#CHAIR2019

11TH ANNUAL

# CHAIR SUMMIT

CME Outfitters

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CME Outfitters

# Tardive Dyskinesia

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# Learning Objectives

Accurately diagnose tardive dyskinesia based on diagnostic criteria and assessment tools.

Apply guideline-based treatment of tardive dyskinesia.

# *DSM-5* Definition of Tardive Dyskinesia (TD)

*"Involuntary athetoid or choreiform movements lasting at least a few weeks, developing in association with the use of a neuroleptic medication for at least a few months, and persisting beyond 4-8 weeks"*

DSM-5 Diagnostic Classification. In: American Psychiatric Association. (2013). *Diagnostic and statistical manual of mental disorders* (5th ed.). Arlington, VA: American Psychiatric Publishing.

# *DSM-5* Definition of TD

*Medication-induced movement disorder, caused by dopamine receptor blocking drugs, that starts after a few months of medication use (or less in an older patient) and persists at least one month after medication change or discontinuation*

DSM-5 Diagnostic Classification. In: American Psychiatric Association. (2013). *Diagnostic and statistical manual of mental disorders* (5th ed.). Arlington, VA: American Psychiatric Publishing.

# Implications of *DSM-5* Definition of TD

DELAYED IN ONSET

PERSISTENT but REVERSIBLE

*or*

PERSISTENT and IRREVERSIBLE

# Tardive Syndromes

## Oro-bucco-lingual dyskinesia

- Classic oro-bucco-lingual dyskinesia
- Tardive dyskinesia

## Tardive dystonia

## Tardive akathisia

## Tardive tics

- Tardive tourettism

Tardive tremor
Tardive myoclonus
Tardive parkinsonism

Savitt T, Jankovic J. *J Neurol Sci*. 2018;389:35-42.

# Classic (Tardive) Oro-Bucco-Lingual Dyskinesia

**INDUCED BY EXPOSURE TO DOPAMINE-BLOCKING DRUGS**

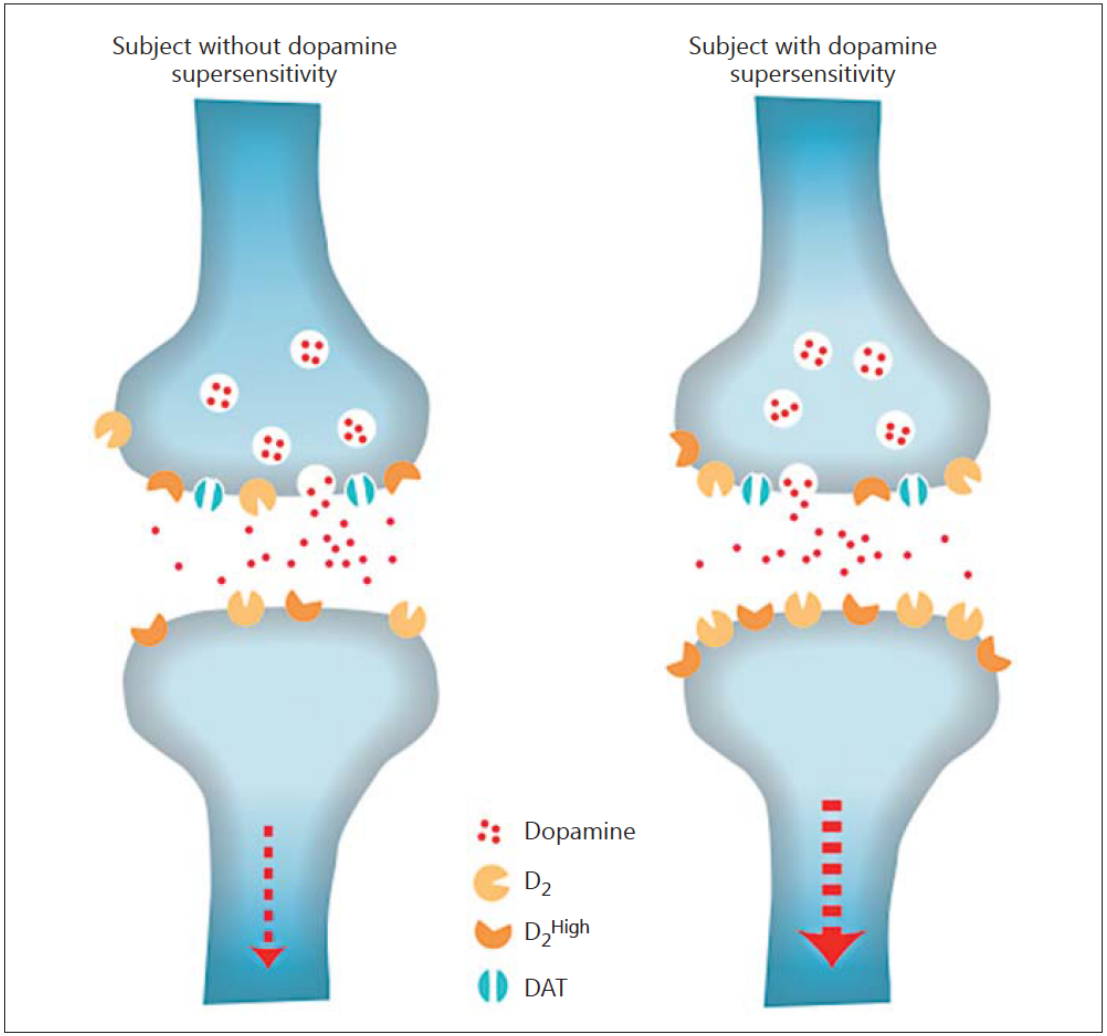
| | |
|---|---|
| Anatomical sites involved | Stereotypical appearance |
| “Late” appearance | Persistence – *for a while*<br>Persistence – *for good* |

