 year, without regard for tic frequency. Onset is before 18 years of age, and tics cannot be attributed to the use of drugs or other medical condition. Note that multiple characteristics overlap in individuals with chronic motor tic disorder and individuals with Tourette syndrome.[31] u Tourette disorder is also called Tourette syndrome, and both have very similar formal criteria,[27,32] except that when originally proposed, the age of onset for Tourette syndrome was before 21 years of age as compared to before 18 years of age for Tourette disorder. Other criteria include the presence of multiple motor tics and at least one vocal tic, a waxing and waning course, a duration of longer than 1 year, and tics that are neither substance-induced nor due to a general medical condition.

EPIDEMIOLOGY

- Simple tics are relatively common in childhood being 6% to 12% (range of 4% to 24%)
- Tourette syndrome, which occurs worldwide with common features in all cultures and races, prevalence estimates have been variable, with estimates ranging from 0.3% to 1%.
- Mortality rates are reportedly higher in Tourette syndrome and chronic motor or vocal tic disorder, irrespective of the presence of comorbidities.

COMORBIDITIES

- Most individuals with Tourette syndrome (an estimated 86% to 90%) have at least one comorbid/coexisting neuropsychological problem.
- Coexisting neuropsychological issues add a significant additional burden to patients with Tourette syndrome or chronic motor or vocal tic disorder.
- In a study examining parent attribution of impairment in home activities, non–tic-related concerns were a greater problem.[48]

ADHD

- ADHD symptoms (inattentiveness, hyperactivity-impulsivity, or both) usually precede the onset of tics by 2 to 3 years. ADHD is reported to affec t about 50% of referred patients with Tourette syndrome.
- In patients with tics, the addition of ADHD symptoms correlates with increased deficits in the ability to plan, working memory, and inhibitory control and increased psychosocial and school difficulties, aggressiveness, disruptive behaviors, emotional problems, functional impairment, and learning disabilities.

OCD

- Obsessive-compulsive behaviors usually emerge during early adolescence, several years after the onset of tics, although an earlier age of onset has been suggested
- A lifetime comorbid diagnosis of OCD is present in about 50% of patients with Tourette syndrome
- In Tourette syndrome, obsessive-compulsive behaviors usually include a need for order or routine and a requirement for things to be symmetric or "just right." Hence, the execution of tics must occur in a particular fashion and sequence (eg, number of times, order, both sides of the body)

Anxiety and Mood Disorders

- the presence of generalized anxiety disorder in subjects with Tourette syndrome has ranged from 19% to 80%, with increased rates in children and youth with Tourette syndrome
- A high-risk period for anxiety issues begins at age 4, and a high-risk period for mood disorders begins at age 7
- The presence of depression in patients with Tourette syndrome has correlated positively with earlier onset and a longer duration of tics.

Disruptive Behaviors

- Episodic behavioral outbursts and anger control problems are reported in 25% to 70% of Tourette syndrome

- Other Neuropsychological Symptoms: Poor self-concept, reduced self-esteem, antisocial activities, oppositional behaviors, schizotypal traits, and personality disorders are more frequent in individuals with Tourette syndrome
- Sleep Disorders :difficulties falling and staying asleep, restlessness, arousals, and parasomnias, are common in Tourette syndrome

Possible Autoimmune Disorder

- several immune-mediated mechanisms, including microglial dysfunction, reduced numbers of regulatory T cells, altered gamma globulin, and an increased response to pathogens, have been proposed as potential contributing etiologic factors for tics.
- Tic symptoms have also been claimed to be associated with a preceding group A ß-hemolytic streptococcal infection, known as pediatric autoimmune neuropsychiatric disorders associated with streptococcal infections (PANDAS)

TREATMENT

- The establishment of an effective therapeutic plan requires the careful initial assessment of tics, determining the presence of co-occurring issues, and clarifying the resulting impairment of each issue. Further, it is essential to clarify whether tics or associated problems, such as ADHD, OCD, anxiety, school problems, or behavioral disorders, represent the greatest impairment.

The first step in treatment is education of the patient, his/her family, and the school or workplace about the diagnosis, its potential coexisting issues, and indications for therapy. Tics have no cure and fluctuate, and supportive care is often sufficient for many individuals with milder tics

- Specific criteria for initiating behavioral or pharmacologic tic-suppressing therapy include the presence of psychosocial problems (eg, loss of self-esteem; peer problems; difficulty participating in academic, work, family, social, and after-school activities), tic-induced musculoskeletal/physical difficulties, and disruption of classroom/work settings. The goal of treatment is to reduce tics to a degree at which they are no longer causing significant problems.

