

Antipsychotic Use in Children and Adolescents

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Objectives

At the end of this workshop, the participants will be able to:

- Recognize mental health diagnoses of children and adolescents treated with antipsychotics.
- Determine how the risks and benefits of treatment of children and adolescents with antipsychotics are estimated.
- Interpret response of child or adolescent's targeted symptoms to treatment with antipsychotics.
- Distinguish between symptoms of side effects and adverse effects that children and adolescents might display while taking antipsychotics.

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Antipsychotics

Indications:

- Psychosis
- Aggression/agitation/ self injurious behaviors/autism/
- Autism spectrum disorders and disruptive behavior disorders
- Severe OCD/ severe anxiety
- Mania/severe depression
- Tics/Tourette' s
- Personality disorders/insomnia/delirium etc

Antipsychotics

Behaviors Seen:

- Psychosis
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- Autism spectrum disorders and disruptive behavior disorders
- Severe OCD/ severe anxiety
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Antipsychotics

Theories regarding psychosis:

- Disruption in **flow of Dopamine**... like gas flooded car
- **Excess of dopamine** – positive symptoms of hallucinations...?
- **Diseases & drugs that increase dopamine** will produce positive symptoms
- All known antipsychotics are **blockers of dopamine receptors (esp. D2)**
- Negative symptoms / cognitive symptoms may be **due to a deficit of dopamine in mesocortical areas**
- **Neurodegeneration due to excitotoxicity** – excess stimulation of

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WHY DO YOU TREAT CHILDREN AND ADOLESCENTS WITH Antipsychotics?

- **HARMING SELF**
- **HARMING OTHERS**
- **DETERIORATING EMOTIONALLY/BEHAVIORALLY**
- **CLEARLY PSYCHOTIC**
- **CLEARLY CYCLING**
- **INABILITY TO SLEEP**
- **INABILITY TO FUNCTION IN SCHOOL, HOME, COMMUNITY**
- **RISK OF HOSPITALIZATION**
- **MULTIPLE TRIALS OF LESS RISKY MEDS WITHOUT CLEAR BENEFIT OR LIMITED BENEFIT**
- **SEVERE TRAUMA**

Risks and Benefits of Treating with Antipsychotics

RISKS

- **SIDE EFFECTS**
- **STIGMA**
- **ADVERSE EFFECTS**
- **WEIGHT GAIN**
- **MOVEMENT DISORDERS**

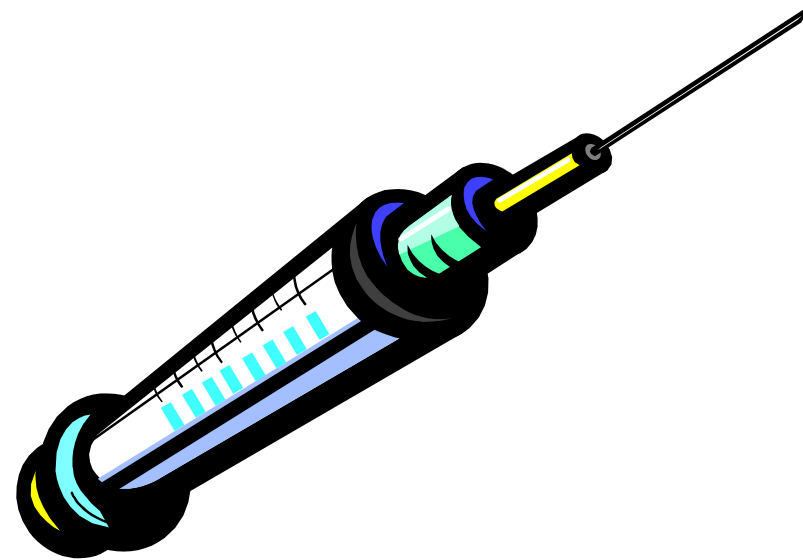
BENEFITS

- **SAFETY OF SELF**
- **SAFETY OF OTHERS**
- **REDUCES SUFFERING**
- **IMPROVED FUNCTIONING**
- **CLEARER THINKING**
- **IMPROVED SELF ESTEEM**
- **CAN STAY IN HOME VS HOSPITALIZATION**

