Office Management of Patients Living With Schizophrenia

Dr. Richardson O. Tachere, MD; MPH; M.A (Health Mgt.); FRCPC.

Psychiatrist, CMHA, Kitchener.

A Day in Psychiatry - 2017

Wednesday November 8th, 2017

Bingeman's Conference Centre

Kitchener, Ontario.

Office Management of Patients Living with Schizophrenia

Dr. Richardson .O. Tachere

Day in Psychiatry 2017

Declaration of Conflict of Interest:

I DO NOT have any affiliation with any pharmaceutical, medical device or communication organization.

I DO NOT INTEND to make therapeutic recommendations for medications that have not received regulatory approval

(e.g. “off-label”use).

Office Management of Patients Living with Schizophrenia

This 2017 **Day in Psychiatry** educational event has received unrestricted educational grants from the following organizations:

- Lundbeck
- Otsuka
- Pfizer
- Janssen
- Purdue
- Shire
- Sunovion
- KW Guardian Pharmacy
- HLS Therapeutics
- Allergan

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Mitigating Potential Conflicts of Interest:

Not applicable

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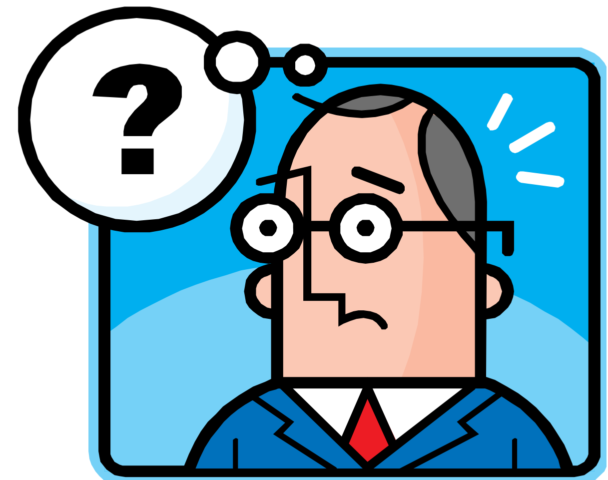
Learning Goals

1. Discuss the emerging trends in the concept of “psychosis” and its differential diagnoses.
2. Outline the diagnostic criteria and clinical features of schizophrenia.
3. Describe evidence-based treatment options for schizophrenia, including strategies for monitoring and management of side-effects.
4. Summarize resources available in our community for patients with schizophrenia and other severe & persistent mental illnesses.

- What is the relevance of this topic?



Introduction:

- Schizophrenia is a devastating illness:
  - ➢ robs young people of their potentials;
  - ➢ tears families apart;
  - ➢ has an enormous burden on society (financial, legal, social, etc.)

Facts:

- Among the top 25 leading causes of disability globally
- ~ 3% of the total burden of human disease
- ~ 1% point prevalence
- > 60% of patients with the first episode of the illness have persistence of symptoms & impairment in various domains of functioning.

Facts:

- In Canada:

  - hospital bed occupancy: 1 in 12

    (higher than any other single disease)

  - direct health & non-health care costs ~ $2 billion/yr.

  - indirect costs (loss of productivity, etc.) ~$4.8 bill/yr.

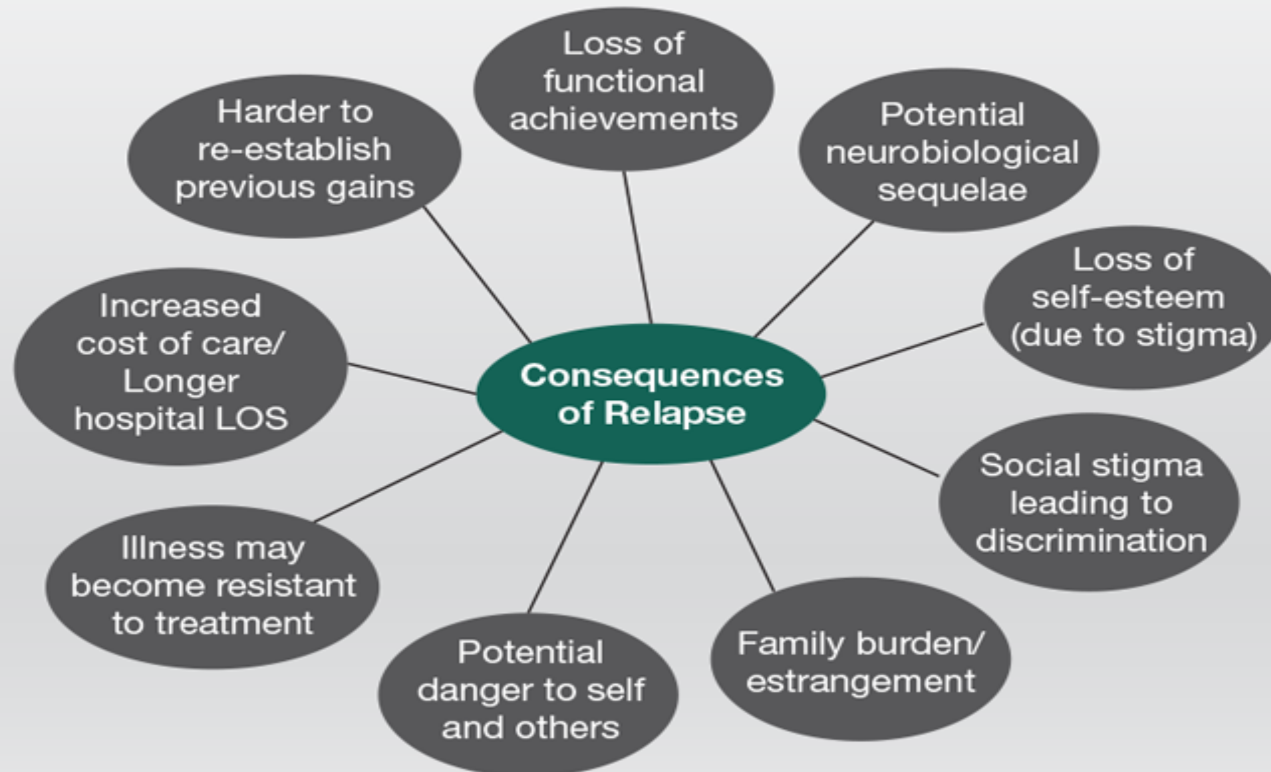
Facts:

