



# Psychotropic Medications – What You Need to Know

# Series Format

- 4 One-hour talks - 2 in November and 2 in January, provided by Syl Apps Psychiatric Consultants
- Open to All Staff – and all are encouraged to attend
- Talks will be videotaped for future reference
- Slide decks and reference materials will be provided.

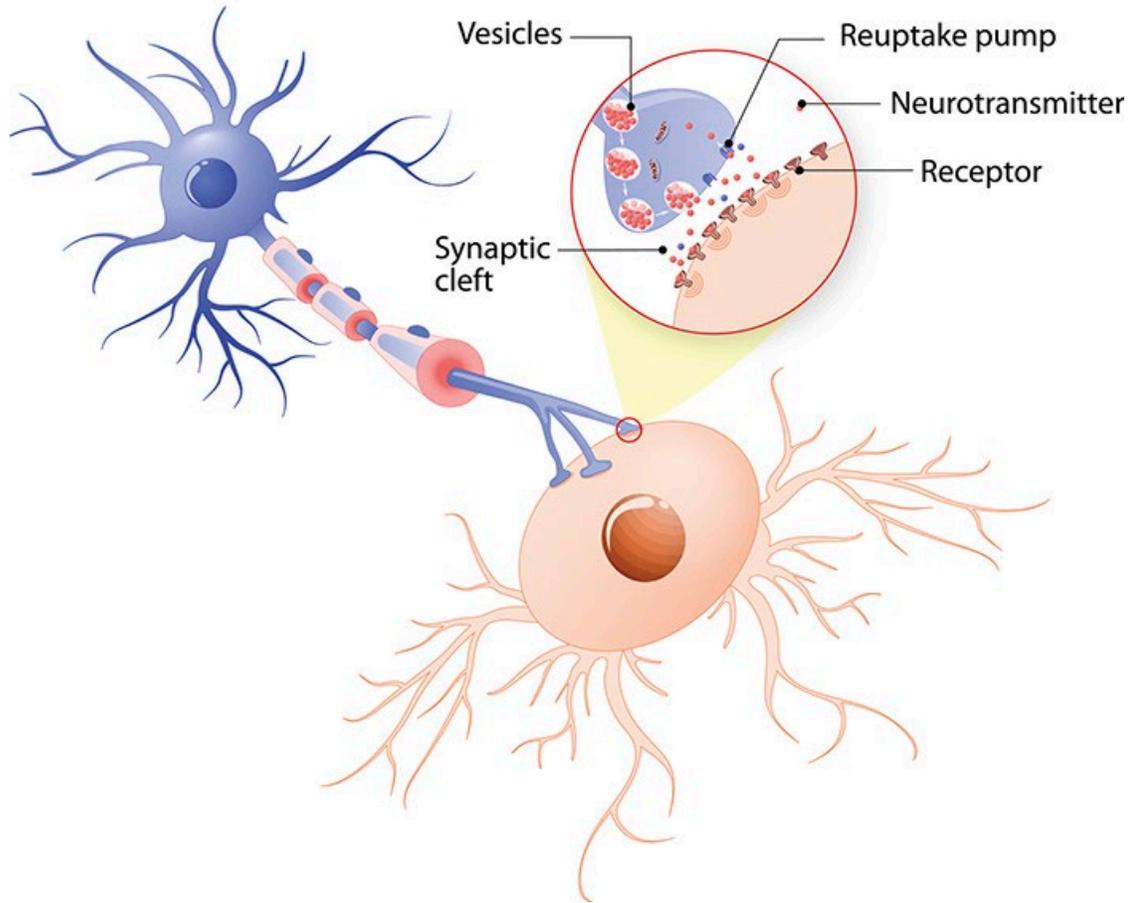
# Session One – Introduction – Principles of Administration and Monitoring

- Neurotransmission for Beginners
- Medication Classes to be discussed in the 3 next Sessions
- Consent to Treatment and Standing vs. “PRN” Medications
- Work-up for Administration and Monitoring (i.e. monitoring instruments – PMMC, Lab Work, BMI, etc.)
- Evaluation of Treatment Response
- Hypnotic Agents – Meds for Sleep

# A Brief Guide to Neurotransmission

- Psychotropic substances and medications work by impacting chemically-based communication between neurons in the central or peripheral nervous system.
- A Psychotropic Medicine will therefore increase or decrease activity in a targeted neurological system or pathway – those involved in regulation of moods, anxiety, stress, thought form and perception, etc.