# TD: Neuroleptics

- First-generation antipsychotics (FGAs)
  - Prevalence of TD at 5 years: 32%
    at 15 years: 57%
    at 25 years: 68%
  - Annual incidence of TD: 7.7%
- Second-generation antipsychotics (SGAs)
  - Prevalence of TD at 5 years: 13%
  - Annual incidence of TD: 2.9%
- Metoclopramide
  - Approved for use up to 12 weeks
  - Risk for TD <1%

Glazer WM, et al. *J Clin Psychiatry*. 1993;54:133-139. Correll CU, Schenk EM. *Curr Opin Psychiatry*. 2008;21(2):151-156. Rao AS, Camilleri M. *Aliment Pharmacol Ther*. 2010;31:11-19. US Food and Drug Administration. https://www.accessdata.fda.gov/drugsatfda_docs/label/2011/017854s058lbl.pdf.

# Mechanism of TD




Chouinard G, et al. *Psychother Psychosom*. 2017;86:189-219.

# TD: Risk Factors

- Dose of antipsychotic drug
- Length of exposure to antipsychotic drug
- Concomitant use of anticholinergics
- **AGE**
- Female gender
- African-American ancestry
- Presence of mood disorder
- Presence of dementia
- Prior history of acute extrapyramidal syndrome

Solmi M, et al. *J Neurol Sci*. 2018;389:21-27.

# TD: Genetics

- Pharmacokinetics
  - CYP2D6, VMAT2, SOD2, HSPG2
- Pharmacodynamics
  - DRD2, DRD3, 5HTRA, 5HTRC
- Examples:
  - rs363224 polymorphism of the VMAT2 gene has been associated with TD
  - rs1799732 polymorphism of the DRD2 gene has been associated with TD in a study sample of European ancestry

Zai CC, et al. J Neurol Sci. 2018;389:28-34.

# Abnormal Involuntary Movement Scale (AIMS)

- Includes an examination procedure
- Developed by NIMH and in the public domain
- The exam can usually be done in 10 minutes or less

NIMH = National Institute of Mental Health.