- Peak age of onset for first psychotic episode:

  - Males: late teens to early/mid-20s;

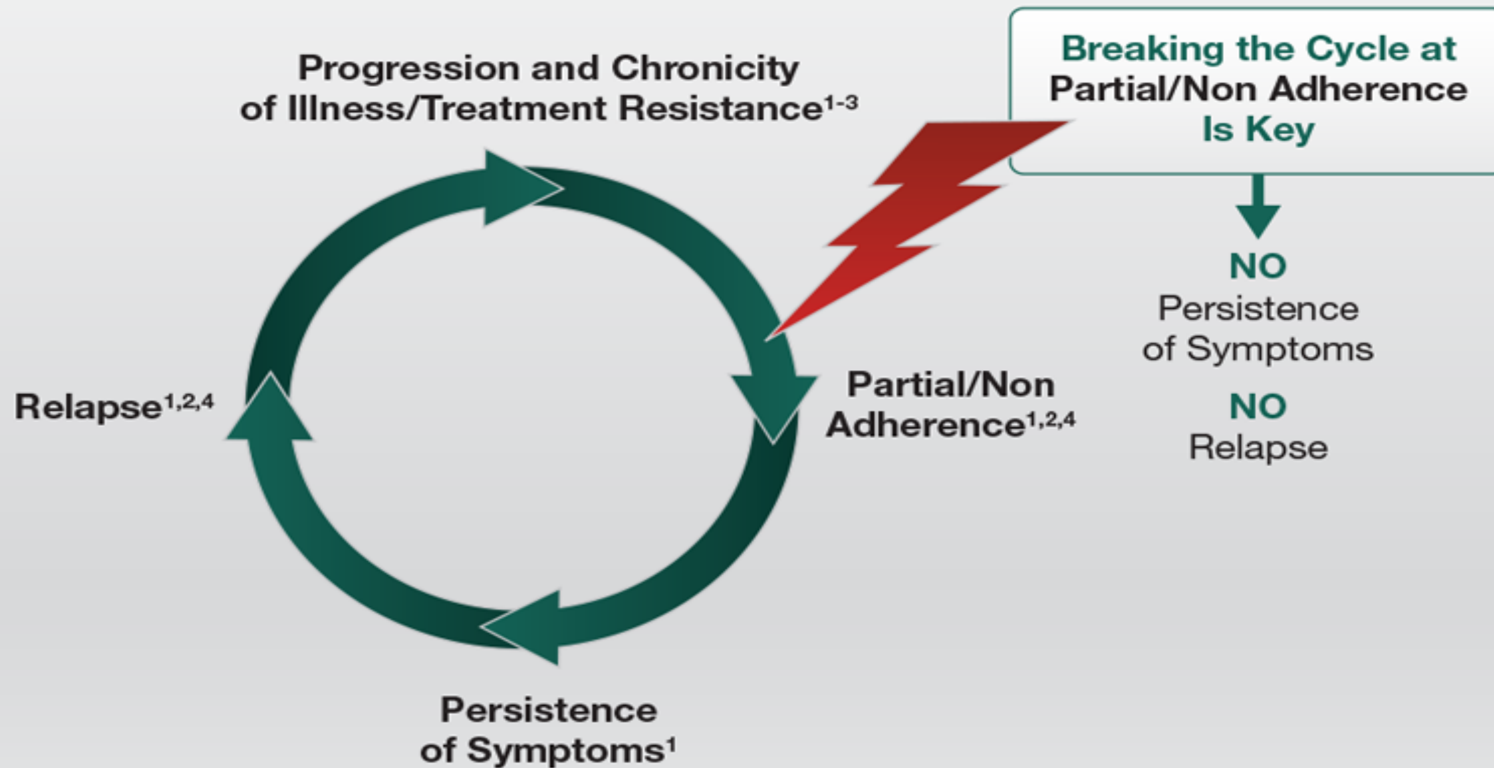
  - Females: mid/late-20s.