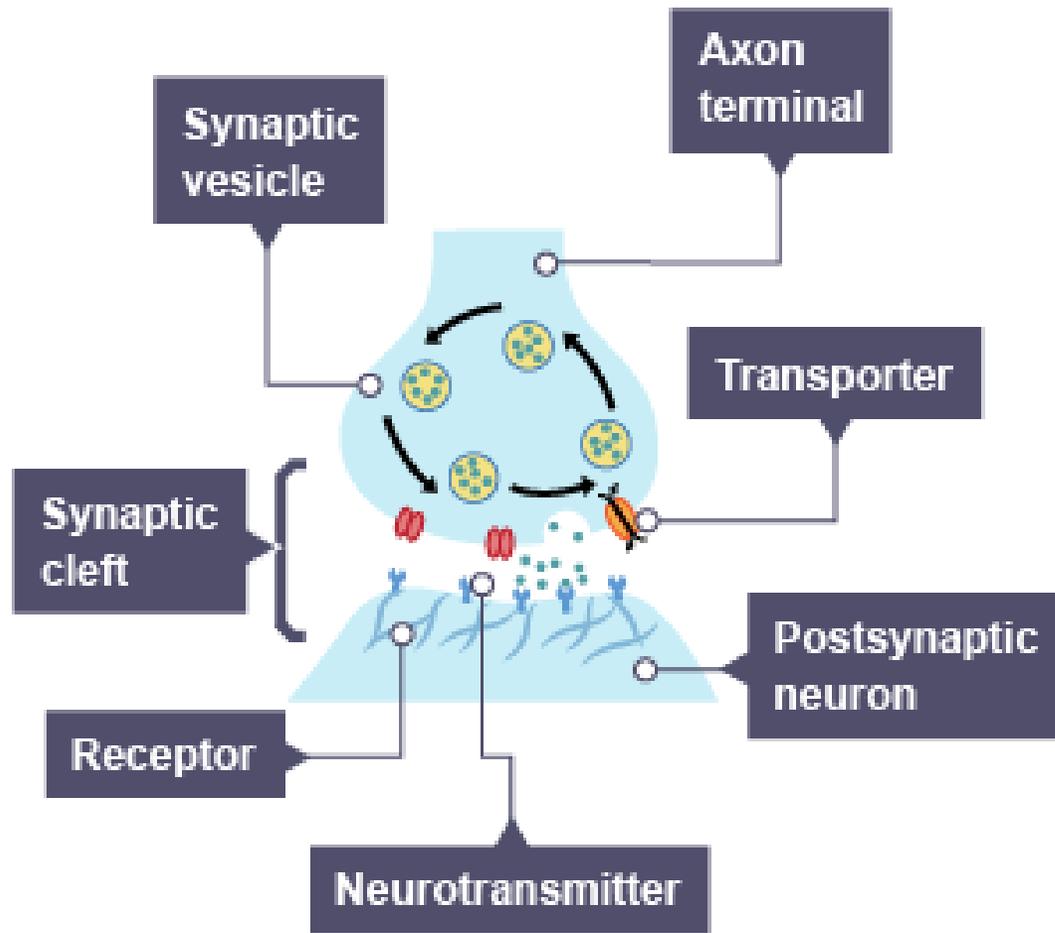
# Neurotransmission – Chemical basis for Psychopharmacology



Electrical Conduction **along** Nerve cells...  
But chemical conduction **between** cells.

We call the chemicals that pass between cells that trigger electrical activity **NEUROTRANSMITTERS**. They work by crossing from the transmitting cell and binding to receptors on the receiving cell

This takes place in the Synapse



Transmitters, stored in vesicles are released into the cleft where they attach to a receptors.

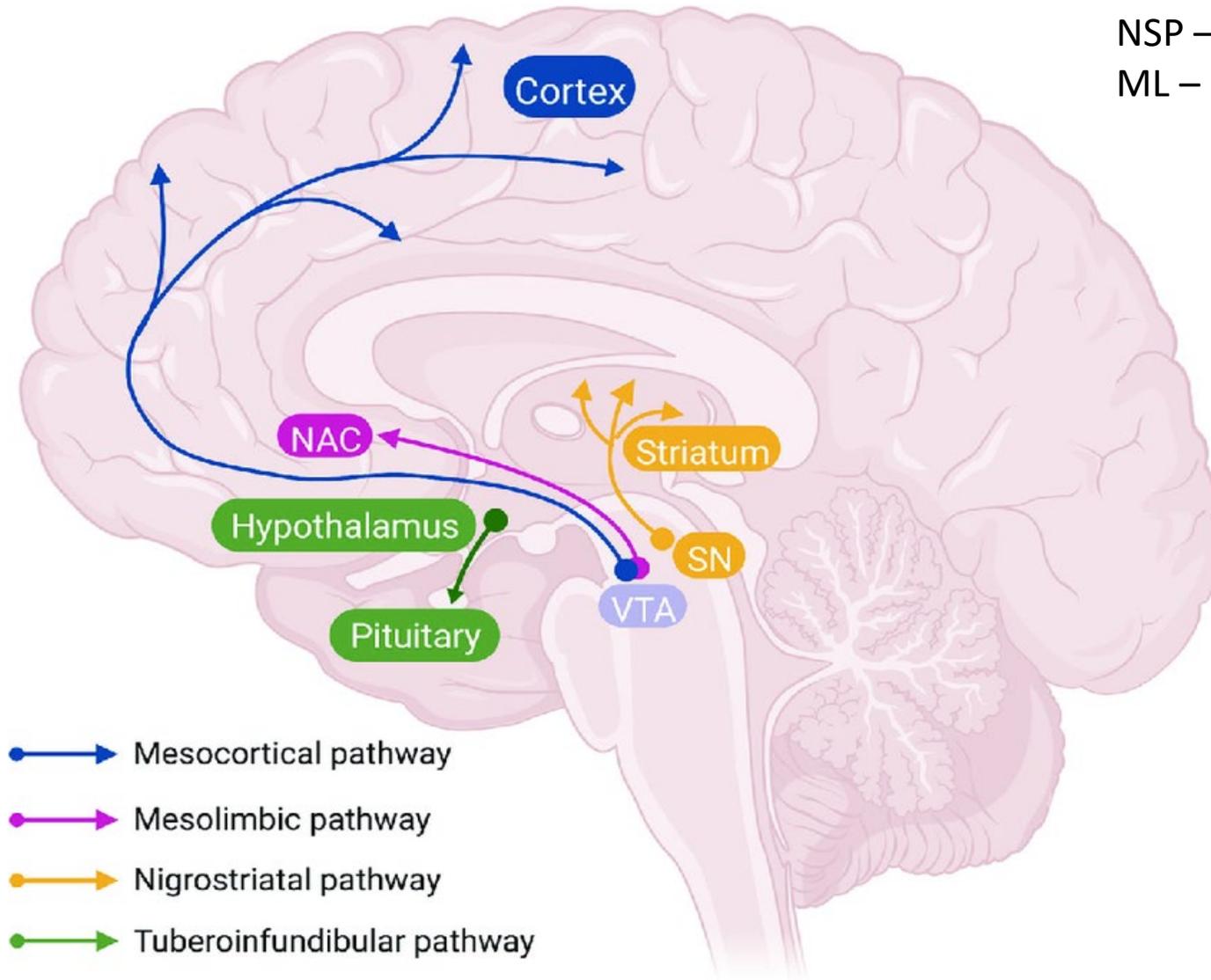
Transmission may be excitatory, inhibitory or modulating, which may result in broader, more sustained or variable effects on neurotransmission.