- **Nonpharmacologic Treatments**: habit reversal training should be the first-line intervention for tics.

- The treatment program now known as CBIT includes three major components: (1) awareness training to make the patient more aware of his/her tics and the premonitory urge, (2) competing response training to provide a substitutive behavior to perform as soon as the tic or urge appears, and (3) functional intervention (self-monitoring, relaxation training, and contingency management)

- CBIT has been shown to be beneficial in several large studies and is particularly appealing given its safety and lack of side effects. Recognizing a deficiency of trained therapists, the use of telemedicine and home-based parent-directed therapy are being assessed

- response prevention, another behavioral technique, asks the patient to experience the urge to tic while actively suppressing tics
- Many families and patients with tics have been attracted to the use of various complementary or alternative medicines, including numerous natural supplements . however, evidence regarding the efficacy or safety of complementary or alternative medicine treatments for tics is limited.
- Acupuncture, self-hypnosis, and plum blossom needle therapy also have very limited support

Pharmacotherapy

- In general, a two-tiered approach to the use of pharmacotherapy is recommended for treating tics with use of tier 1 medications for milder tics and use of tier 2 medications reserved for more difficult to control symptoms
- Therapeutic agents should initially be prescribed at their lowest effective dosage and gradually increased as needed. Patients should be carefully followed and have periodic evaluations assessing medication efficacy, side effects, and the requirement for continued therapy
- Recognizing that treatment is symptomatic, if tics remain under good control for a significant period, a gradual taper of the medication during a nonstressful time should be considered

TIER 1 MEDICATIONS

- tier 1 medications are less effective in suppressing tics but have fewer and generally less significant side effects. Medications in this category typically include clonidine, guanfacine, topiramate, clonazepam, and baclofen.
- two α-adrenergic agonists (clonidine and guanfacine)
- The efficacy of anticonvulsants is varied
- Clonazepam is often prescribed for tics
- Baclofen, a GABA-B receptor agonist ; variably effective

TIER 2 MEDICATIONS

- are more effective in suppressing tics than tier 1 medications but are associated with more significant side effects that frequently limit their usefulness.
- the dopamine receptor antagonists (typical and atypical antipsychotics)
- the vesicular monoamine transporter-2 inhibitors.