- Early recognition and uninterrupted treatment can prevent relapses…



PeerVoice

The Vicious Cycle in Schizophrenia: Can it Be Broken?



- Community-based treatment & extensive collaboration!

Format: Practical & Interactive

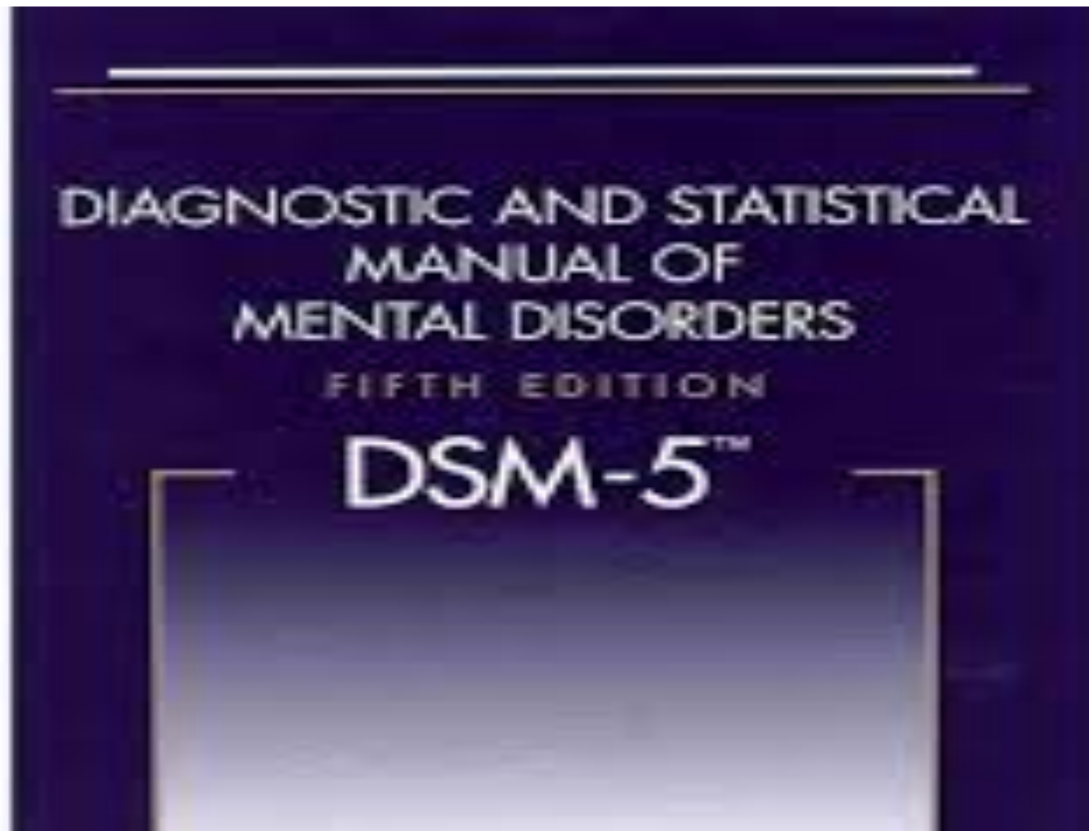
- a) Review of basic knowledge
- b) Knowledge application via:
  - Case-based learning: 2 common scenarios
  - FAQs: 5 common questions

- What is psychosis?

The concept of psychosis

- The word ‘psychosis’ originated from two Greek words – *“psyche”* (soul/mind) & *“osis”* (abnormal condition).
- 1841: Karl Friedrich Canstatt: 1st used the term ‘psychosis’ as an abbreviation of *“psychic neurosis”* (neurosis then referred to any nervous system disease).
- 1845: Ernst von Feuchtersleben: 1st used ‘psychosis’ in place of terms such as insanity & madness.

The contemporary concept of psychosis:



The contemporary concept of psychosis

DSM-5: Symptoms of psychosis occur in 5 domains -

- delusions
- hallucinations
- disorganized thinking (speech)
- grossly disorganized or abnormal motor behavior (including catatonia) &
- negative symptoms.

Reality testing…

- Is the ability to differentiate between the external world & the internal world…to accurately judge the relation between the self & the environment.

Definition of psychosis:

- Psychosis refers to an **impairment of reality testing** & mental functioning *manifested by* hallucinations, delusions, thought disorganization and/or abnormal behavior.

Symptoms of psychosis explained

- Hallucinations — Perception-like experiences that occur without an external stimulus.
- Delusions — Fixed false beliefs that are not amenable to reasoning & not in keeping with patient's sociocultural & religious backgrounds.
- Thought disorganization — Disruption in the logical thought process which may manifest as loose associations, nonsensical speech or bizarre behavior.