# AIMS

**ABNORMAL INVOLUNTARY MOVEMENT SCALE (AIMS)**

Public Health Service
Alcohol, Drug Abuse, and Mental Health Administration
National Institute of Mental Health

**NAME:**_____
**DATE:** _____
**Prescribing Practitioner:** _____

**CODE:** 0 = None
1 = Minimal, may be extreme normal
2 = Mild
3 = Moderate
4 - Severe

**INSTRUCTIONS:**
**Complete Examination Procedure (attachment d.) before making ratings**

| **MOVEMENT RATINGS:** Rate highest severity observed. Rate movements that occur upon activation one less than those observed spontaneously. Circle movement as well as code number that applies. | | RATER Date | RATER Date | RATER Date | RATER Date |
|---|---|---|---|---|---|
| Facial and Oral Movements | **1. Muscles of Facial Expression** e.g. movements of forehead, eyebrows periorbital area, cheeks, including frowning blinking, smiling, grimacing | 0 1 2 3 4 | 0 1 2 3 4 | 0 1 2 3 4 | 0 1 2 3 4 |
| | **2. Lips and Perioral Area** e.g., puckering, pouting, smacking | 0 1 2 3 4 | 0 1 2 3 4 | 0 1 2 3 4 | 0 1 2 3 4 |
| | **3. Jaw** e.g. biting, clenching, chewing, mouth opening, lateral movement | 0 1 2 3 4 | 0 1 2 3 4 | 0 1 2 3 4 | 0 1 2 3 4 |
| | **4. Tongue** Rate only increases in movement both in and out of mouth. NOT inability to sustain movement. Darting in and out of mouth. | 0 1 2 3 4 | 0 1 2 3 4 | 0 1 2 3 4 | O 1 2 3 4 |
| **Extremity Movements** | **5. Upper (arms, wrists,, hands, fingers)** Include choreic movements (i.e., rapid, objectively purposeless, irregular, spontaneous) athetoid movements (i.e., slow, irregular, complex, serpentine). DO NOT INCLUDE TREMOR (i.e., repetitive, regular, rhythmic) | 0 1 2 3 4 | 0 1 2 3 4 | 0 1 2 3 4 | 0 1 2 3 4 |
| | **6. Lower (legs, knees, ankles, toes)** e.g., lateral knee movement, foot tapping, heel dropping, foot squirming, inversion and eversion of foot. | 0 1 2 3 4 | 0 1 2 3 4 | 0 1 2 3 4 | 0 1 2 3 4 |
| **Trunk Movements** | **7. Neck, shoulders, hips** e.g., rocking, twisting, squirming, pelvic gyrations | 0 1 2 3 4 | 0 1 2 3 4 | 0 1 2 3 4 | 0 1 2 3 4 |

# AIMS (Continued)

| | | | | | |
|---|---|---|---|---|---|
| **Global Judgments** | **8. Severity of abnormal movements overall** | 0 1 2 3 4 | 0 1 2 3 4 | 0 1 2 3 4 | 0 1 2 3 4 |
| | **9. Incapacitation due to abnormal movements** | 0 1 2 3 4 | 0 1 2 3 4 | 0 1 2 3 4 | 0 1 2 3 4 |
| | **10. Patient's awareness of abnormal movements.** Rate only patient's report<br>No awareness 0<br>Aware, no distress 1<br>Aware, mild distress 2<br>Aware, moderate distress 3<br>Aware, severe distress 4 | 0<br>1<br>2<br>3<br>4 | 0<br>1<br>2<br>3<br>4 | 0<br>1<br>2<br>3<br>4 | 0<br>1<br>2<br>3<br>4 |
| **Dental Status** | **11. Current problems with teeth and/or dentures** | No Yes | No Yes | No Yes | No Yes |
| | **12. Are dentures usually worn?** | No Yes | No Yes | No Yes | No Yes |
| | **13. Edentia?** | No Yes | No Yes | No Yes | No Yes |
| | **14. Do movements disappear in sleep?** | No Yes | No Yes | No Yes | No Yes |

This scale is available in the public domain and has not been modified. Final 9/2000.

# TD: Differential Diagnosis

- Huntington's disease
- Wilson's disease
- Neuroacanthocytosis
- Prion diseases
- Neurodegeneration with brain
- Sydenham chorea antiphospholipid antibody syndrome
- Systemic lupus erythematosus
- Anti-*N*-methyl-D-aspartate receptor
- Oher autoimmune diseases