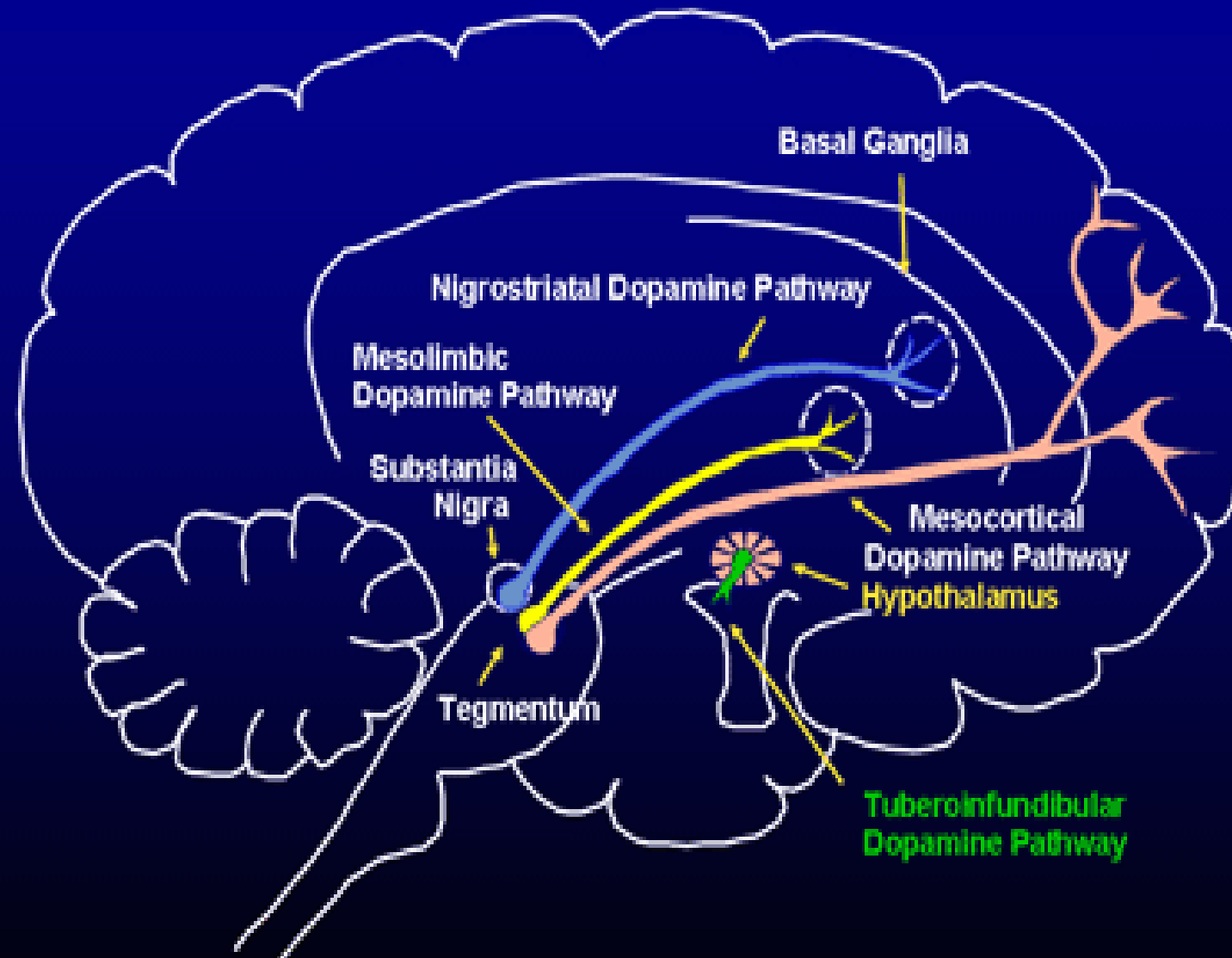
Typical Antipsychotics

❖ 1953 Thorazine

❖ The Single Most Important
Advancement in Treatment of
Psychotic Illnesses



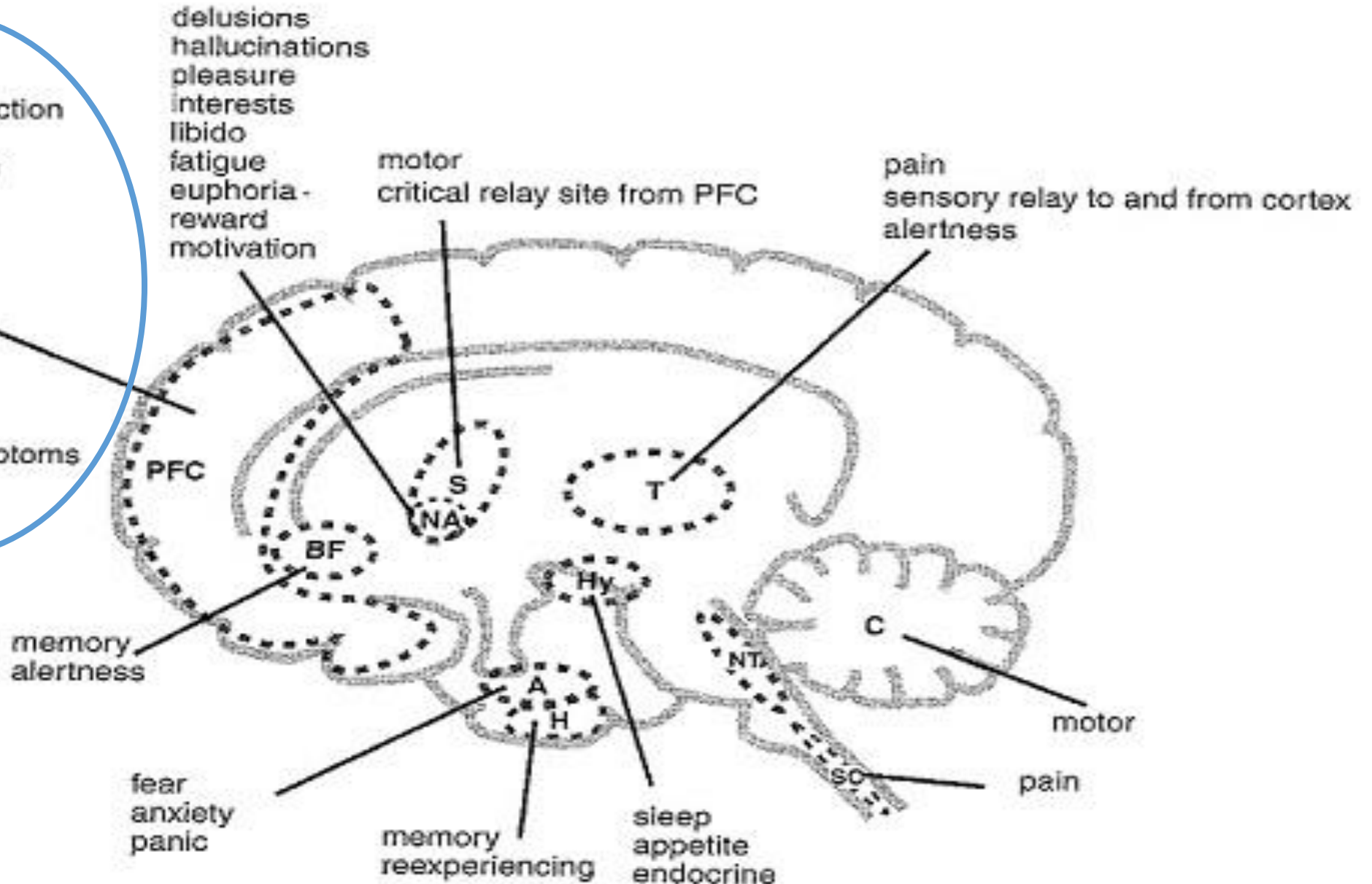
The Dopaminergic Pathways of the Brain



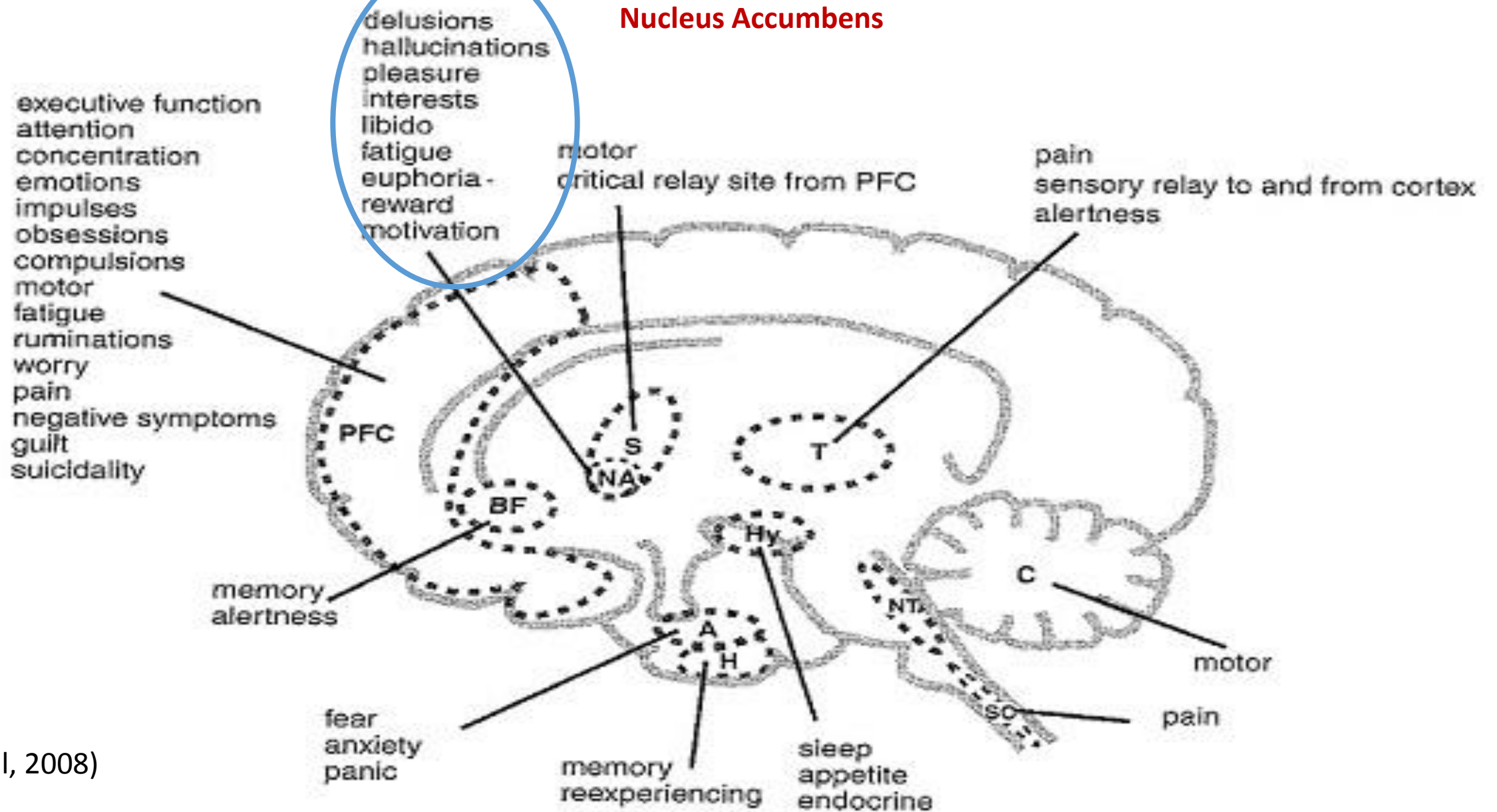
Some Key Behaviors Hypothetically Linked to Specific Brain Regions

PFC- Pre frontal Cortex

- executive function
- attention
- concentration
- emotions
- impulses
- obsessions
- compulsions
- motor
- fatigue
- ruminations
- worry
- pain
- negative symptoms
- guilt
- suicidality



Some Key Behaviors Hypothetically Linked to Specific Brain Regions



(Stahl, 2008)

Typical Antipsychotics

Conventional/typical Antipsychotics:

- AKA Neuroleptics- “seize the neuron”