The effect of the transmitter on the receptor may end by transmitter metabolism, reuptake into a vesicle in the axon or by diffusion away from the cleft.

- Some medicines (such as morphine or Alpha-adrenergic blockers mimic transmitter action. Other drugs (such as the SSRI antidepressants) increase the activity of preexisting neurotransmitters by keeping them longer in the cleft.
- Medicines “target” particular disorders because different chemical neurotransmitters act in different pathways.
- Medicine effects – both desired and unwanted ones – are often related to some systems utilizing multiple transmitters or different systems (other than the desired one) using the same transmitter.

# DOPAMINE PATHWAYS

TIP – Prolactin↓  
NSP – ↓dopamine=↓movement  
ML – ↑dopamine = ↑psychosis



- Mesocortical pathway
- Mesolimbic pathway
- Nigrostriatal pathway
- Tuberoinfundibular pathway

# Neurotransmission System “Overlap”

- Dopamine transmission in the Mesolimbic Pathway regulates thought form + perceptions; too much dopamine activity = psychosis
- Dopamine transmission in the Nigrostriatal Pathway controls movement. Too little transmission = Parkinson’s Disease.
- Early “First Generation” antipsychotics acted broadly to decrease dopamine transmission in multiple pathways...
- Decreased mesolimbic activity would treat psychosis – while decreased nigrostriatal activity would often contribute to Parkinsonism or other movement disorders and decreased Tuberoinfundibular activity might cause gynecomastia or galactorrhea...

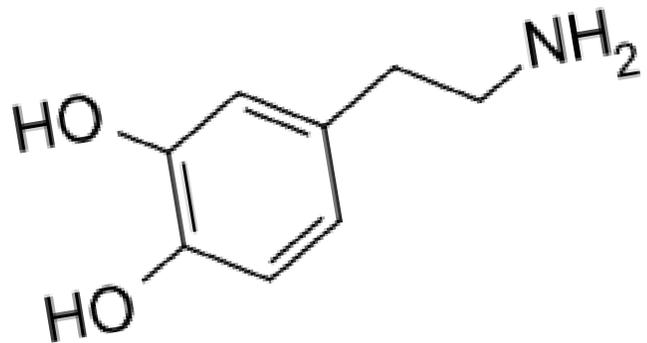
- Research by Seeman in Toronto (1974) found there were differences in the properties of the dopamine receptors in different systems.
- Identification of the D2 receptor – specific to the mesolimbic system led to the development of 2<sup>nd</sup> generation antipsychotics – more selective in binding mesolimbic receptors rather than the receptors for other pathways.
- These drugs were much less active in the motor system, so movement disorders and gynecomastia from antipsychotic use became much less common.



Phillip Seeman (1934-2021)