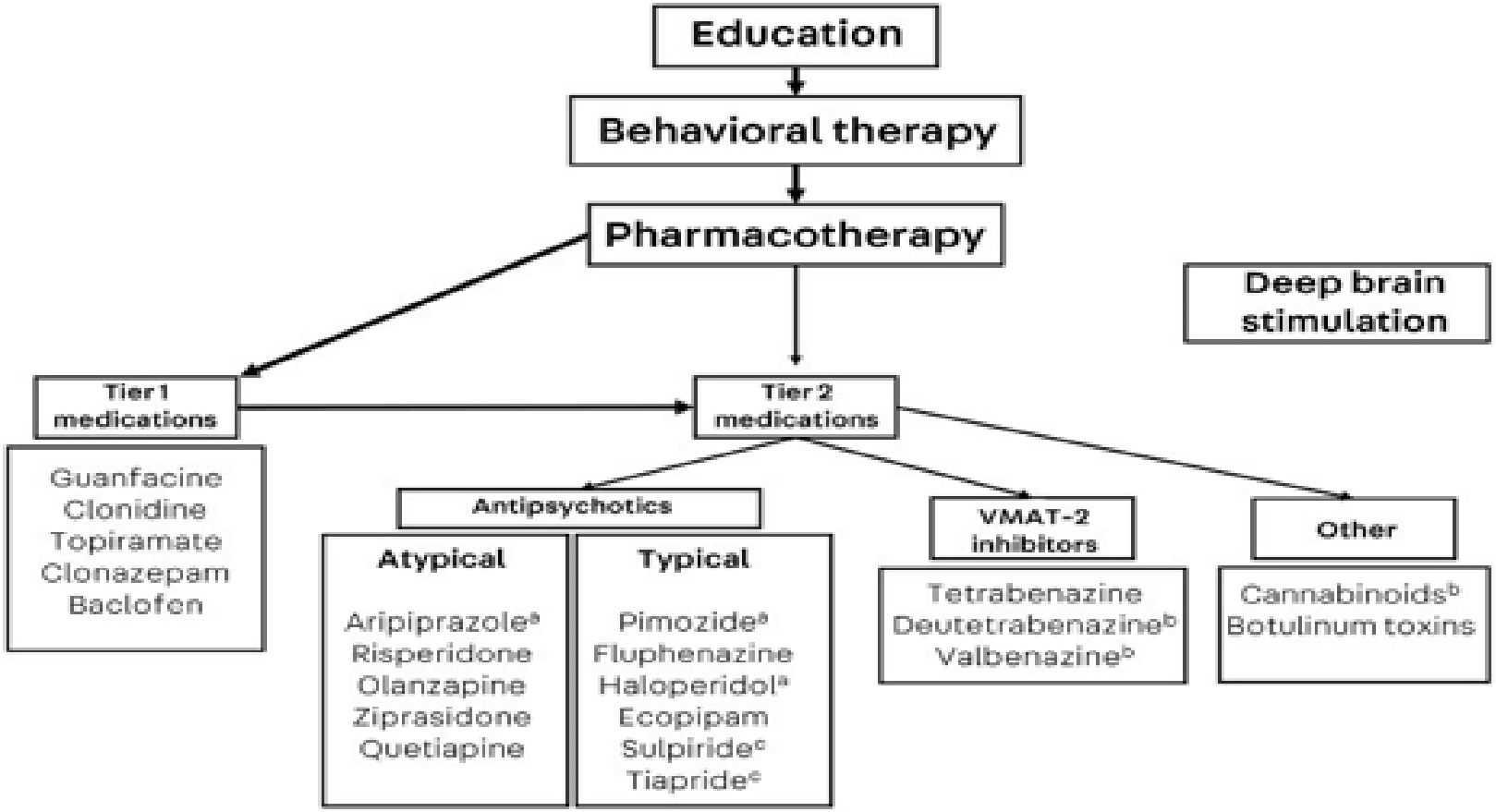


FIGURE 3-2

Approaches to the treatment of tics.

VMAT-2 = vesicular monoamine transporter-2.

[a] Approved by the US Food and Drug Administration for the treatment of tics.

[b] Medications are under investigation. [c] Medications are not available in the United states.

cannabinoids

- Several small studies and case reports have suggested that cannabinoids may have a beneficial effect on tics in patients with Tourette syndrome
- Pharmacologic approaches have included smoking marijuana or using extracts from the cannabis plant, including Δ-9-tetrahydrocannibinol (THC), cannabidiol, and nabiximols (combinations of THC and cannabidiol). The most common side effects are sedation, dizziness, headaches, a “high” (euphoria feeling), red eyes, increased appetite, psychosis, depression, and cognitive impairment
- Several reviews, however, have emphasized the lack of evidence with regard to the use of cannabinoids and the requirement for additional testing.

Botulinum toxin

- has a beneficial chemodenervation effect on severe localized tics (eg, violent head thrusts), dystonic motor tics, and vocal tics and reduces the premonitory sensory component

Brain Stimulation

- brief repetitive intense magnetic fields generated by a coil placed over the scalp to produce an electromagnetic field in the underlying brain region. Several small trials in Tourette syndrome using low-frequency inhibiting repetitive transcranial magnetic stimulation (1 Hz) suggest that it can have a beneficial effect, especially if the supplementary motor area is targeted.

