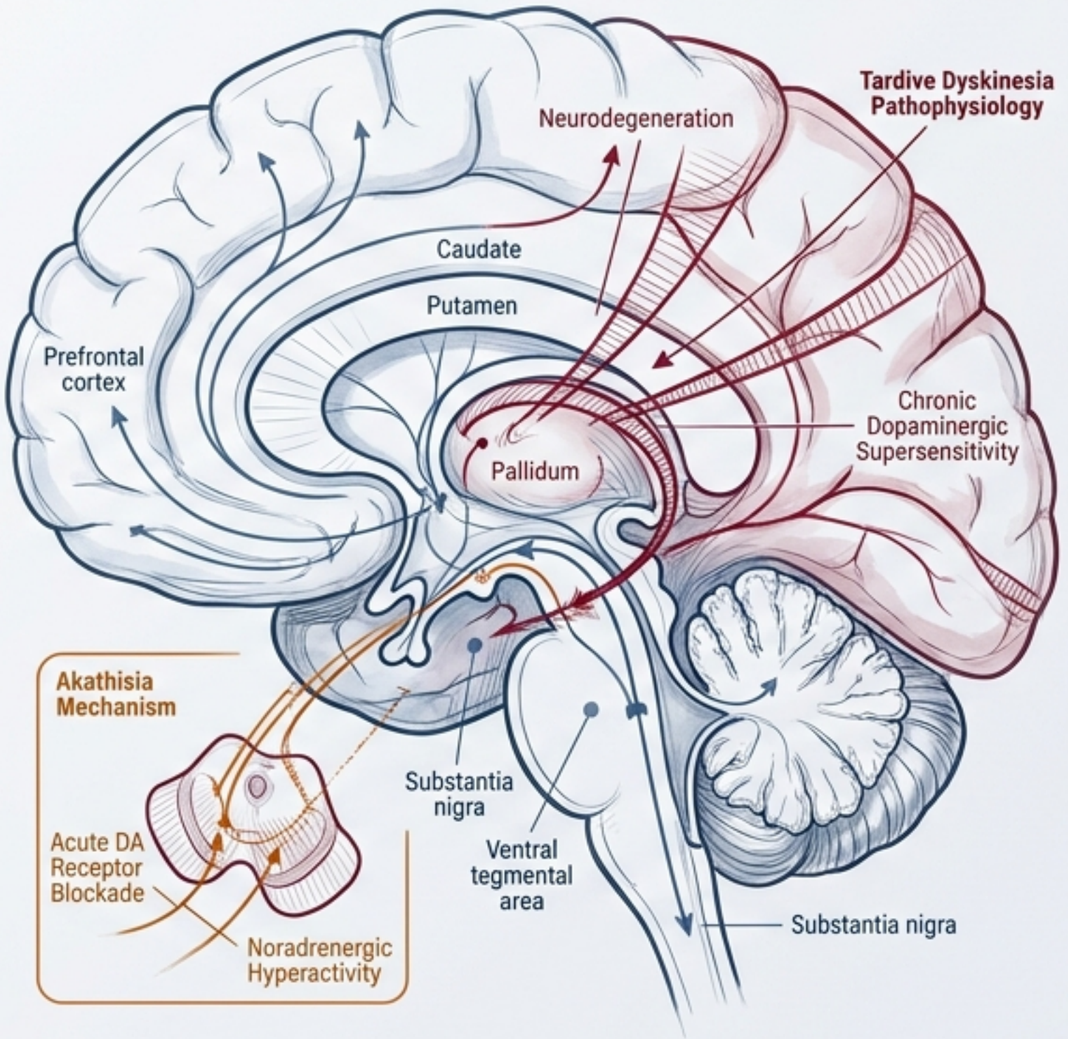
ANTIPSYCHOTIC MOVEMENT DISORDERS

Akathisia and Tardive Dyskinesia: Pathophysiology, Assessment, and Management

EXECUTIVE SUMMARY

- **High Morbidity:** Movement disorders remain a primary driver of distress and medication non-compliance.
- **Distinct Mechanisms:** Acute dopaminergic imbalance (Akathisia) vs. chronic neuroadaptation and degeneration (Tardive Dyskinesia).
- **Divergent Treatments:** Symptom modulators for acute restlessness vs. VMAT2 inhibition for established structural changes.