# Neurotransmitters in Psychiatry

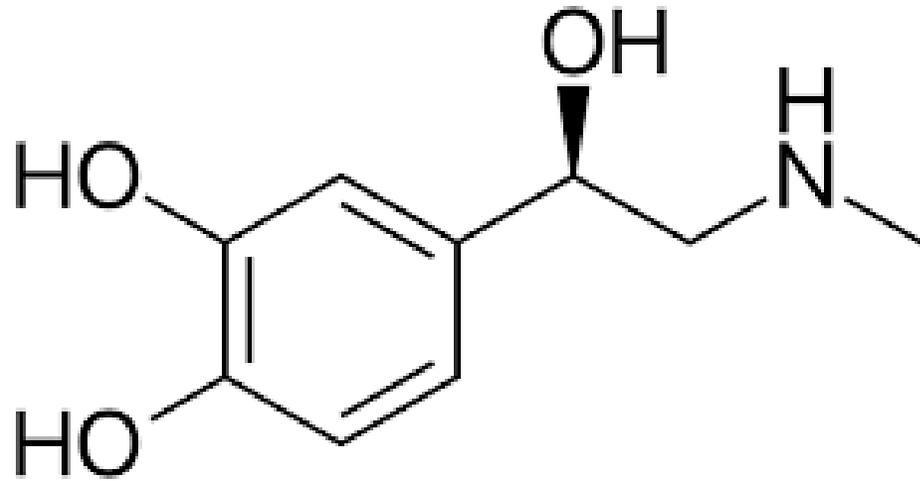
- While well over a hundred neurotransmitters have been identified, most psychotropic medications act on a small number of transmitters related to the mental health problems...
- Serotonin in mood disorders, OCD and anxiety.
- Norepinephrine in mood disorders
- GABA in anxiety and sleep disorders
- Dopamine in psychotic illness



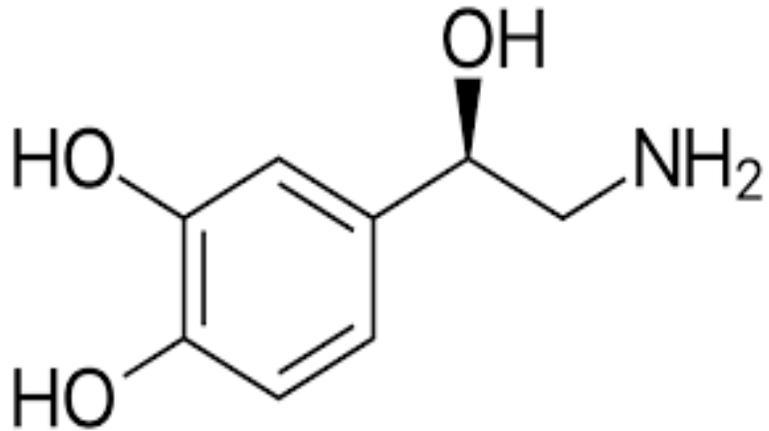
**Dopamine** is involved in control of the brain's 'reward' systems, including feelings of pleasure, achieving heightened arousal and learning. Dopamine also helps with focus, concentration, memory, sleep, mood and motivation.

Diseases associated with dopamine system dysfunction include Parkinson's disease, schizophrenia, bipolar disorder, restless leg syndrome, and ADHD.

Many highly addictive drugs, such as cocaine and amphetamine, act directly on the dopaminergic system.

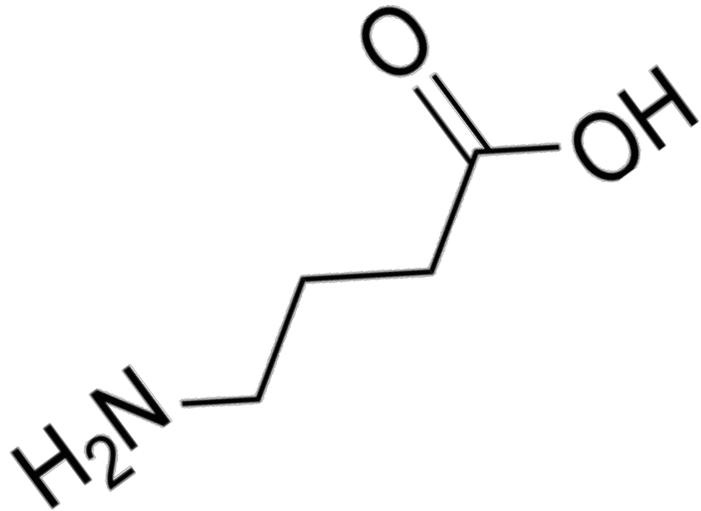


**Epinephrine** (also called adrenaline) and norepinephrine control a person's "fight-or-flight response" to stress. These neurotransmitters stimulate this response by increasing heart and respiratory rates, blood pressure, blood flow to your muscles, as well as heighten attention and focus to allow rapid, strong responses to threat or danger.