- **What clinical conditions cause psychosis?**

Differential Diagnosis of Psychosis

- Endless List!

Differential Diagnosis: 3 broad groups

- **Psychoses:**
- (a) due to a mental or psychological disorder
- (b) due to a another medical condition
- (c) due to a substance (medication or drug of abuse)

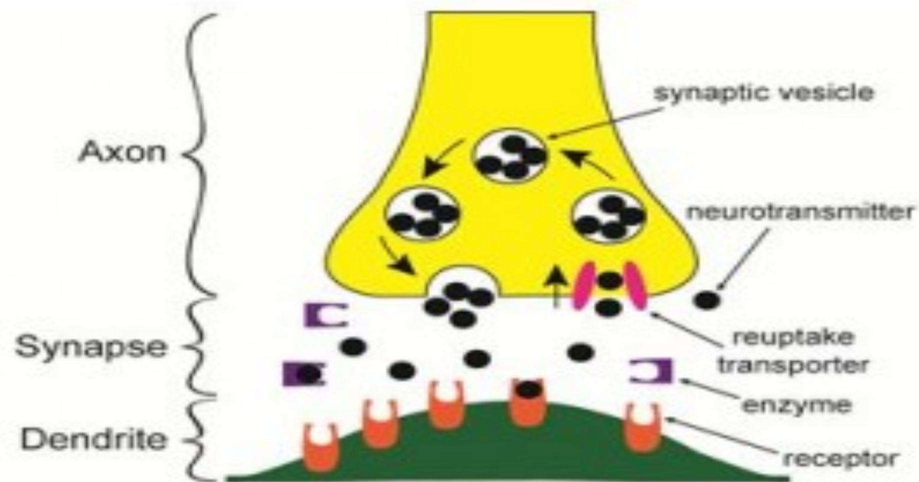
Examples…

Mental or Psychological	Other medical illnesses	Substances
Schizophrenia	Infections	Cocaine
Bipolar	Electrolyte imbalances	LSD
MDD, etc.	Brain tumors, etc.	Amphetamines, etc.

- **What is the pathophysiology of psychosis?**

Pathophysiology:

- Neurotransmitter Systems



Neurotransmitter systems: (a) Dopamine

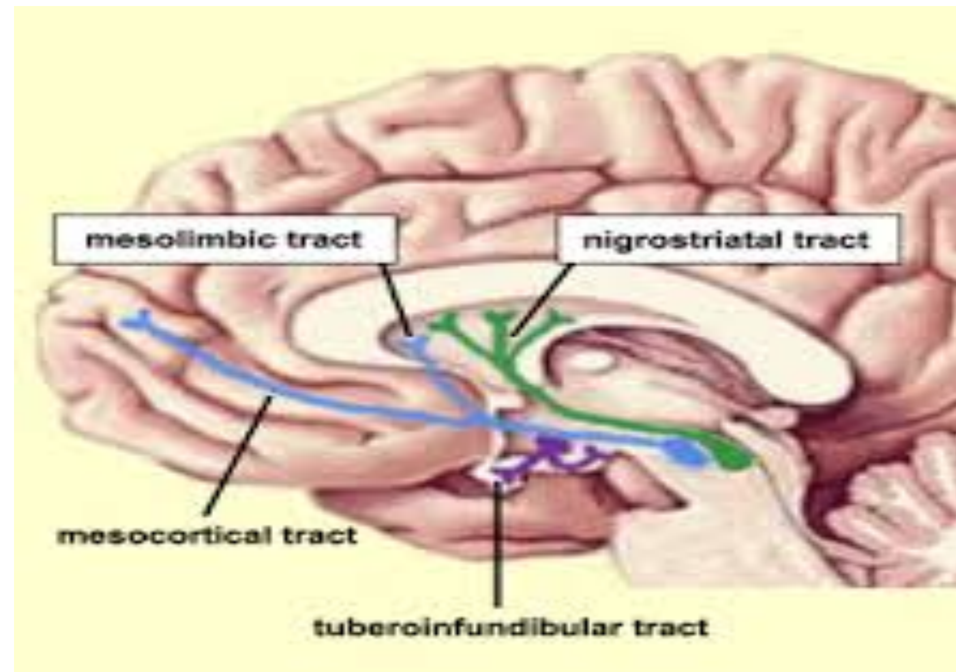
- **Hypothesis:* Hyperactivity in ML & hypoactivity in MS.
- 4 main Pathways:

