Tourette Syndrome and Attention Deficit Disorders: A Pharmacological Approach

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Tourette Syndrome - definition

- A neurological disorder manifested by motor and phonic tics with onset during childhood
Tourette Syndrome DSM-IV Criteria

- Both multiple motor and one or more vocal tics have been present at some time during the illness, although not necessarily concurrently
- The tics occur many times a day (usually in bouts) nearly every day or intermittently throughout a period of more than 1 year, and during this period there was never a tic-free period of more than 3 consecutive months
- The onset is before age 18
- The disturbance is not due to the direct physiological effects of a substance (e.g. stimulants) or a general medical condition (e.g. Huntington’s disease or post-viral encephalitis)

Characteristics of Tics

- Stereotyped, repetitive movements or sounds
- Premonitory feelings or sensations
- Partial voluntary suppression
- Suggestibility
- Usually increase with stress and/or relaxation
- Often decrease with distraction and concentration

Motor Tics

- Simple - fast, darting, “meaningless”
  - Eye blinking, grimacing, jaw snapping, shoulder shrugging
- Complex - slower, “purposeful”
  - Hopping, clapping, jumping, kissing, cursing by gesture (copropraxia)
Verbal Tics

- Simple - fast, darting, “meaningless”
  - Coughing, grunting, sniffing, animal noises

- Complex - slower, “purposeful”
  - Linguistically meaningful words or phrases, cursing (coprolalia), repetition (echolalia)

Neurobiology of Tourette Syndrome

Role of the Basal Ganglia in Tourette Syndrome

- Normally, basal ganglia provides mechanism for desired motor pattern to proceed (selective facilitation) while inhibiting interference by competing motor patterns (surround inhibition)

- In TS, increased areas of excitability within basal ganglia (excessive facilitation) with normal surround inhibition leading to exaggerated activity or spread to other body parts
Pathophysiology of Tourette Syndrome: Current Understanding

Genetic predisposition coupled with external factors

Impairment of normal programmed cell death (developmental apoptosis)?

DA hyperinnervation and/or increased DA transmission in striatum and limbic system

Impaired cortico-striatal-thalamic loop

Tics, ADHD, OCD

Tourette Syndrome Co-Morbidities

- ADHD - 60-75%
- Obsessive-Compulsive mannerisms - 50-60%
  - 20-30% meet full DSM IV diagnosis for OCD
- Other anxiety disorders
  - Separation anxiety, panic attacks, generalized anxiety disorder
- Mood disorders, emotional lability, aggression, rage attacks
- Learning disabilities
- Sleep disorders (night terrors)
- Migraine

PANDAS

- Pediatric Autoimmune Neuropsychiatric Disorders Associated with Streptococcal Infections
- Explosive onset of tic disorder and/or OCD with exacerbations and remissions in childhood
- Temporal association with Group A β-hemolytic strep (GABHS) infection
- Presence of neurologic abnormalities including choreaform movements, hyperactivity
- Psychiatric co-morbidity including emotional lability, separation anxiety

**Treatment of TS-Tic Suppression**

- **Tier 1 medications**: Clonidine (Catapres), Guanficine (Tenex), Clonazepam (Klonopin, et al), Gabapentin (Neurontin), Toparimate (Topamax), Levetiracetam (Keppra)

- **Tier 2 Medications**: Pimozide (Orap), Fluphenazine (Prolixin), Risperidone (Risperdal), Olanzapine (Zyprexa), Haloperidol (Haldol), Aripiprazole (Abilify), Quetiapine (Seroquel), Trifluoperazine (Stelazine), Pergolide (Permax), Donepezil (Aricept), Botulinum Toxic, Nicotine patch, Delta 9-tetra hydrocannabinol

**Treatment of TS-OCD**

- Fluoxetine (Prozac)
- Sertraline (Zoloft)
- Paroxetine (Paxil)
- Fluvoxamine (Luvox)
- Clomipramine (Anafranil)

**Attention Deficit Disorders-DSM IV Criteria**

**INATTENTION**

(need 6 of 9)

- often fails to give close attention to details or makes careless mistakes in schoolwork, work or other activities
- often has difficulty sustaining attention in tasks or play activities
- often does not seem to listen when spoken to directly
- often does not follow through on instructions and fails to finish schoolwork, chores, or duties in the workplace (no if oppositional behavior or doesn’t understand instructions)
- often has difficulty organizing tasks and activities
- often avoids, dislikes, or is reluctant to engage in tasks or activities that require sustained mental effort (such as schoolwork or homework)
- often loses things necessary for tasks or activities (e.g., toys, school assignments, pencils, books, or tools)
- often easily distracted by extraneous stimuli
- often forgetful in daily activities
Attention Deficit Disorders - DSM-IV Criteria

HyPERACTIVITY-IMPULSIVITY (need 6 of 9):
- often fidgets with hands or feet or squirms in seat
- often leaves seat in classroom or in other situations in which remaining seated is expected
- often runs about or climbs excessively in situations in which it is inappropriate (in adolescents or adults, may be limited to subjective feelings of restlessness)
- often has difficulty playing or engaging in leisure activities quietly
- is often "on the go" or often acts as if "driven by a motor"
- often talks excessively
- often blurts out answers before questions have been completed
- often has difficulty awaiting turn
- often interrupts or intrudes on others (e.g., butts into conversations or games)

Attention Deficit Disorders - DSM-IV Criteria

- Present at least 6 months, maladaptive and inconsistent with development level
- Some symptoms that caused impairment were present before age 7
- Some impairment from the symptoms is present in two or more settings (e.g., at school (or work) and at home)
- There must be clear evidence of clinically significant impairment in social, academic or occupational functioning

Attention Deficit Disorders - Types

- Attention-Deficit-Hyperactivity Disorder, Combined Type
- Attention-Deficit-Hyperactivity Disorder, Predominantly Inattentive Type
- Attention-Deficit-Hyperactivity Disorder, Predominantly Hyperactive –Impulsive Type
Treatment of TS-ADHD

- **Common Medications**: Methylphenidate (Ritalin, Concerta, et al), Dextroamphetamine (Dexedrine), Clonidine (Catapres), Atomoxetine (Strattera)

- **Other Medications**: Guanficine (Tenex), Depramine, Nortriptyline (Pamelor, Aventyl), Imipramine (Antideprin, Deprimin, et al), Brupropion (Wellbutrin, et al), Deprenyl

Tics and Stimulant Medication

- Early reports suggested that stimulant medication were associated with potential to provoke or intensify tics and that tics might persist even when medication was withdrawn Barkley (1990), Borchering (1990) and Pollack (1977)

- Other investigators countered that patients did not have significant worsening of tics Law and Nolan (1999) Palumbo (2004)

- Some have postulated that tic exacerbations occur only with starting doses or higher doses

- Some have postulated methylphenidate better than dextroamphetamine

Tics and Stimulant Medication - Summary

- There is significant evidence that stimulants are beneficial for attention deficit disorder symptoms in children with a tic disorders

- Methylphenidate therapy does not induce or exacerbate tics

- Atomoxetine, Clonidine and Guanficine are alternatives
Tourette Syndrome - A Pharmacological Approach

- Identify the symptom that needs treatment
- Explore non-pharmacological approaches
- If there is more than one symptom that needs to be treated, usually better to use monotherapy
- If two or more drugs need to be used, must be aware of cumulative side effects and interactions