

Movement Disorders Induced by Dopamine Blocking Agents

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Disclosures

- Accordia Pharma
- Amneal Pharma
- Kyowa Kirin Pharma
- Neurocrine Pharma
- Teva Pharma
- Supernus Pharma

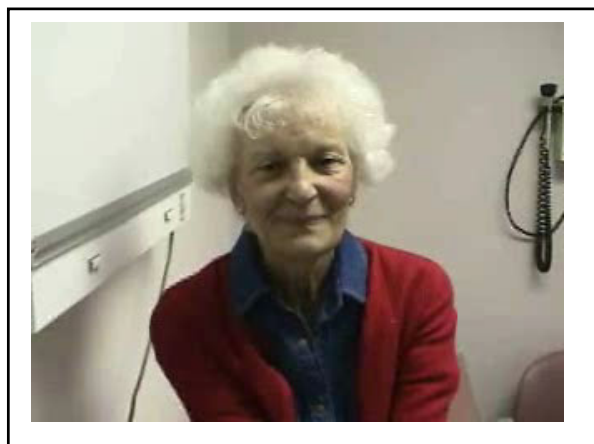


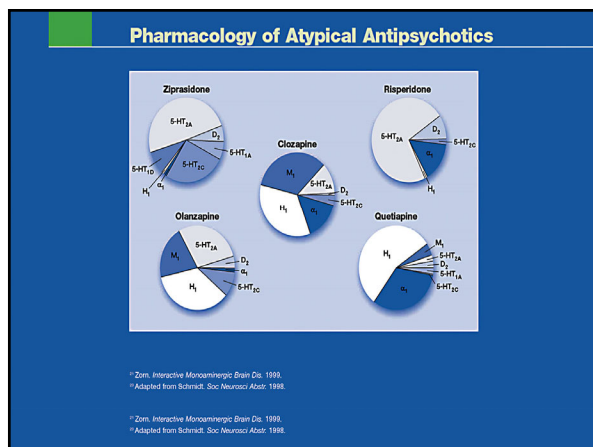




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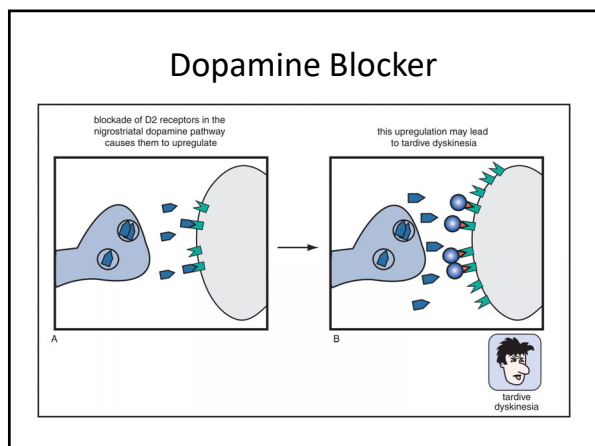
- Chlorpromazine introduced in France in 1952 (Delay and Deniker)
- Soon afterwards, it was recognized that in addition to sedation these drugs were associated with other side effects
- Schonecker described abnormal neck movements (Tardive Dystonia)
- Uherbrand and Forbye described classic orobuccolingual dyskinesia





Relative Frequency of Dopamine blocking agents Induced Movement Disorders

- Classic TD from 1st gen D2 blockers • 30%
- Classic TD from 2nd gen D2 Blockers • 13%
- Drug induced parkinsonism • 30%



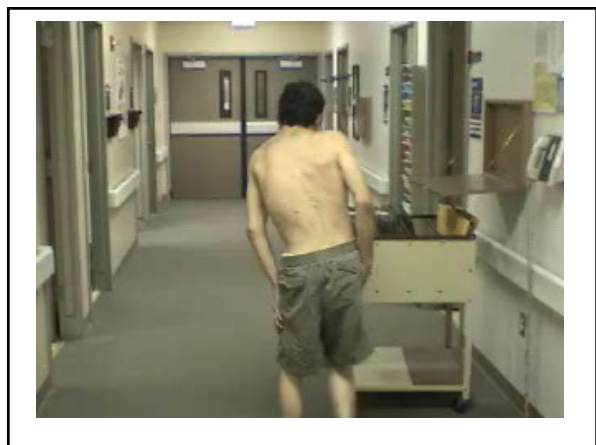
Relative Frequency of Tardive Dyskinesia phenomenology

• Tardive Chorea	• 70%
• Tardive Dystonia	• 30%
• Tardive Akathesia	• 15%
• Tardive tics	• 1%

Relative Location of Tardive Dyskinesia phenomenology

• Oral/facial	• 70%
• Upper extremity	• 65%
• Lower extremity	• 60%
• Trunk	• 50%





Pisa Syndrome



Tardive Dystonia Retrocollis





Tardive Akathesia



Severe Tardive Dyskinesia



Severe Tardive Dyskinesia



Which patients are at increased risk factors for TD?