-Mesolimbic

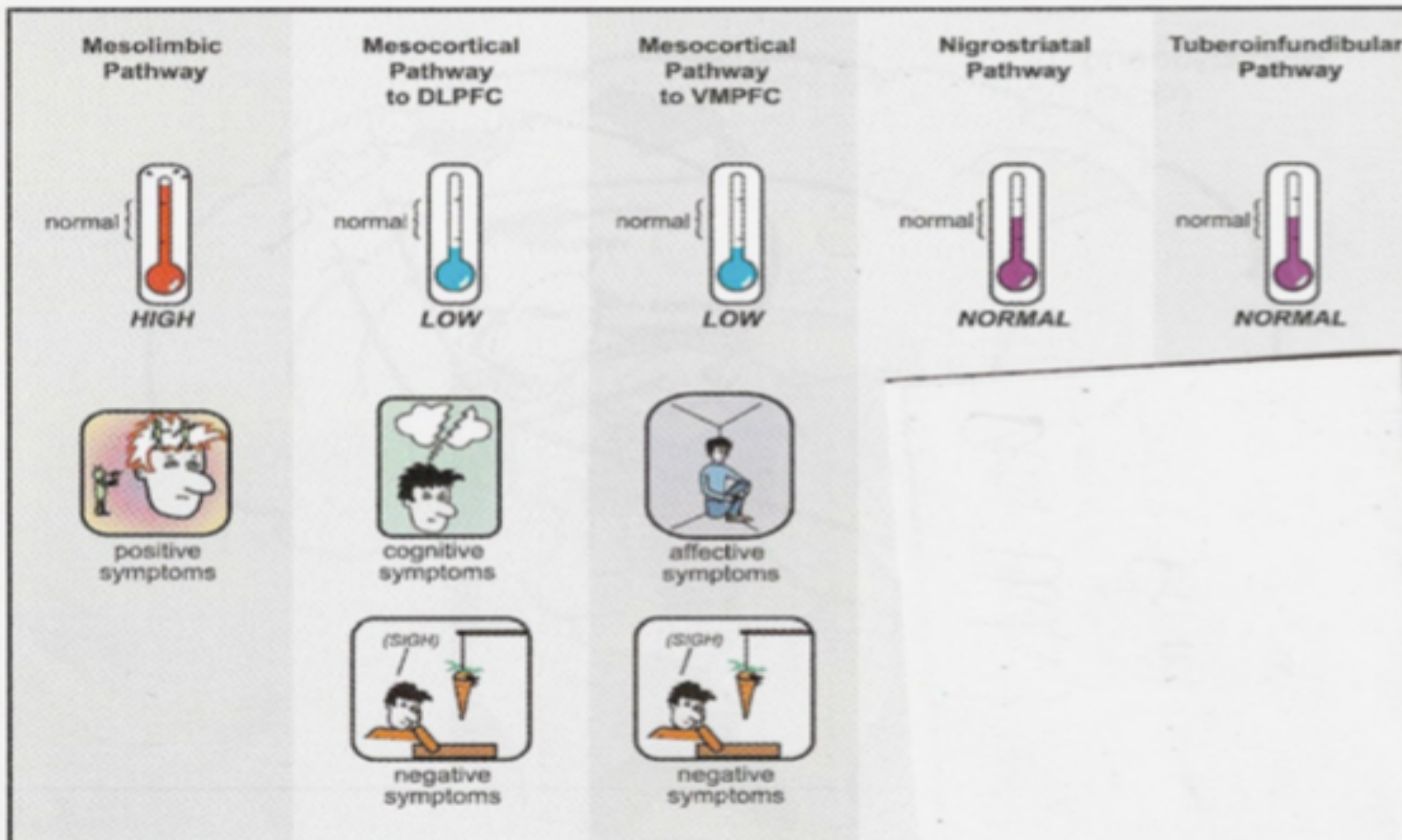
-Mesocortical

-Nigrostriatal

-Tuberoinfundibular



The Integrated DA Hypothesis of Schizophrenia



Neurotransmitter systems: (a) Dopamine…

- *Merits:* *Amphetamine causes psychotic symptoms.
  *All known antipsychotic drugs block dopamine (esp. D_2).

- *Demerits:* *Does not account for negative symptoms.
  *Patients still have persistent psychotic symptoms despite effective D_2 blockade.

Neurotransmitter systems: (b) Glutamate

- The major excitatory neurotransmitter in the brain.
- 3 groups of receptors:

-**NMDA**: N-methyl-D-aspartate

-**AMPA**: α-amino-3-hydroxyl-5methyl-4-isoxazolepropionic acid

-**Kainate**

Neurotransmitter systems: (b) Glutamate…

- *Hypothesis:* NMDA receptor hypoactivity.
- *Merits:* *Inhibition of NMDA receptors with Ketamine & PCP causes a cluster of psychotic symptoms (both positive & negative).

*Many of the schizophrenia-susceptible genes identified also regulate glutamate transmission.