- Neuroleptosis= Slowing/affective indifference
- Block all D2 receptors in the brain (including the Mesocortical pathway which worsens negative symptoms)

Typical Antipsychotics

Typical Antipsychotics: tightly adhered to neuron

- Haldol (haloperidol) (depot, IM, liquid forms)
- Orap (pimozide)
- Prolixin (fluphenazine) (depot form)
- Moban (molindone)
- Navane (thiothixene)
- Thorazine (chlorpromazine) (IM form)
- Mellaril (thioridazine)
- Stelazine (trifluoperazine)

Atypical Antipsychotics

Atypical Antipsychotics: Less tightly bound at D2

- Dopamine has **rapid dissociation off** of neuron
- **Block serotonin receptors** (esp. 5HT 2A)
- Serotonin **blockade in nigrostratum** reduces EPS
- Serotonin blockade in mesocortical areas **may improve negative symptoms**

Atypical Antipsychotics

Antipsychotics Novel/Atypical :

- Clozaril (clozapine) – agranulocytosis!
- Zyprexa (olanzapine) – weight gain
- Risperidal (risperidone) EPS at higher doses
 - Invega (paliperidone)- active metabolite of risperidone
- Seroquel (quetiapine) – no prolactin increase/galactorrea
- Abilify (aripiprazole) – partial agonist, less weight gain
 - Rexulti (brexpiprazola)
- Geodon (ziprasidone) – EKG changes but less weight gain
- Latuda (lurasidone)
- Fanapt (iloperidone)
- Saphris (asenapine maleate)

Clozaril (clozapine)

- The **first atypical**
- **Agranulocytosis** (low white count) limits use
- Need for **weekly then biweekly blood draws**
- Effective for **recalcitrant conditions**
- Dose range is 50 to 800mg/day
- SE: weight gain, seizures, sedation