**Norepinephrine** is known for its effects on alertness, arousal, decision-making, attention and focus.

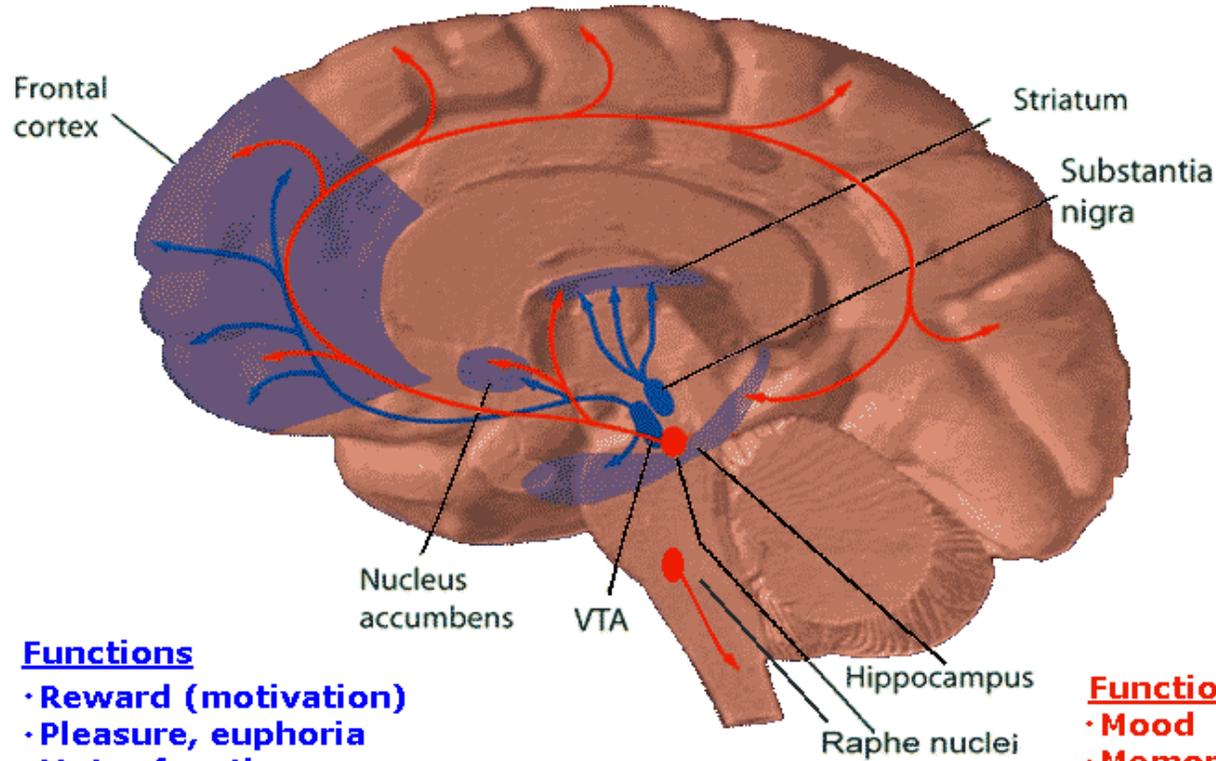
Many medications (stimulants and antidepressants medications) aim to increase norepinephrine levels – to improve focus or concentration to treat ADHD or to modulate norepinephrine to improve depression symptoms.



**GABA** (Gamma-Aminobutyric Acid) is a major inhibitory neurotransmitter, important in the control and relief of anxiety, regulation and maintenance of sleep and containing seizure activity.

Benzodiazepines act to enhance GABA's effect on GABA receptor activity, while alcohol binds to GABA-A receptors directly.

## Dopamine Pathways



### Functions

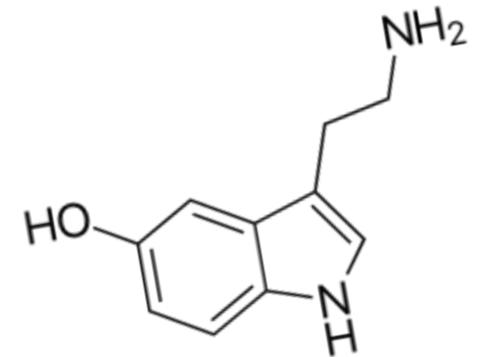
- Reward (motivation)
- Pleasure, euphoria
- Motor function (fine tuning)
- Compulsion
- Perseveration

## Serotonin Pathways

### Functions

- Mood
- Memory processing
- Sleep
- Cognition

**Serotonin (5-hydroxytryptamine)** is involved in cognition, memory, reward, learning, in regulation of mood, appetite and sleep and such physiological processes such as vomiting and vasoconstriction.



# Session 2 – Antipsychotics

Monday, November 24 at Noon

Jeremy Butler MD FRCP

- Uses in Psychiatry for various conditions
- Antipsychotic Groups ( i.e. 1<sup>st</sup>, 2<sup>nd</sup> and 3<sup>rd</sup> generation and Clozaril)
- Antipsychotic delivery (i.e. Oral, injectable short-acting and depot)
- Side effects (i.e. movement, metabolic, hematologic, etc.)
- Monitoring of response and tolerance and safety
- Patterns of response, duration of use for various conditions, “PRN” versus standing

# Session 3 – Treatments for ADHD

Christina McDonald MD FRCP

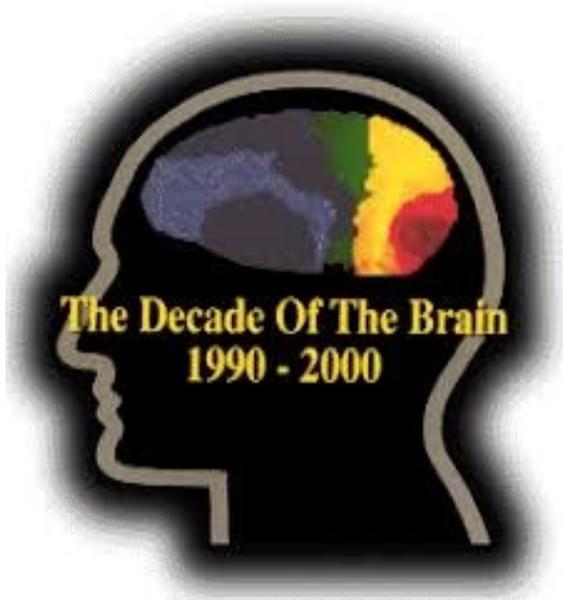
- Overview of ADHD Signs, Symptoms and Differential Dx
- Evaluation, Diagnosis and Monitoring
- Comprehensive Treatment Planning
- Use of Medications in Treatment
- Types of medications and their Use – Stimulants, nonstimulants and others