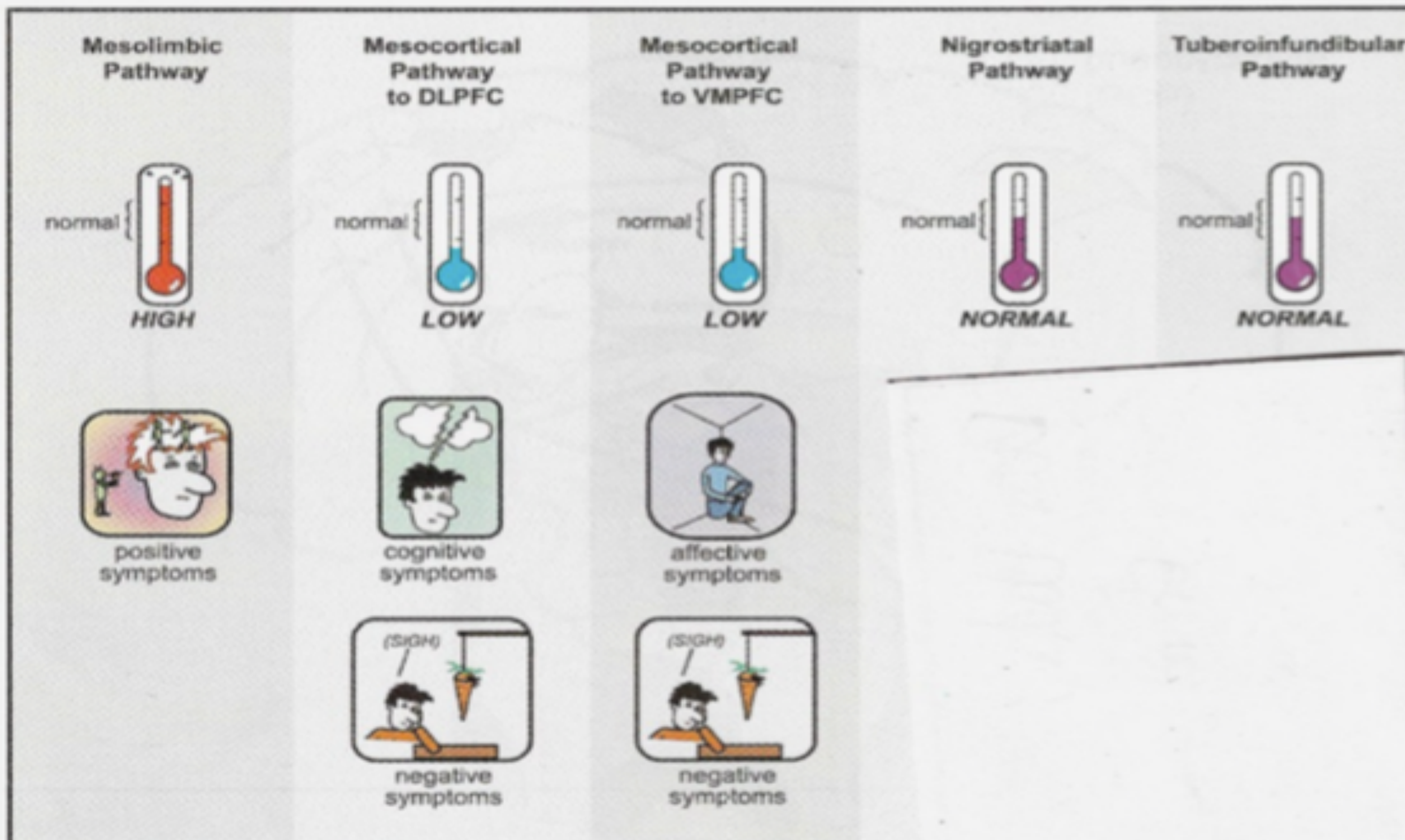
*Post-mortem studies show abnormalities in glutamatergic synapses.

Contemporary Hybrid Hypothesis : Glutamate & Dopamine

- Dopamine hyperactivity is the downstream consequence of glutamate dysfunction in the prefrontal cortex & hippocampus.

- How do antipsychotic medications work?

The Integrated DA Hypothesis of Schizophrenia



Mechanisms of Action

- Exact mechanism is unknown - primary action is mainly attributed to D2 blockade.
- SGAs have affinities for multiple DA & 5HT receptors, e.g. D2, D3, D4, 5-HT_{1A}, 5-HT_{2A}, 5-HT_{2C}, 5-HT_7 etc. PLUS actions at DA, 5HT & Nor-E reuptake transporters.