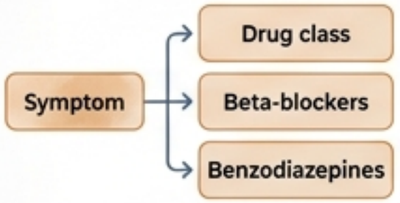
AKATHISIA
(Without Sitting)

Onset:
Acute (Days to Weeks).

Core Pathology:
Subjective inner restlessness paired with objective fidgeting.

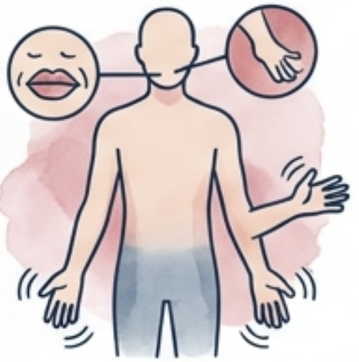
Clinical Impact:
High dysphoria, severe psychological distress, elevated suicide risk.

Primary Resolution:
Symptom modulators (Beta-blockers, Benzodiazepines).



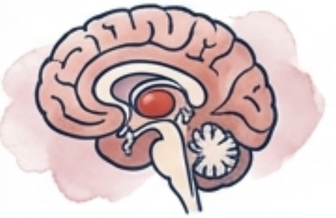
TARDIVE DYSKINESIA
(Delayed Abnormal Movement)

Onset:
Delayed (Months to Years).

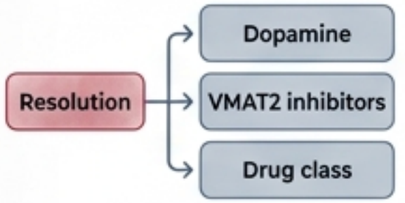


Core Pathology:
Involuntary choreiform, athetoid, or rhythmic movements.

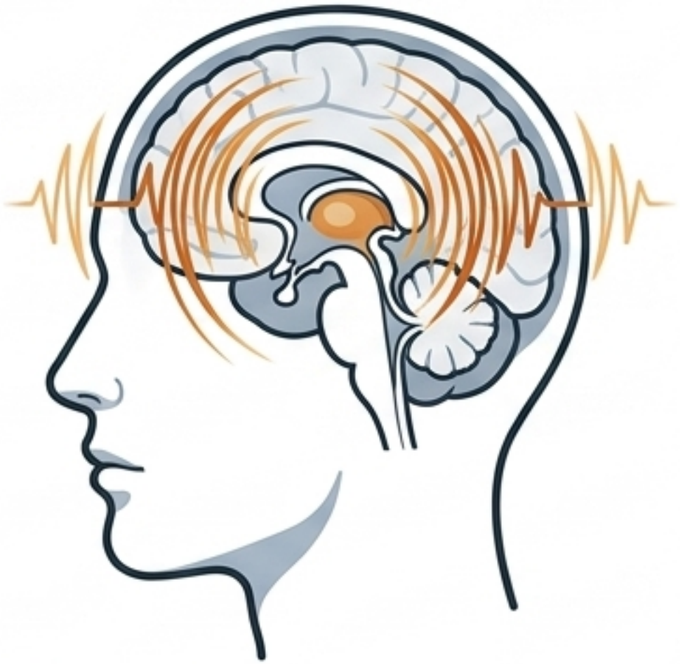
Clinical Impact:
Insidious physical manifestation, structural neurodegeneration.



Primary Resolution:
Dopamine depletion (VMAT2 inhibitors).



AKATHISIA: THE DUAL PRESENTATION



THE MIND (SUBJECTIVE)

- Intense inner restlessness and anxiety.
- Profound dysphoria, tension, and unbearable discomfort.

⚠ **CLINICAL ALERT:** Highly correlated with medication non-compliance and acute suicide risk.

THE BODY (OBJECTIVE)

- Constant fidgeting and inability to sit still.
- Pacing, rocking, and weight-shifting.
- Repetitive crossing and uncrossing of legs.