# Session 4 – Medicines for Mood and Anxiety Disorders

Jeremy Butler MD FRCP

- Uses in Psychiatry
- Types of Antidepressants – similarities and differences, Tx course/duration
- Medicines for Bipolar disorders, Tx course/duration
- Nature of Anxiety and Panic – Anxiolytic Agents (i.e. antidepressants, benzodiazepines, other agents); standing vs. PRN use

# Comprehensive Treatment Planning



- Medications are rarely a single solution to mental health challenges – especially for the complex youth that we work with.
- Medicines are only likely to be of much use if they are utilized as part of a comprehensive treatment plan.

As such, where psychiatry is involved in provision of care, I think that it is important that psychiatry works in collaboration with the family and other professional – not providing medication in isolation from the team.

# Consent to Treatment

- In Ontario, there is no defined lower age for when an individual has the right to personal consent to treatment, including for medications, surgical interventions or other procedures. Ability to provide consent is based on the individual's capacity to understand the risks versus benefits and alternatives to a treatment intervention.
- A treatment should not be administered without consent, outside of Emergency "life or death" situations where the individual is unable to provide consent and where there is no appropriate alternative 3<sup>rd</sup> party available to provide consent.
- Individuals age **16 and older** are presumed to be capable of consenting to their own treatment unless there are reasonable grounds to believe otherwise. For those under 16, a healthcare provider must assess the child's capacity to consent.

# Standing Versus “PRN” (As Needed) Medicines

- Psychotropic “PRN” medication may be appropriate in a limited number of circumstances.
- These situations are usually where a person’s complaint is intermittent or episodic, brief - but significant, rather than chronic, longstanding or continuous.
- Even so, the situation is such that we only want to treat the present episode – NOT prevent recurrence. (i.e. not epilepsy, where treatment is standing for prevention of seizures)

# Therapeutic Alliance and “PRNs”

- As “PRN” use is voluntary, there should be a discussion about risks and benefits of “PRN” use BEFORE they becoming available. This is the process of obtaining informed consent.
- Even with 3<sup>rd</sup> party consent, the patient should understand about shared responsibility for “PRN” use – medicine will not be given if either the responsible staff and the patient do not agree to use it. If threats or coercion enter into the discussion, the utility of these medicines will be undermined.
- Medications for agitation – often injectable antipsychotics...similar to the use of mechanical or physical restraint – cannot be part of “PRN” protocols – by definition these situations are emergencies.

# “PRN” Medications may commonly or occasionally be used for...

- Sleep Disorders (Hypnotics)
- Situational Anxiety (Anxiolytics, Antipsychotics)
- Panic Disorders or Attacks (Anxiolytics, Antipsychotics)
- Pain Syndromes (Analgesics)
- Agitation/Temper Outbursts/Emotional Dysregulation
- Delirium/Acute Confusional States, Brief Psychotic Reactions, intoxications “Bad trips” (more “stat” than “PRN”)
- Drug Withdrawal Syndromes

# Caveats and Cautions - I

- “PRN” may often be used in an effort to decrease the use of a drug by not supplying it regularly...but creation of an “intermittent” reinforcement schedule, may sometimes inadvertently lead to drug-seeking behaviours.
- Regular monitoring of patterns and frequency of “PRN” use is needed to ensure that use is neither excessive or interfering with the effectiveness of “standing” medications.
- This can be a problem most especially where there is irregular contact between the most responsible/prescribing physician and the rest of the clinical team.

# Caveats and Cautions - II

- “PRN” and Standing Combination Therapy may be an option to treat behavioural dysregulation; while this practice may be reasonable, it is fraught with clinical challenges...this requires good communication within the team and a positive therapeutic alliance to be effective.
- This approach presumes that standing medication provides a helpful “floor” for dysregulation. As such, having additional “PRN” medication available provides incremental additional control when it may be needed...

# Caveats and Cautions - III

- In this case, review of frequency, patterns and response to the use of “PRNs” is needed to ensure effectiveness about dosing and scheduling of the standing medicine.
- Too frequent use of “PRNs” might suggest that standing medication as administered is not doing its work...
- On the other hand, very infrequent use of “PRNs” might suggest that standing doses are higher than necessary, reluctance to use “PRNs” on the part of the staff or patient, or other barriers to their use.

# Work-up, Administration and Monitoring

- For psychotropic medications to be employed safely, there is a basic protocol of investigation and monitoring that will be required to ensure that the medication is both safe, well tolerated and effective.