Some commonly used antipsychotics

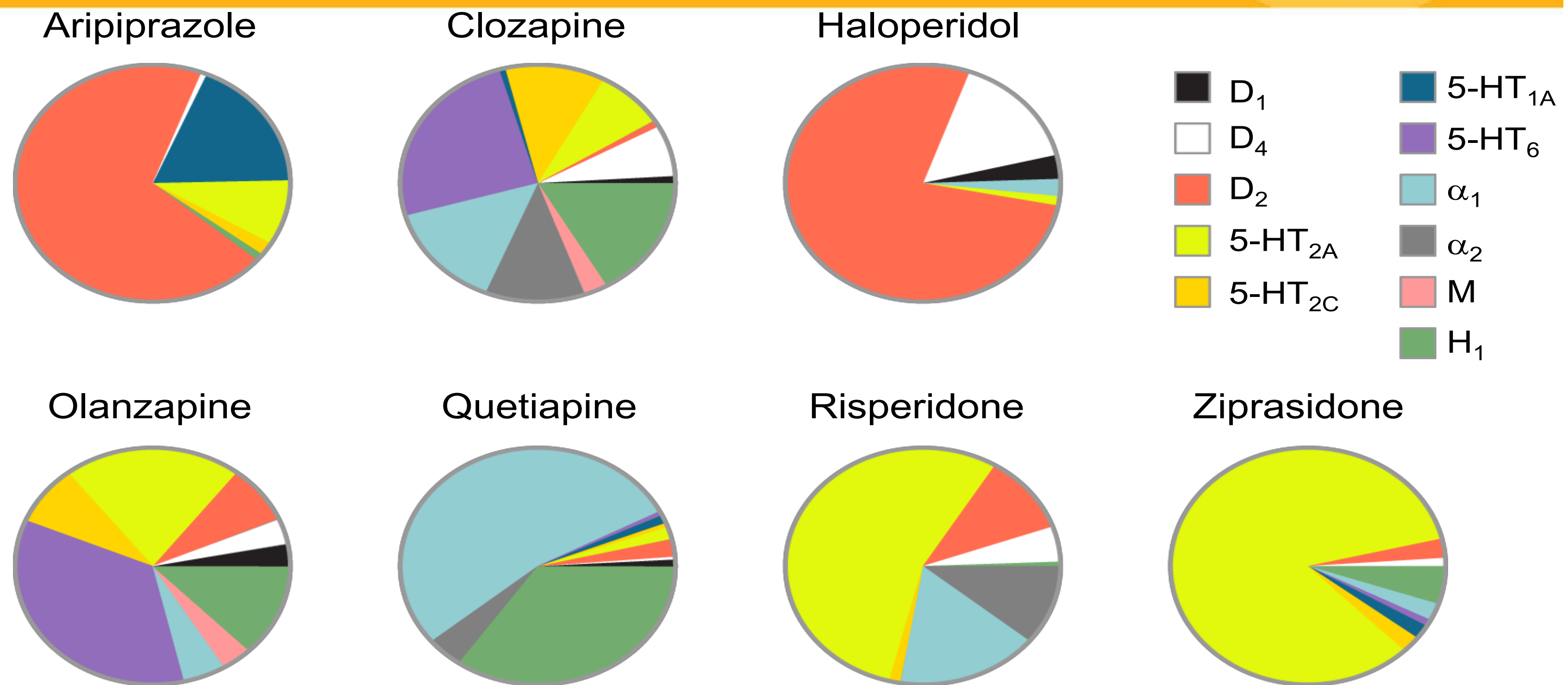
❖ FGAs

- Haloperidol
- Chlopromazine
- Perphenazine
- Zuclopenthixol
- Fluphenazine

❖ SGAs

- Risperidone
- Olanzapine
- Quetiapine
- Aripriprazole
- Clozapine

Variation in receptor profiles (slide courtesy: Dr. A. Labelle – Univ. of Ottawa)



Bymaster FP et al. Neuropsychopharmacology 1996;14(2):87-96. Schotte A et al. Psychopharmacology (Berl) 1996;124(1-2):57-73.
Lawler C et al. Neuropsychopharmacology 1999;20(6):612-27. Corbett R et al. CNS Drug Reviews 1997;3(2):120-47.

Mechanisms of Action

- SGAs are distinguished by:
  - (a) greater affinity for antagonism of the $5HT_{2A}$ vs. D2 receptor;
  - (b) fast dissociation from the D2 receptor (rapid dissociation theory).

Mechanisms of Action

- The clinical significance of actions at many of these receptors is presently unknown but may contribute to the clinical effects of these agents.
- There is significant variation in the receptor profiles of the SGAs .

- **How do we diagnose schizophrenia?**

Schizophrenia

Diagnostic Criteria **295.90 (F20.9)**

A. Two (or more) of the following, each present for a significant portion of time during a 1-month period (or less if successfully treated). At least one of these must be (1), (2), or (3):

1. Delusions.
2. Hallucinations.
3. Disorganized speech (e.g., frequent derailment or incoherence).
4. Grossly disorganized or catatonic behavior.
5. Negative symptoms (i.e., diminished emotional expression or avolition).

B. For a significant portion of the time since the onset of the disturbance, level of functioning in one or more major areas, such as work, interpersonal relations, or self-care, is markedly below the level achieved prior to the onset (or when the onset is in childhood or adolescence, there is failure to achieve expected level of interpersonal, academic, or occupational functioning).

C. Continuous signs of the disturbance persist for at least 6 months. This 6-month period must include at least 1 month of symptoms (or less if successfully treated) that meet Criterion A (i.e., active-phase symptoms) and may include periods of prodromal or residual symptoms. During these prodromal or residual periods, the signs of the disturbance may be manifested by only negative symptoms or by two or more symptoms listed in Criterion A present in an attenuated form (e.g., odd beliefs, unusual perceptual experiences).

D. Schizoaffective disorder and depressive or bipolar disorder with psychotic features have been ruled out because either 1) no major depressive or manic episodes have occurred concurrently with the active-phase symptoms, or 2) if mood episodes have occurred during active-phase symptoms, they have been present for a minority of the total duration of the active and residual periods of the illness.

E. The disturbance is not attributable to the physiological effects of a substance (e.g., a drug of abuse, a medication) or another medical condition.