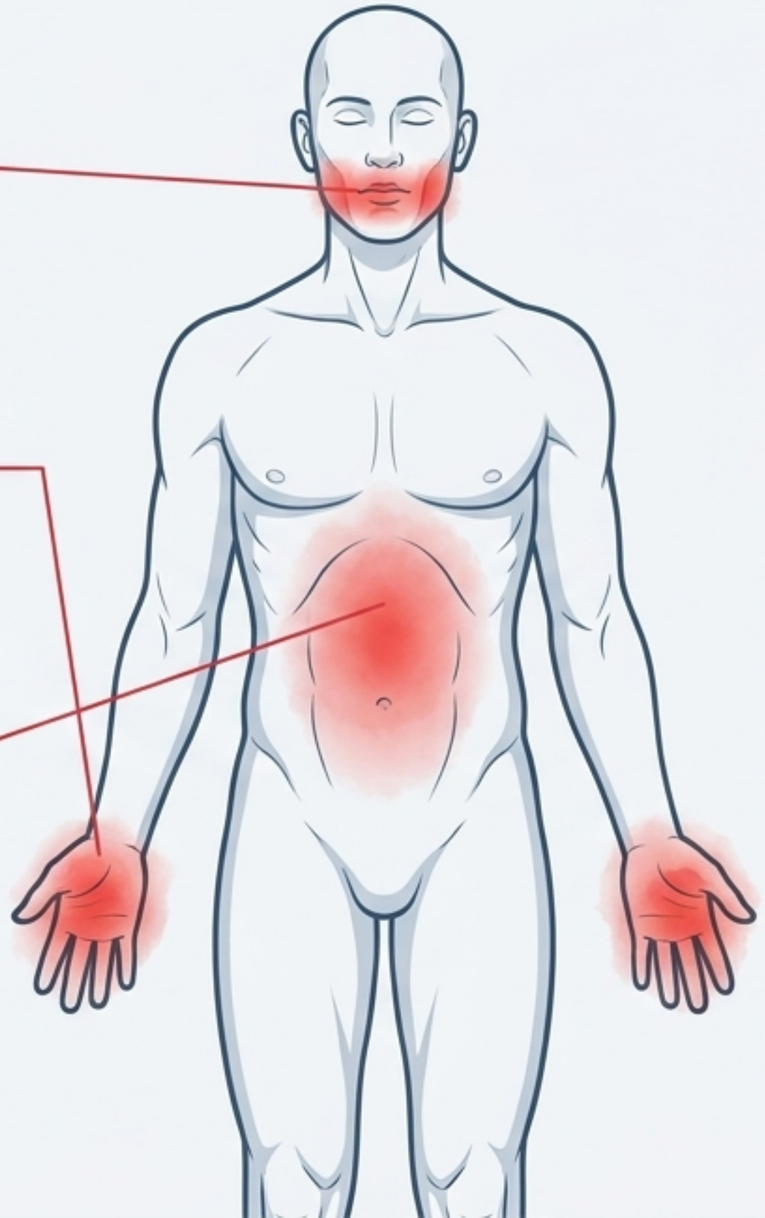
TARDIVE DYSKINESIA: MANIFESTATIONS

OROFACIAL
Involuntary tongue protrusion, lip smacking, puckering, perioral tremor, bruxism.

EXTREMITIES
Writhing movements of hands/feet, choreiform finger movements.

TRUNK & RESPIRATORY
Rocking, twisting, irregular breathing patterns, vocal dyskinesia.

Behavioral Modifiers: Symptoms increase with stress/concentration; decrease with relaxation/sleep.



EPIDEMIOLOGY

3-5%
Annual incidence with First-Generation Antipsychotics.

25-30%
Cumulative prevalence in chronic antipsychotic treatment.

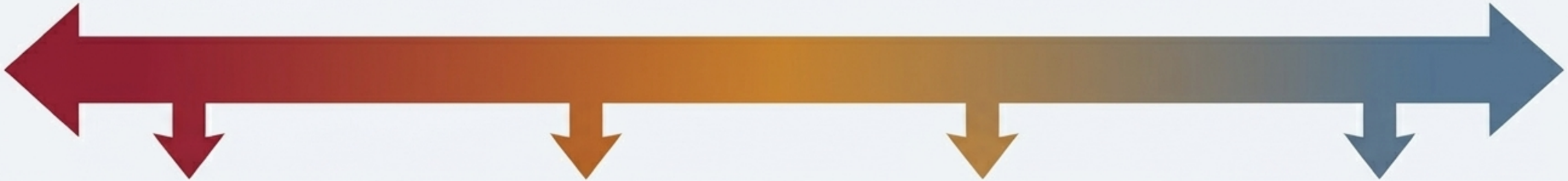
40-60%
Prevalence in elderly patients receiving antipsychotics.