“Baseline” Evaluation should include

- physical examination, note height, weight and BMI, menstrual cycle
- Lab work – blood, urine, electrocardiogram, Note allergies and history of drug sensitivities.
- Screen for medical conditions that might impact on the safety or response to medication – notably, iron deficiency and anemia, diabetes mellitus, thyroid disorders and sleep problems are relatively common and may produce symptoms that worsen or mimic mental health concerns. R/O Pregnancy

# Screening and Monitoring Tools

- Various 3<sup>rd</sup> party or self-administered instruments may be used to measure 'symptom and sign' severity, to help establish a diagnosis and assess treatment response.
- For example, Beck and Hamilton Depression Scales may be useful for mood symptoms, while the Beck or Hamilton Anxiety Scales and GAD-7 screen for Anxiety. The SNAP-IV rating scale and others may be used to monitor for ADHD. All these tools may be easily found online.
- **CADDRA.CA** is an excellent resource for information as well as tools to understand and monitor treatment of ADHD.

# Tools for Monitoring Medication Side Effects

- Tracking BMI, height and weight will help avoid problems with weight gain or loss, glucose intolerance or lipid profile.
- Dyskinesias and movement disorders are not infrequent and concerning side effects of various psychotropic medications; the AIMS (Abnormal Involuntary Movement Checklist) is useful for monitoring.
- The PMCC - Psychotropic Medication Monitoring Checklist System, developed by CPRI (Child & Parent Resource Institute) in London, provides a useful set of side-effect screens specific to various classes of medications. While Kinark is not planning formally to implement this tool, it may be helpful to become familiar with the items noted on the checklists, particularly when new medications are being introduced to a patient.

# Sleep Problems and Medications

[kinark.on.ca](http://kinark.on.ca)

BETTER OUTCOMES. TOGETHER.

# Approach to Sleep Medication Selection

- Take a history of the problem – sleep routines, diet, exercise and daytime routines. Does the person night. Weekday/weekend differences.
- Nature of sleep/wake cycle, napping, fatigue...note that snoring, drooling obesity may suggest apnea, “sheets everywhere” may suggest “restless legs,” nightmares, night terrors, sleep-walking or talking, enuresis, etc.
- Difficulty suggesting Apnea or airway obstruction may require and ENT consult and a sleep study to correctly diagnose.

# **BEARS: A screening tool for children's sleep problems from the Canadian Sleep Society.**

- Bedtime problems
- Excessive daytime sleepiness
- Awakenings during the night
- Regularity of sleep schedule
- Snoring and other sleep-related breathing problems

# ABCs of Sleep Issues for Children

- Age-appropriate bedtimes and wake-times with consistency
- **B**edtime schedules and routines
- **C**onsistency in schedules
- **D**ark and quiet location, exercise, and diet
- **E**lectronics should be avoided in the bedroom
- **F**ocus on positive sleep associations
- **G**et enough sleep each night
- **H**ealthy sleep is a great goal
- **I**ndependence when falling asleep
- **J**ust note all substances, including caffeine, alcohol, and medication

# STOP-BANG Mnemonic for Sleep Apnea

- **S** - Snoring (Do you snore loudly?)
- **T** - Tiredness (Are you tired during the day?)
- **O** - Observed (Has anyone observed you stop breathing or choke while sleeping?)
- **P** - Pressure (Do you have high blood pressure?)
- **B** - BMI (Is your body mass index over ?)
- **A** - Age (Are you middle-aged or older?)
- **N** - Neck circumference (Is your neck circumference large?)
- **G** - Gender (Are you male?)

# “Natural Products”

- **Melatonin** promotes sleep primarily by signaling darkness to the brain's "master clock," the suprachiasmatic nucleus (SCN) of the hypothalamus, helping to diminish wakefulness signals, preparing the body for rest.
- **Tryptophan** is an Amino Acid precursor to Serotonin and Melatonin
- **Magnesium** modulates GABA and reduces the activity of the N-methyl-D-aspartate (NMDA) receptor. This calms the nervous system and relax muscles, while also decreasing stress hormones such as cortisol and increasing the production of melatonin.
- **Valerian Root** may increase GABA activity

# OTC medications

- Most often these are antihistamines. The histaminergic neurotransmission system located in the posterior hypothalamus and projecting to almost all the major regions of the CNS. Strong evidence suggests that histamine has a pivotal role in the regulation of sleep-wakefulness.
- Antihistamines should generally not be a first choice – while sedating, so antihistamines may cause drowsiness, they can decrease deep sleep duration, resulting in poor quality, un-restorative sleep.
- Antihistamines will often have troublesome side effects and can be abused, addictive and dangerous in overdose.

# Sleep Medications

- Multiple Classes of Medications may be useful on either a standing or an “as needed” basis.
- Very often, doctors will not use “Hypnotics” as a first choice
- They may try to harness the sedating effects of other types of medications, believing that these may be less likely to be abused, create dependency, or be more useful to treat the underlying cause of sleep problems than a hypnotic would be.

# Prescription Hypnotics

- For many decades, insomnia treatment was dominated by benzodiazepines (Valium, Serax, Dalmane). Although these were effective for short-term insomnia, next-day residual effects, such as reduced alertness and sleepiness could affect daily activities.
- Development of tolerance, dependence, withdrawal effects, and abuse potential led to the development of new hypnotic drugs. These nonbenzodiazepine hypnotics, collectively called the “Z-drugs,” include zopiclone, zolpidem, and zaleplon.
- Zaleplon binds preferentially at the  $\alpha 1\beta 2\gamma 2$  subunit of GABA  $\gamma$ -type A receptors in the CNS, with a half-life of about one hour.