Zyprexa (olanzapine)

FDA approved for **Schizophrenia and Bipolar mania/mixed** (13 and up)

Dosage range 2.5mg to 20mg/day

Zydis form – orally disintegrating tablet

Q day or BID

Weight gain/metabolic syndrome

Mood stabilizing



Risperdal (risperidone)

FDA approved for **treatment of *autism related irritability** (5 to 16),
***schizophrenia** (13 and up) and
***bipolar mania or mixed state** (10 and up)

Dosage range 0.25 – 6mg

Atypical at lower doses

Becomes **typical at higher doses**

Liquid form and injectable form (Consta)



Seroquel (quetiapine)

FDA approved to treat

Schizophrenia (13 and up),

Mania (10 and up)

Dosage range 25mg to 800mg/day

Highly **sedating**

Requires slow dosage titration

? Anxiolytic

Mood stabilizing effects

QD, BID or TID dosing especially in children

Minimal EPS and no elevation of prolactin



Abilify (aripiprazole)

FDA approved for treatment of *autism related irritability(6-18),

*schizophrenia (13-18), *bipolar disorder – manic and mixed episodes (10 and above)

Partial **agonist at D2 and 5HT1A**

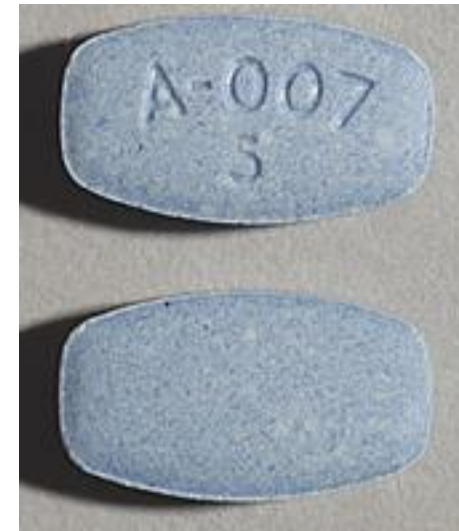
Dosage range 2.5mg/day to 30mg/day

Q day or BID dosing

? Less robust as antipsychotic

Mood stabilizing

Less weight gain/No EKG changes,



Geodon (ziprasidone)