THE DIAGNOSTIC TOOLKIT

SCALE	TARGET DISORDER	MEASURED COMPONENTS	CLINICAL APPLICATION
BARS	**Akathisia**	Subjective distress, objective movement, ability to sit still	Gold standard for akathisia.
AIMS	**Tardive Dyskinesia**	Orofacial, extremity, and trunk movements	Standard for TD screening.
SAS	**Parkinsonism**	Gait, rigidity, and tremors	Acute extrapyramidal side effects.
ESRS	**Comprehensive EPS**	Parkinsonism, akathisia, dystonia, dyskinesia	Comprehensive cross-disorder assessment.
IMS	**Tardive Dyskinesia**	Comprehensive TD assessment with severity ratings	Research and specialized clinical settings.

CLINICAL BEST PRACTICE: Baseline AIMS assessment must be performed before antipsychotic initiation. Readminister every 6-12 months. Assess BARS immediately whenever akathisia is suspected.

ETIOLOGY: THE PHARMACOLOGICAL RISK SPECTRUM



HIGHEST RISK

First-Generation Antipsychotics

Haloperidol, chlorpromazine, fluphenazine.

Potency directly correlates with a 10-20% akathisia risk and 3-5% annual TD risk.

VARIABLE RISK

Second-Generation Antipsychotics

Risperidone (intermediate) >

Olanzapine >

Quetiapine & Aripiprazole (lowest risk).

PRECIPITATORS

Dopamine Agonists & Stimulants

Bromocriptine, ropinirole, methylphenidate, amphetamines.

Induce or exacerbate motor dysregulation.

OFTEN OVERLOOKED

Antiemetics & SSRIs

Metoclopramide and

prochlorperazine (highly antidopaminergic; frequent cause of acute dystonia/akathisia).

High-dose Fluoxetine/Sertraline.

PATIENT VULNERABILITY: THE RISK FACTOR MATRIX

DEMOGRAPHIC VULNERABILITY

- Age >60 years (creates a 3-4 fold increased TD risk).
- African and Hispanic descent.
- Female gender.

CLINICAL VULNERABILITY

- Affective and Bipolar disorders.
- Cognitive impairment.
- Organic brain syndromes.
- Baseline diabetes.