# Benzodiazepines versus Z-drugs

- Benzodiazepines such as Valium, Ativan or Xanax bind non-selectively to a site of the GABA<sub>A</sub> receptor complex, enhancing GABA activity.
- Whereas most benzodiazepine hypnotics bind to all GABA<sub>A</sub> receptors with similar affinity, zaleplon and zolpidem **have a more selective affinity for some of its subunits**. This more limited binding seems to significantly decrease the risks of addiction, tolerance and withdrawal associated with regular or high dose use of benzodiazepines.

# Other Prescription Medications

- Antidepressants – most SSRI antidepressants aren't very sedating, so they tend to have small direct impact on sleep. They may improve sleep quality by decreasing REM ("dream") sleep...so for nightmares, SSRIs may decrease their frequency and intensity. REM sleep is increased on sleep studies of depressed individuals.
- Some Antidepressants such as Trazadone and Mirtazapine may be quite sedating. Mirtazapine decreases sleep latency and increases deep sleep without suppressing REM sleep (unlike SSRIs). It acts on serotonin, alpha1-adrenergic and histamine systems. Weight gain is a common side effect of mirtazapine use.

# Antipsychotics and Sleep

- **Dopamine receptor antagonism:** While antipsychotics treat psychosis by blocking D2 dopamine receptors, this action also reduces the wake-promoting effects of dopamine, resulting in sedation. Similar to trazadone and mirtazapine, antipsychotics act on serotonin, alpha-adrenergic and histamine systems.
- Excessive use or reliance on these medications, because of their more concerning side-effect profiles, should be reserved for patients who require antipsychotics on a regular basis for treatment of their underlying condition.

# Alpha-Adrenergic Antagonists Agents

- Agents such as prazosin, guanfacine and clonidine have been used for years in the treatment of high blood pressure and tachy-arrhythmias.
- Because of their ability to decrease stress and “fight or flight” responses, they may be very useful in decreasing the frequency or severity of night terrors (panicky hyper-arousal taking place during deep, Stage IV sleep) as well as panic attacks, high-anxiety or irritability states during the day.

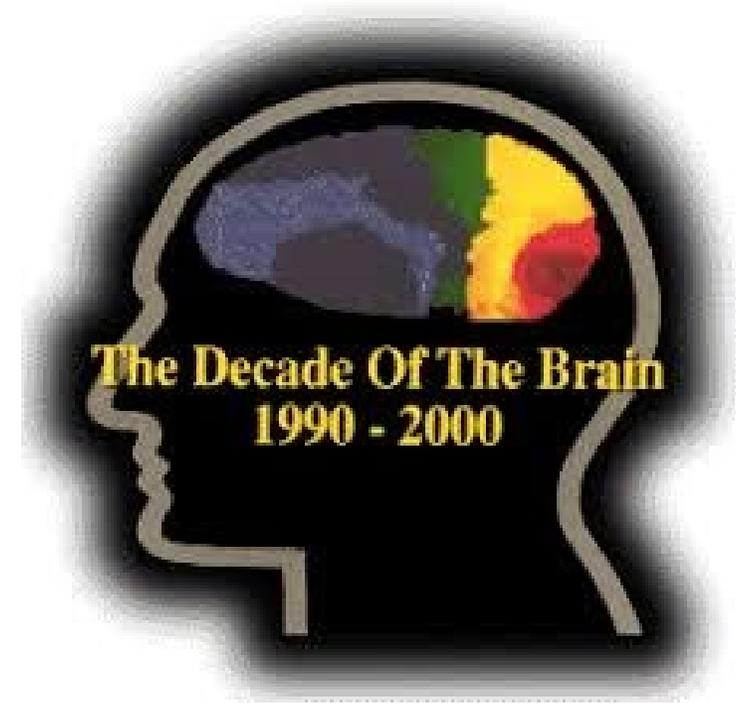
# Choice of Medication - I

- For occasional and minor disturbance, “PRN” treatment will likely be more appropriate than standing medicine.
- Use natural products and supplements as a first choice where possible. Warm milk is a good source of tryptophan. Some brands of melatonin are more effective than others- so if you find one brand particularly helpful – stick with it. Melatonin is mainly for sleep induction; tryptophan is often more effective than Melatonin for sleep maintenance, but high doses may be needed.
- Avoid Antihistamines and benzodiazepines, because of possible abuse, dependency or toxicity.

# Choice of Medication - II

- Avoid antipsychotics except where useful for managing dysregulation or symptoms where an antipsychotic is otherwise appropriate.
- Avoid the benzodiazepines where possible, the “Z-drugs” may be as effective, better tolerated and safer.
- For standing nightly treatment, sedating antidepressants may be most appropriate where mood and anxiety/PTSD features are part of the clinical pictures. Side effects may be problematic. For many of these patients, alpha-adrenergic blockers are a good choice. Long-term use may be required, but is never suggested, and tapering will be helpful.

Thank You !!!



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