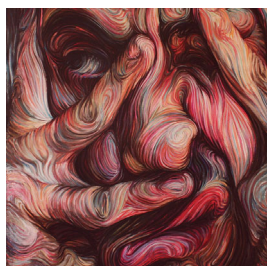
- Cumulative exposure to antipsychotics
- Treatment with anticholinergics
- Potency of DBA
- History of "EPS"
- Increased age
- Postmenopausal women
- Current substance abuse
- Diagnosis of mood disorder

Withdrawal -Emergent Syndrome

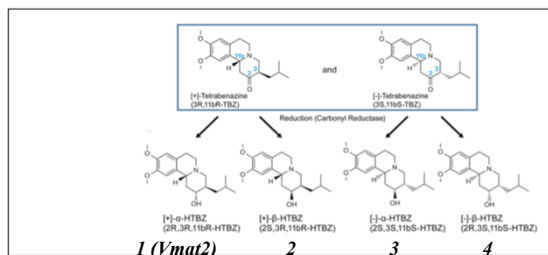
- The movements appear upon discontinuation of the DBA and last up-to 3 months
- More frequent in children
- The movements often choreic involve the limbs, neck, trunk primarily and seldom the lower facial region
- Another term is covert dyskinesia

Withdrawal emergent dyskinesia is real

- Communication with PCP and psychiatry
- Patient education
- Reasonable patient expectation



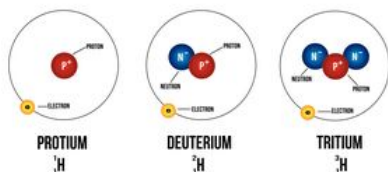
Tetrabenazine



Source: Skor et al., 2017

What is deuterium?

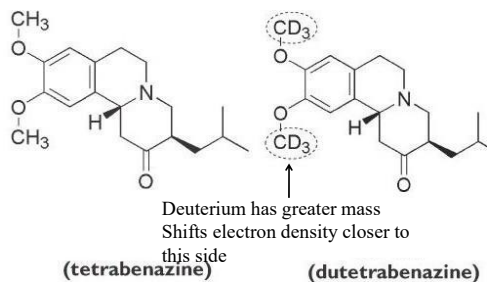
THE THREE ISOTOPES OF HYDROGEN



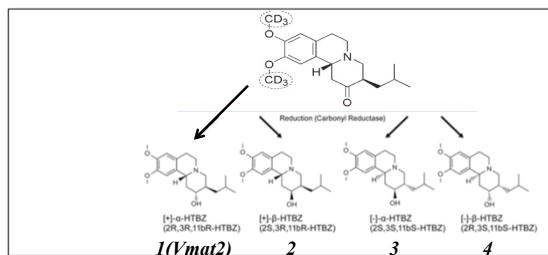
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One in every 6420 hydrogen atoms in the universe is a deuterium atom.

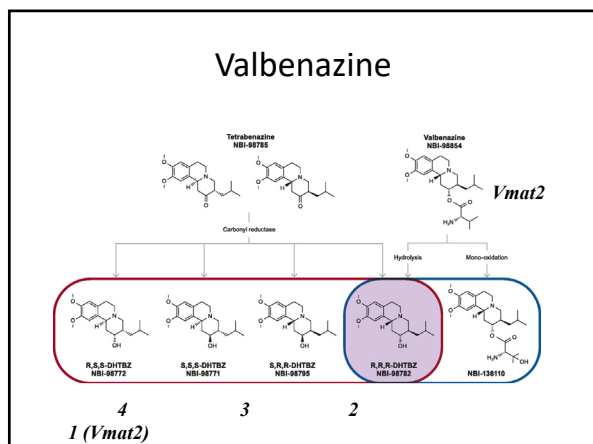
Deuterated Tetrabenazine



Deuterated Tetrabenazine



Valbenazine



1 (Vmat2)

Drug Induced Parkinsonism

- 20-40% of patients treated with dopamine blocking agents
- Often subacute in onset and may resolve even with continuing use of the offending drugs
- More common and severe in older individuals
- May be tremor predominant or akinesia may overshadow other features
- Often asymmetrical

Parkinsonism



TD vs PD

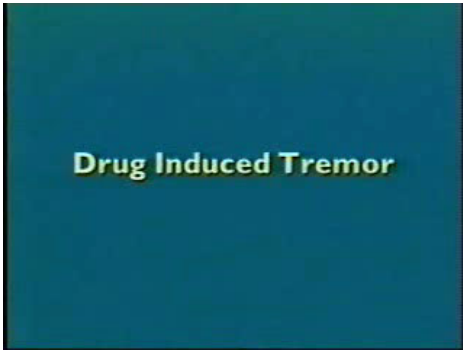


- The Washout time frame for drug induced parkinsonism is 6-12 months after stopping dopamine blockade.

What about anticholinergics and “EPS”?



What about Depakote?



DBA Induced Movement Disorders

- Prevention is the most important
- Patients on neuroleptics should be kept on the lowest dosages possible and regularly evaluated for the continuing need for the DBA
- Atypical agents should be used where possible

Questions?