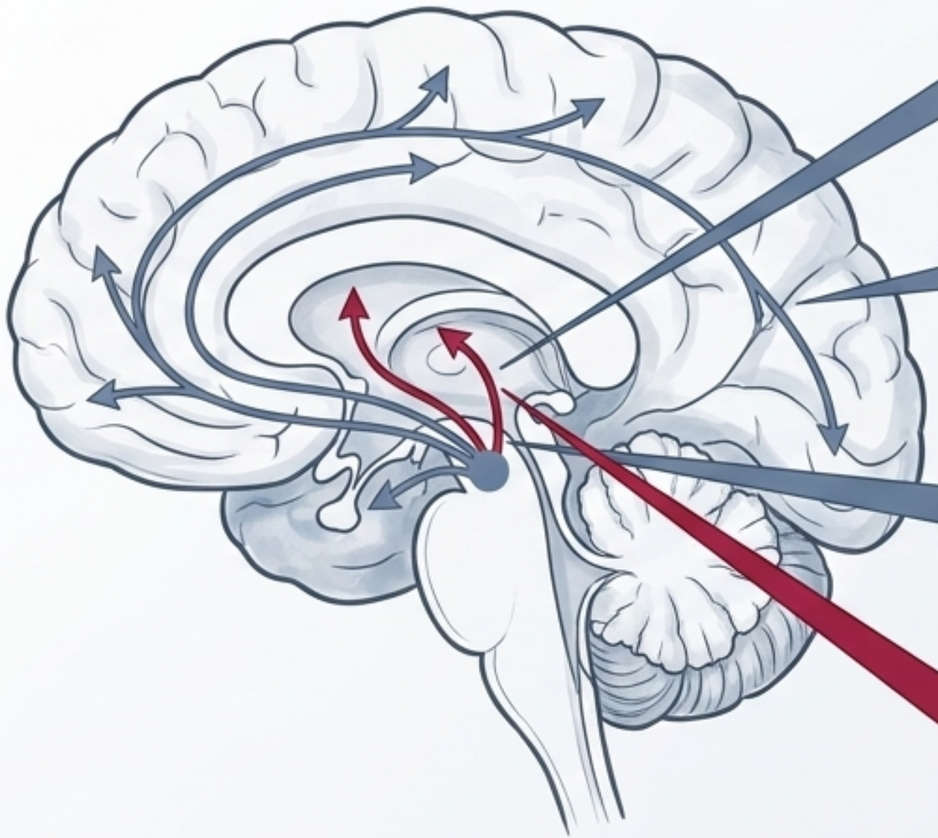
PHARMACOLOGICAL DRIVERS

- High-potency typical agents.
- High cumulative lifetime dose.
- Prolonged chronological exposure.
- Rapid dose titration.

GENETIC PREDISPOSITION

- Polymorphisms in dopamine receptors (DRD2, DRD3).
- COMT (catechol-O-methyltransferase) variations affecting individual susceptibility.

NEUROANATOMY OF ANTIPSYCHOTICS



MESOLIMBIC (VTA to NAcc)

Blockade Effect: Therapeutic reduction of psychosis.

MESOCORTICAL (VTA to PFC)

Blockade Effect: Worsening of cognitive deficits and negative symptoms.

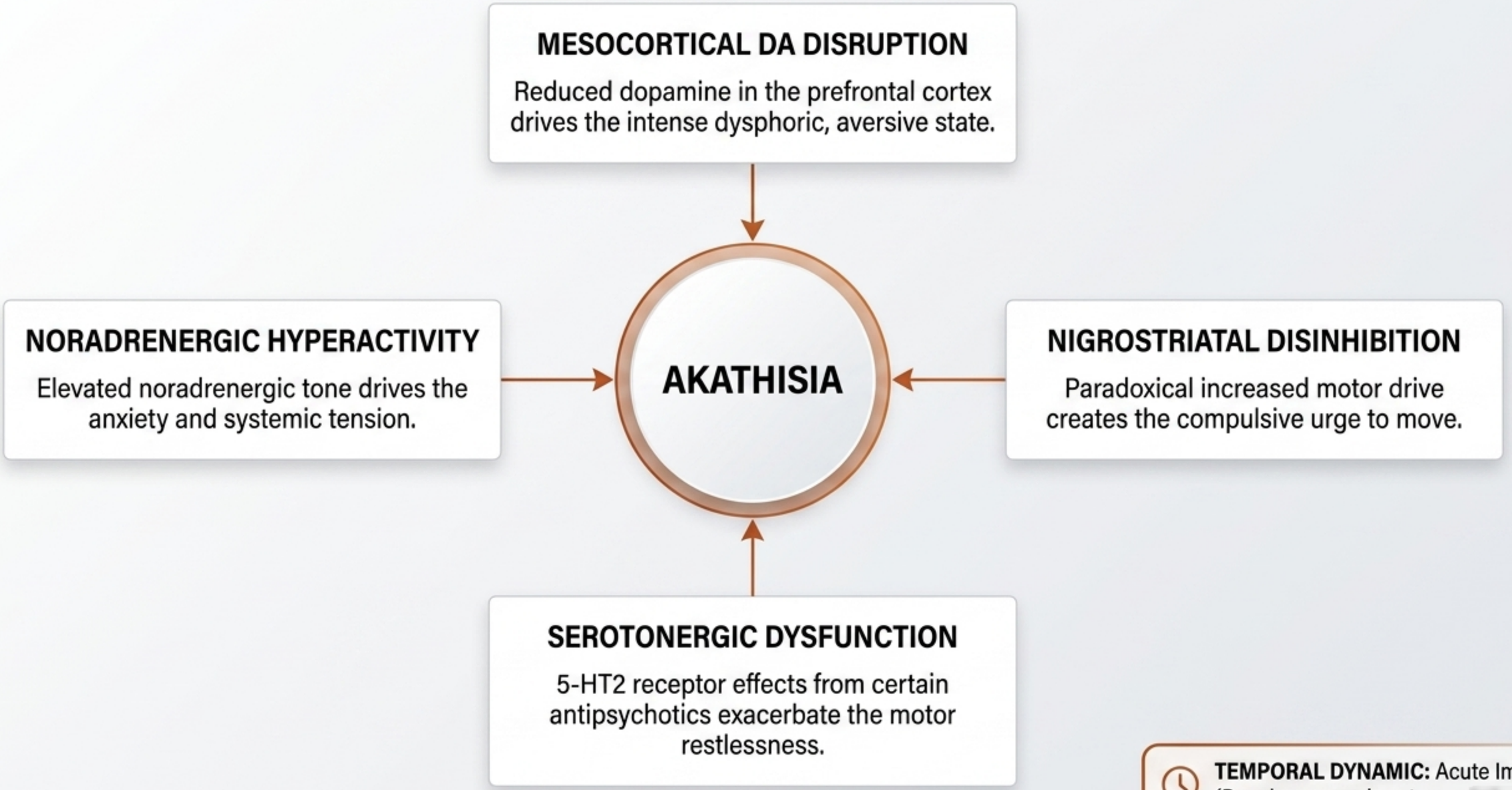
TUBEROINFUNDIBULAR (Hypothalamus to Pituitary)