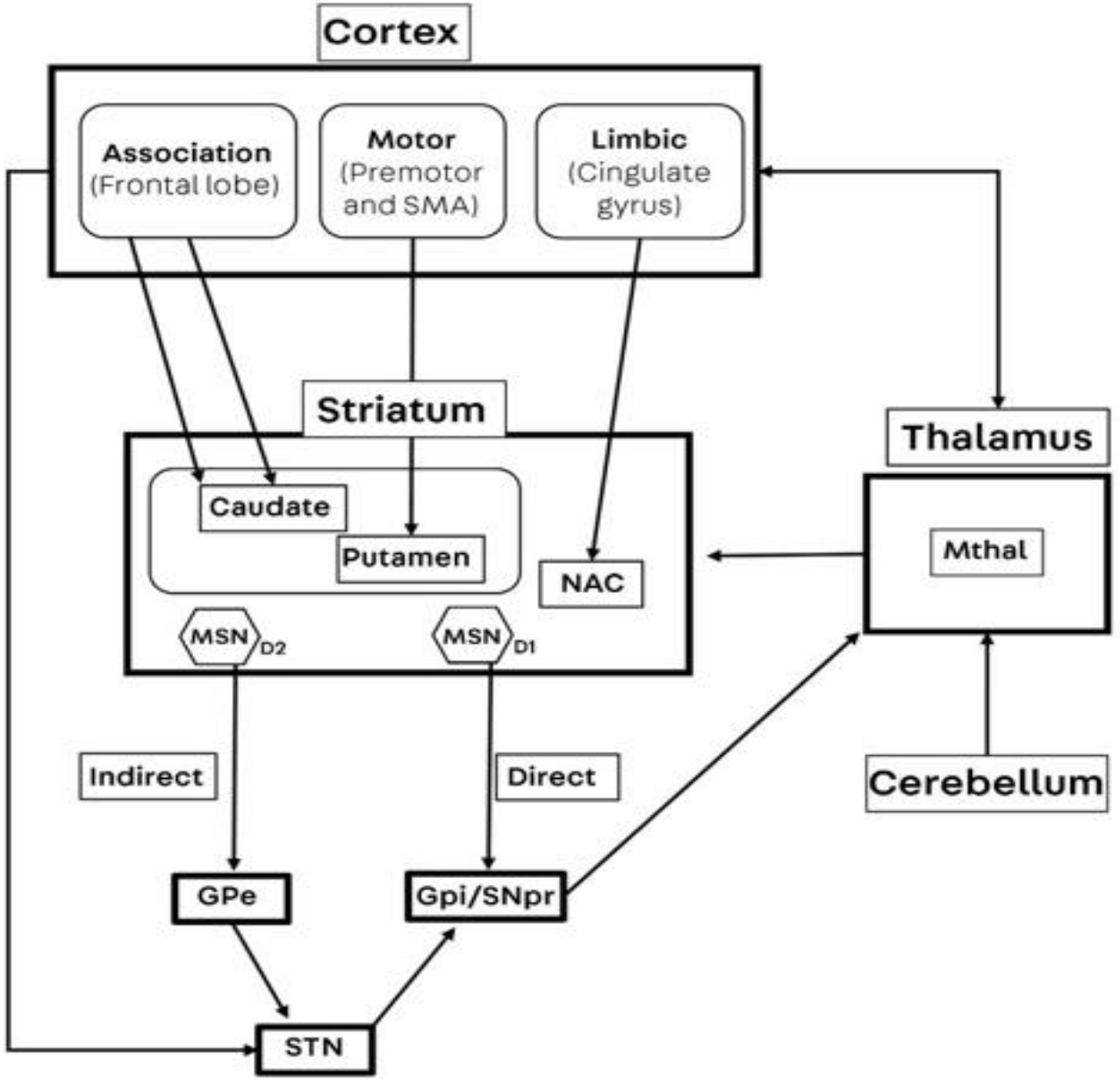
- Deep brain stimulation is a stereotactic treatment that has significant potential for the treatment of tics. The centromedian parafascicular complex of the thalamus and anteromedial globus pallidus internus have been the most commonly stimulated sites, but the optimal target has yet to be determined.

Suggested criteria for the use of deep brain stimulation in patients with tics include the following:

- Disabling tics with a Yale Global Tic Severity Scale score of more than 35/50
- Failed behavioral therapy (CBIT)
- Failed medication trials from pharmacologic groups including α-adrenergic agonists (guanfacine, clonidine) and dopamine antagonists (including one typical and one atypical antipsychotic), plus one additional category (vesicular monoamine transporter-2 inhibitors)
- Evaluation by a multidisciplinary team (eg, neurologist, neurosurgeon, psychiatrist, neuropsychologist, deep brain stimulation programmer)

Treated and stable comorbid conditions[110]

Thank you


Cortex
Association
(Frontal lobe)
Motor
(Premotor
and SMA)
Limbic
(Cingulate
gyrus)
Striatum
Caudate
Putamen
NAC
MSN D2
MSN D1
Thalamus
Mthal
Indirect
Direct
Cerebellum
GPe
Gpi/SNpr
STN