5HT and norepinephrine reuptake inhibition

Dosage range 40mg/day to 160mg/day

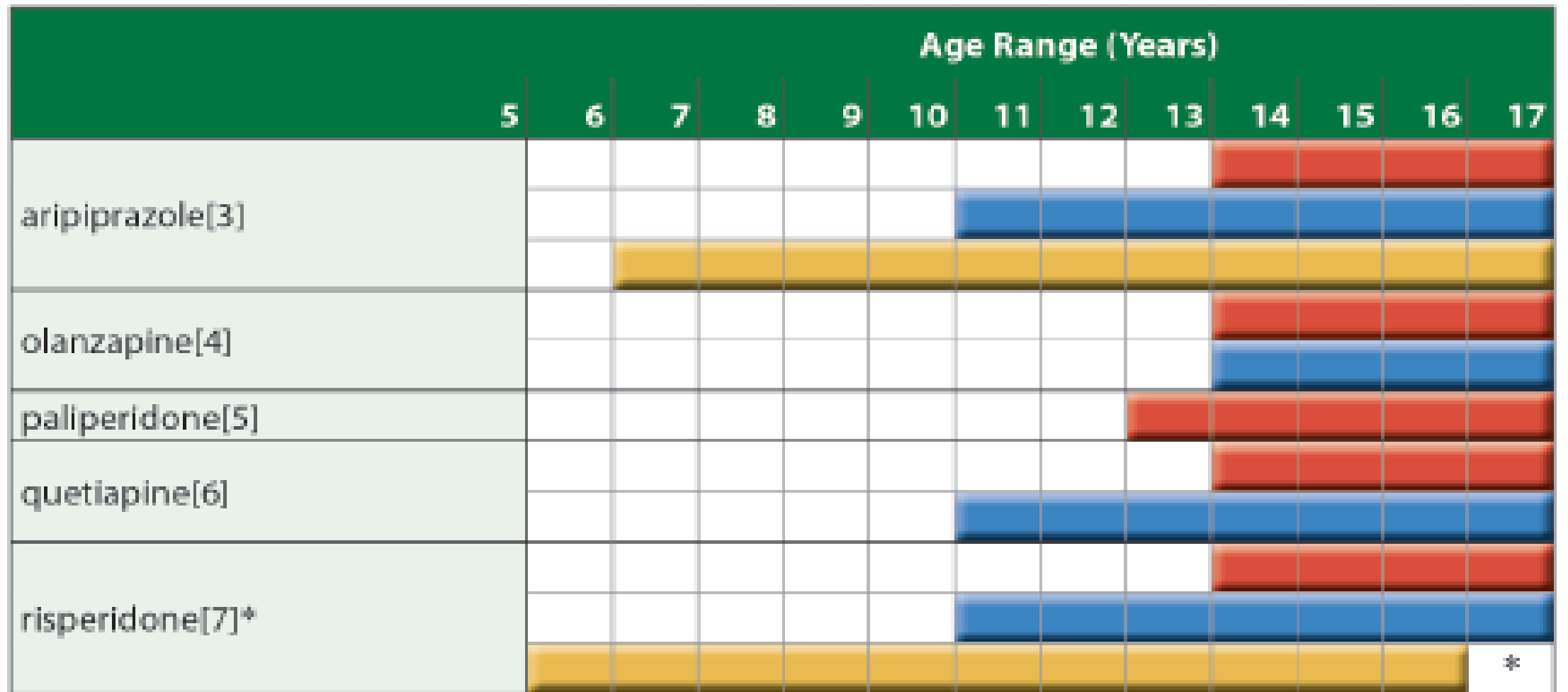
BID dosing

Effects on **EKG** Potential **QTc**
prolongation

Less weight gain



Figure 1. FDA-Approved Pediatric Age Ranges and Indications for Atypical Antipsychotics



■ schizophrenia ■ bipolar I disorder: manic or mixed ■ irritability with autistic disorder

*Risperidone should not be used by patients older than age 16 who have been diagnosed with irritability with autistic disorder.

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TARGETED SYMPTOM RESPONSE

- **Follow up closely with child over phone with mother and in person either weekly or every other week due to dangerousness (intensity and frequency)of symptoms**
 - **Eg. "Recommended aripiprazole 2.5 mg daily targeting severe impulsivity and aggression (tried to choke brother). Mother has to monitor closely as episodes of aggression towards brother (hitting, pushing, choking) occur daily and his tantrums last up to 20 minutes"**
- Identify whether those symptoms are improved, worse or the same
 - **"Follow up after 1 week on aripiprazole 2.5 mg daily and aggressive episodes have reduced in frequency from daily to 2 x per week and have reduced to episodes of 5 minutes of tantrumming."**

TARGETED SYMPTOM RESPONSE

- **Follow up closely with child over phone with mother and in person either weekly or every other week according to acuity (intensity and frequency) of symptoms**
 - Eg. "Recommended 0.25 mg risperidone bid targeting daily, almost constant, auditory hallucinations of father telling him he is a bad boy and should be punished. Can't focus in school, the voice won't let him concentrate"
- Identify whether those symptoms are improved, worse or the same
 - "Follow up after 1 week on 0.25 mg bid of risperidone for auditory hallucinations which have reduced to 2 x per day, when he awakens and when he tries to go to sleep."

What you might see in the classroom or your office

- Child is calmer, **more coherent in their conversations and behavior** with you and others
- **Less irritable**
- More focused, less distracted
- **Tired, less energetic**
- More attentive
- **More cooperative and possibly engaged**