Blockade Effect: Hyperprolactinemia.

NIGROSTRIATAL (SNc to Striatum) [THE DANGER ZONE]

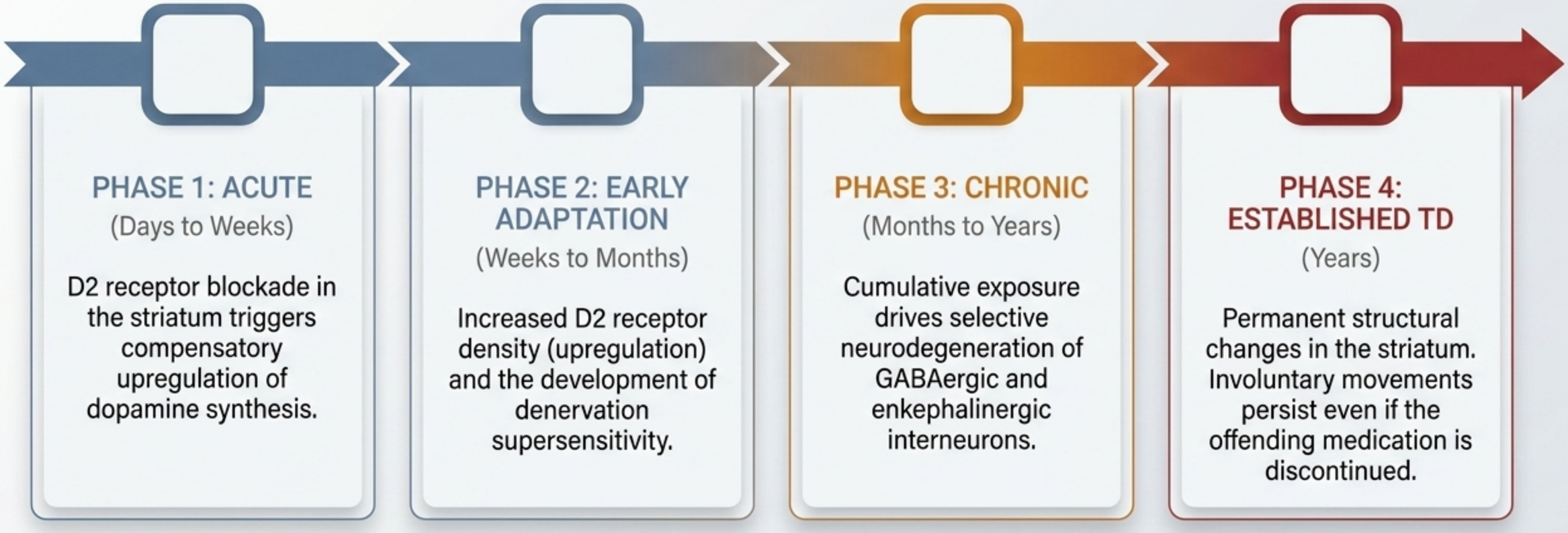
Blockade Effect: Disruption of motor control leading to Parkinsonism, Akathisia, and Tardive Dyskinesia.

PATHOPHYSIOLOGY 1: THE AKATHISIA IMBALANCE



TEMPORAL DYNAMIC: Acute Imbalance (Develops over days to wee

PATHOPHYSIOLOGY 2: THE TD NEUROADAPTATION TIMELINE



MECHANISM SYNTHESIS: THE STRIATAL SCALE

NORMAL STRIATUM

Balanced activity between the Direct Pathway (which facilitates movement) and Indirect Pathway (which inhibits movement).