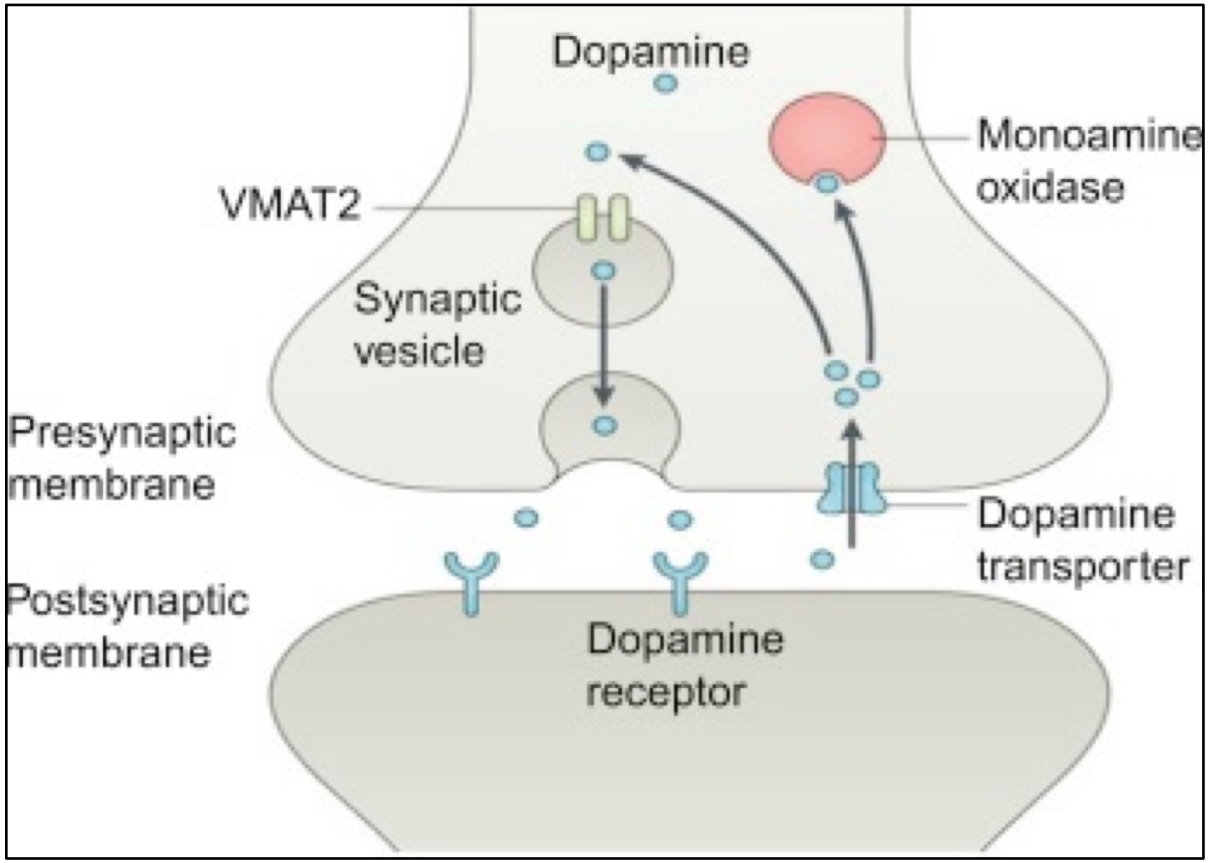
Waln O, Jankovic J. *Tremor Other Hyperkinet Mov (N Y)*. 2013;3. pii: tre-03-161-4138-1.

# TD: Treatment

- Insufficient evidence for withdrawal of dopamine receptor blocking agents
- Insufficient evidence for switching from first generation antipsychotics to second generation antipsychotics