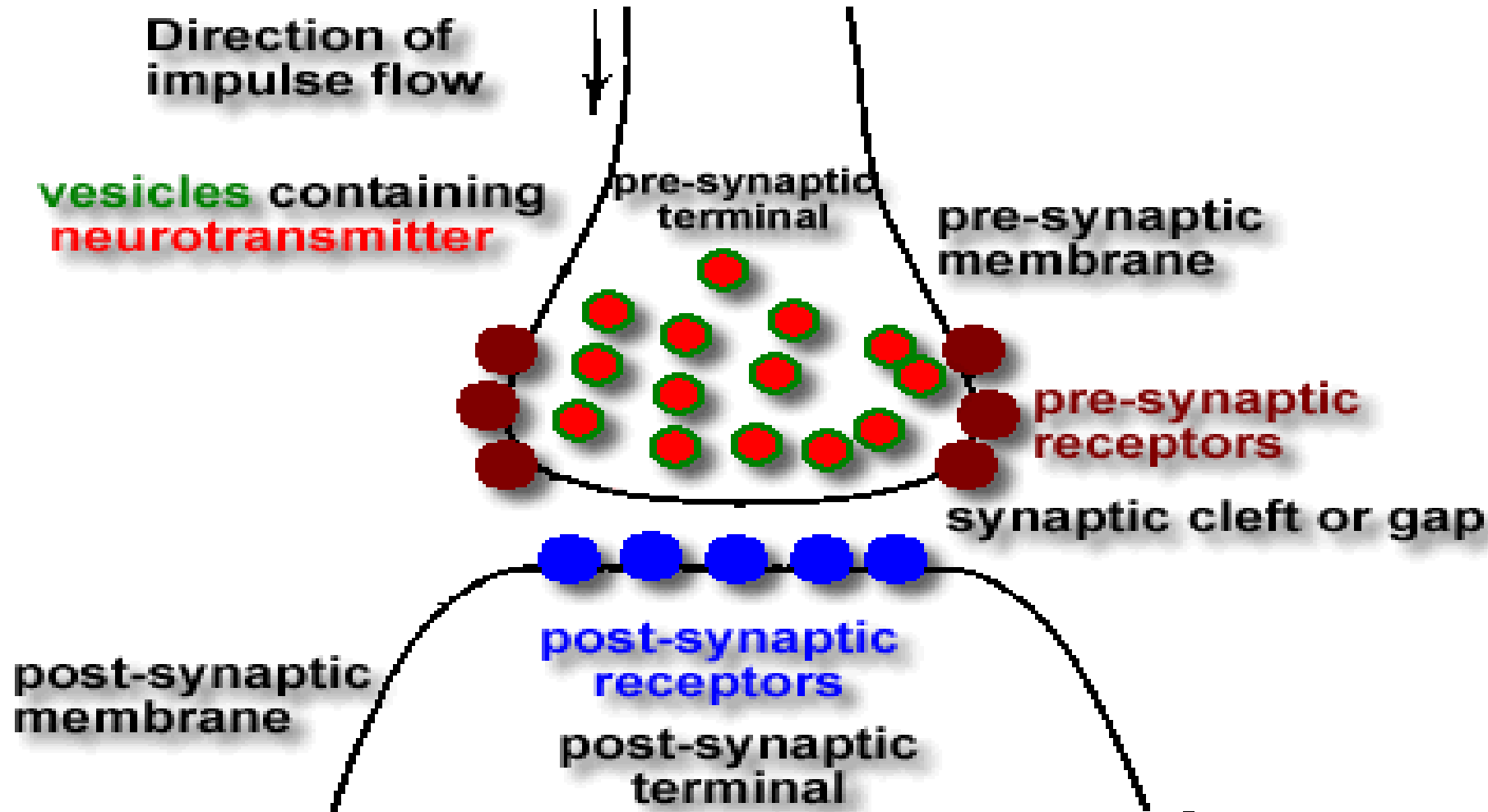
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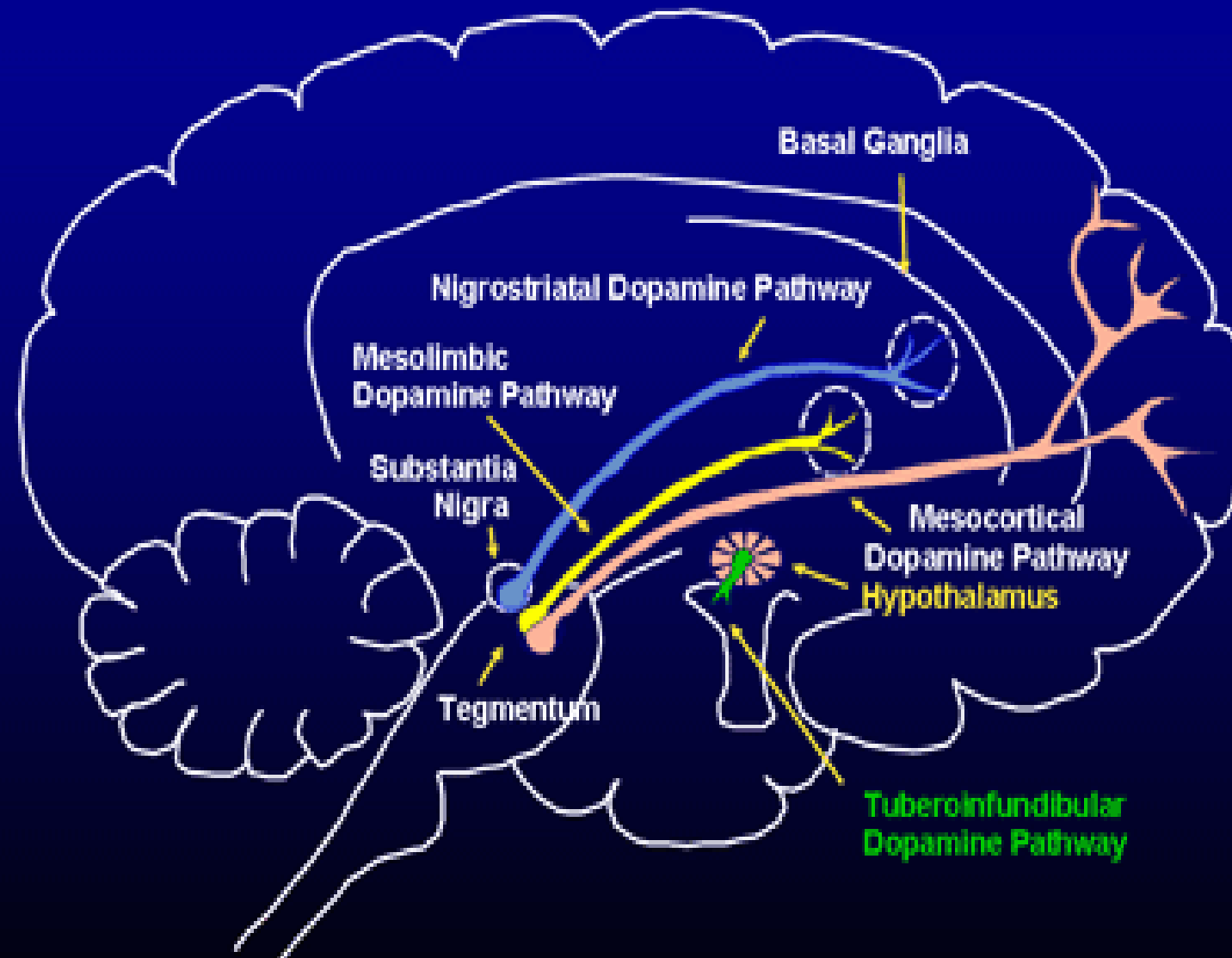
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Antipsychotics