Result: Normal, fluid motor control.

TARDIVE DYSKINESIA STRIATUM

Direct Pathway is hyperactive (↑↑) due to massive dopamine receptor supersensitivity.

Indirect Pathway is weakened (↓) due to chronic loss of GABA and enkephalin inhibitory tone.

Result: Unopposed motor facilitation leading to hyperkinetic, involuntary choreiform movements.

THE PREVENTION PARADIGM

STRATEGIC SELECTION

Prefer Second-Generation Antipsychotics (e.g., aripiprazole, quetiapine) over FGA agents when clinically appropriate.

DOSING DISCIPLINE

Utilize the lowest effective dose for the shortest duration necessary; implement gradual titration to allow neuroadaptation.

ACTIVE MONITORING

Baseline AIMS prior to initiation; routine re-assessment every 6-12 months. BARS assessment immediately upon signs of restlessness.

METABOLIC DEFENSE

Maintain strict metabolic monitoring, as comorbid diabetes acts as an independent risk multiplier for TD.

EXPOSURE REDUCTION

Consider medication-free periods or cautious dose reductions when psychiatric stability permits.

TREATMENT MATRIX: ACUTE AKATHISIA

FIRST-LINE INTERVENTIONS

- **Beta-Blockers:** Propranolol (20-40 mg BID). Excellent efficacy (70-90% response); targets noradrenergic tone. Watch for bradycardia/hypotension.
- **Benzodiazepines**: Lorazepam (0.5-2 mg PRN). Good efficacy, rapid onset via GABA potentiation. Watch for sedation/dependence.

SECOND-LINE INTERVENTIONS

- **Anticholinergics**: Benztropine. Moderate efficacy (30-50%); limited by dry mouth and cognitive effects.
- 5-HT1A **Agonists**: Buspirone. Moderate efficacy; requires 2-4 weeks for onset.

ROOT CAUSE INTERVENTION

- **Antipsychotic Dose Adjustment**: Dose reduction or switch to a lower-risk agent. Highly effective but requires carefully balancing the risk of psychiatric relapse.

TREATMENT ALGORITHM: TARDIVE DYSKINESIA

STEP 1: ANTIPSYCHOTIC SWITCH

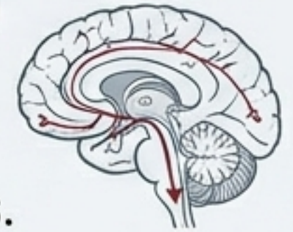
Transition to a low-risk agent to eliminate ongoing dopaminergic assault.

Special Note: Clozapine (300-600mg) is uniquely capable of improving TD while simultaneously treating psychosis, though it requires strict hematologic monitoring.

STEP 2: DOPAMINE DEPLETION (First-Line Treatment)

VMAT2 Inhibitors (Superior safety to legacy tetrabenazine).

- **Valbenazine**: 40-80 mg/day. Minimal CNS effects.
- **Deutetrabenazine**: 36-48 mg/day. Deuteration improves pharmacokinetics.



STEP 3: ADJUNCTIVE NEUROPROTECTION

For inadequate response or early-phase TD intervention.

- **Ginkgo biloba extract**: 240 mg/day. Antioxidant that enhances dopamine depletion efficacy.
- **Vitamin E**: 1200-1600 IU/day. Primarily useful in prevention or early phases.

SYNTHESIS & FUTURE HORIZONS

CLINICAL PEARLS

Standardized Assessment

Integrate BARS (Akathisia) and AIMS (TD) into routine workflows; prevention fundamentally outpaces treatment.

The VMAT2 Revolution

Valbenazine and deutetrabenazine are the definitive, evidence-based gold standards for established TD.

The Clozapine Exception

Clozapine remains the sole antipsychotic capable of actively improving established tardive dyskinesia.

FUTURE HORIZONS

Neuromodulation:

Pallidum-directed Deep Brain Stimulation (DBS) for severe, refractory TD.

Circuit Restorers:

Glutamatergic modulators (NMDA (NMDA antagonists) and GABA-enhancing agents currently in trials.

Precision Psychiatry:

Pharmacogenetic screening to identify high-risk DRD2/COMT profiles prior to prescribing.