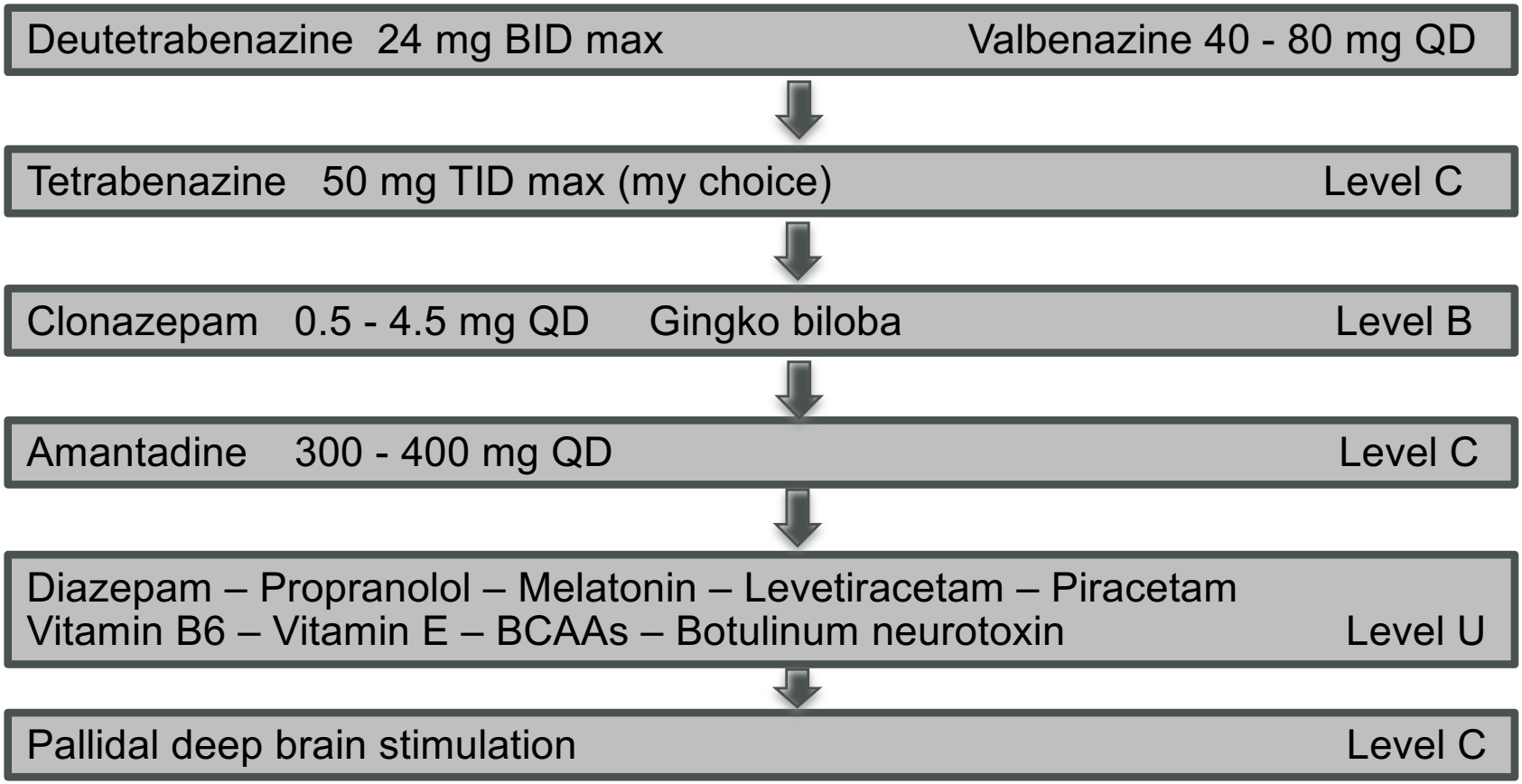
Bhidayasiri R, et al. *J Neurol Sci*. 2018;389:67-75.

# Mechanism of Action of VMAT2 Inhibitors




Jankovic J. *Nat Rev Neurol*. 2017;13:76-78.

# TD: Treatment




BCAAs = branched-chain amino acids.

Bhidayasiri, et al. 2013;81(5):463-469. Bhidayasiri, et al. *J Neurol Sci*. 2018;389:67-75.

# Conclusions

- The term TD may denote tardive syndromes in general or may denote only one of the tardive syndromes (the classic oro-bucco-lingual dyskinesia)
- Exposure to dopamine receptor blocking agents (DRBAs) is usually at least 3 months; TD persists after discontinuation of the DBRAs, sometimes for only a while, sometimes forever
- The classic oro-bucco-lingual dyskinesia may include involvement of trunk and limbs (especially hands and feet)
- The pathogenesis of TD is still viewed as the result of induction of dopamine receptor supersensitivity
- The advent of VMAT2 inhibitors has brought about a significant change for the better in the treatment of TD

# SMART Goals

## **S**pecific, **M**easurable, **A**ttainable, **R**elevant, **T**imel

- Assess the signs and symptoms of TD in patients treated with antipsychotic medications
- Determine appropriate evidence-based treatment of TD

# Questions & Answers

Don’t forget to fill out your evaluations to collect your credit.