Paroxysmal NonKinesigenic Dyskinesia (PNKD)

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Symptoms
- Spontaneous attacks of involuntary, jerking or ballistic movements
- 4 minutes - 4 hours
- Initiated by stress, alcohol, and caffeine.
- Patient with PNKD

Cause
- Autosomal dominant disorder
- Single amino acid mutations in the PNKD gene (of unknown function)
- Dyskinesias are likely caused by dominance of the Direct Pathway
- Caffeine antagonizes adenosine receptors
- A2a receptor only on Indirect Pathway

Circuit Mechanism
- Caffeine shuts down iMSNs
- A2a blockade enhances Indirect Pathway LTD in PNKD model
  - Reduced mini frequency
  - Cannot induce LTD in slice (because it has already occurred)
- ↓Indirect Pathway : ↑Direct Pathway

Goldberg, 2014

Kreitzer, 2014
Treatment

- Clonazepam - benzodiazepine
  - GABA agonist
  - Increases the opening frequency of C3 channel
- Avoiding stress, alcohol, and caffeine
- Potential future treatment: CB1 antagonist
  - Prevents attacks by blocking LTD at indirect pathway corticostriatal synapses

References