Different antipsychotics have different receptor binding profiles and thus differ in SE profile



The Dopaminergic Pathways of the Brain



Antipsychotic Side Effects

Mechanism of action:

Dopamine (D2) receptor blockade as with conventional antipsychotics

Side Effects:

- D2 blockade in the **nigrostriatum causes EPS** (extrapyramidal symptoms), chronic D2 blockade causes **tardive dyskinesia**
- D2 blockade in the **tuberoinfundibular pathway** cause increase in prolactin : **galactorrea** (breast liquid secretion) which in turn effects causes **amenorrhea** (no menses)

Antipsychotic Side Effects

Muscarinic cholinergic blockade> Dry mouth, blurry vision, cognitive blunting, constipation; Prevents EPS

α 1 (alpha 1) adrenergic blockade> Cardiovascular effects, decrease in blood pressure

H1 (histaminic) blockade> weight gain, sedation

Antipsychotic Side Effects

Other side effects

- Reduced seizure threshold
- Anergia- *abnormal lack of energy*
- Metabolic syndrome
 - Weight gain “central obesity”
 - Insulin resistance
 - Elevated triglycerides

Antipsychotics

Extrapyramidal symptoms (EPS)

- **Dystonia** Brief or prolonged contractions of muscles (oculogyric crisis, torticollis, trismus) Parkinsonism – tremor, stiffness, slow movements, shuffling gait, cogwheeling, mask like face, **blepharospasm**
- **Akathisia**– extreme motoric restlessness that may be localized to legs

Antipsychotics

Tardive dyskinesia—Caused by **chronic D2 blockade** in the NS pathway: receptors become “**super sensitive**” and **up-regulate** –

Facial & tongue movements, chewing, tongue protrusions, grimacing, limb movements (quick jerks, choreoathetoid movements)...withdrawal dyskinesia

Potentially Life Threatening Adverse Effect Antipsychotics

Neuroleptic Malignant Syndrome (life threatening)

- Muscular rigidity
- Fever
- Encephalopathy – confusion, stupor, coma
- Vital sign instability
- Muscle enzyme elevation

Atypical Antipsychotics

Medications given with antipsychotics :

Indications: to prevent or treat EPS

- Cogentin (benztropine)
- Benadryl (diphenhydramine)
- Symmetrel (amantadine)
- Inderal (propranolol)

SUMMARY: What to watch for in the classroom or office

SIDE EFFECTS

- Fatigue
- Dry mouth
- Akathisia
- Extra pyramidal symptoms
- Weight gain
- Decreased blood pressure

ADVERSE EFFECTS

- **Neuroleptic Malignant Syndrome**
- Tardive Dyskinesia
- Oculogyric Crisis

Antipsychotics

Monitoring:

- AIMS test
- Weight/vitals
- Lipids/triglycerides
 - Glucose
 - ?EKG

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