F. If there is a history of autism spectrum disorder or a communication disorder of childhood onset, the additional diagnosis of schizophrenia is made only if prominent delusions or hallucinations, in addition to the other required symptoms of schizophrenia, are also present for at least 1 month (or less if successfully treated).

DSM 5 Criteria: Summary

- Symptoms: 2 or more of the 5 psychotic symptoms
- Duration: at least for 6months (with > 1mth of acute phase symptoms, i.e. delusions, hallucinations & disorganized speech/incoherence/derailment)
- Functional impairment
- **Note:** One of the obstacles to early recognition and treatment is **lack of insight**.

Format: Practical & Interactive

- a) Review of basic knowledge ✓
- b) Knowledge application via:
  - Case-based learning: 2 common scenarios
  - FAQs: 5 common questions

Please

Case 1:

Case 2:

HOT TOPICS!

HOT TOPICS…

- The following seven slides are courtesy:

Dr. J. Richard, MD; MSc; FRCPC.

- Psychiatrist, Prevention & Early Intervention in Psychosis (PEPP) Program, London Health Sciences Centre;
- Asst. Professor of Psychiatry,

University of Western Ontario, London.

Hot Topics: Long acting injectables

- The proportion of community patients with schizophrenia reported to be partially or totally nonadherent to oral APs ranges from 45% to 90%, with no differences evident between oral FGAs and oral SGAs
- Physician attitudes represent a major barrier to LAI use
- The existence and potential use of LAIs for AP therapy should be discussed with patients and families at all phases of illness, including the critical period of the first 2 to 5 years.
- In all cases, patients' opinion about the choice of an LAI should be considered regarding knowledge of its effectiveness, ease of administration, frequency of injections, and cost.

Long-Acting Injectable Antipsychotics: Recommendations for Clinicians
CJP. **2013; Malla et al. 58(5 Suppl 1)1S-36S**

Violence in Psychotic Disorders

- Most people with schizophrenia are NOT aggressive and are more frequently victimized than general population
- ***Aggression***: more frequent in:
  - younger males
  - past history of violence
  - non-adherence to treatment
  - substance abuse
  - History of impulsivity

Nielssen et al. 2012. Overview of Violence to Self and Others During the First Episode of Psychosis. Journal of Clinical Psychiatry 73(5)

Suicide and Schizophrenia

- Studies in 1970s and 1980s put the risk of suicide in schizophrenia at 10%
- More recent large cohort follow up studies have put the risk at 5-6%
- Time trend data supports that the risk has declined since 1980s
- Risk is highest earlier in the illness, especially after hospital discharges
- Additional risk factors are

Young age	Poor medication adherence
Male	Comorbid substance use
Social isolation	History of suicide attempts
Higher education level	Family history of depression
Depressed mood	Family history of suicide attempts

- 20% of individuals with schizophrenia will attempt suicide on one or more occasions

Nordentoft et al. 2015. Suicidal behaviour and mortality in first episode psychosis. *J Nervous & Mental Diseases*. 203: 387-394.

Trauma and Psychosis

- Childhood trauma and neglect has been established as an independent risk factor in psychosis.
- Meta analyses suggest that individuals with a history of childhood trauma have nearly 3x the risk of developing psychosis
- It is also associated with more severe and treatment resistant positive symptoms in individuals suffering from schizophrenia

Davis et al. 2016. *Neurosci Biobehav. Rev* 65: 185-94.
Van Winket et al. 2013 *Can J. Psychiatry* 58(1) 44-51

Hot Topics: Cannabis and psychosis

- In the last few years, there is strong evidence that cannabis use ***among youth*** plays a causal role in inducing first episode psychosis
- Younger age at onset of cannabis use and regular cannabis use was significantly related to younger age at onset and causing new incident cases of psychosis

Cannabis use and age at onset of symptoms in subjects at clinical high risk for psychosis. 2012.Dragt et al. *Acta Psychiatrica Scandinavia. 125: 45-53*

Age of onset of cannabis use is associated with age of onset of high-risk symptoms for psychosis. 2010. Dragt et al. *Canadian Journal of Psychiatry*. Mar;55(3):165-71

Cannabis Use and Earlier Onset of Psychosis. Large et al. 2011. *Archives of general psychiatry*. 2011;68(6):555-561

Hot Topics: Cannabis and Psychosis

- The Swedish Conscript Study found a dose response relationship between use prior to age 18 and incident schizophrenia by age 45, with a 3-fold increase in risk in those who reported using cannabis more than 50 times prior to age 18
- The Dunedin birth cohort study found a particularly strong association in young people who used prior to age 15 (OR 11 95% CI 1.8 – 70) and a psychotic disorder
- higher potency cannabis confers higher risk of psychosis
- Cannabis users have, on average, a 2 to 6 year younger age of onset
- Meta analyses of all studies suggest that regular cannabis use at least doubles the risk of developing a chronic psychotic disorder
- But MOST cannabis users do not develop psychosis, suggesting unknown gene/environment mediators for this effect

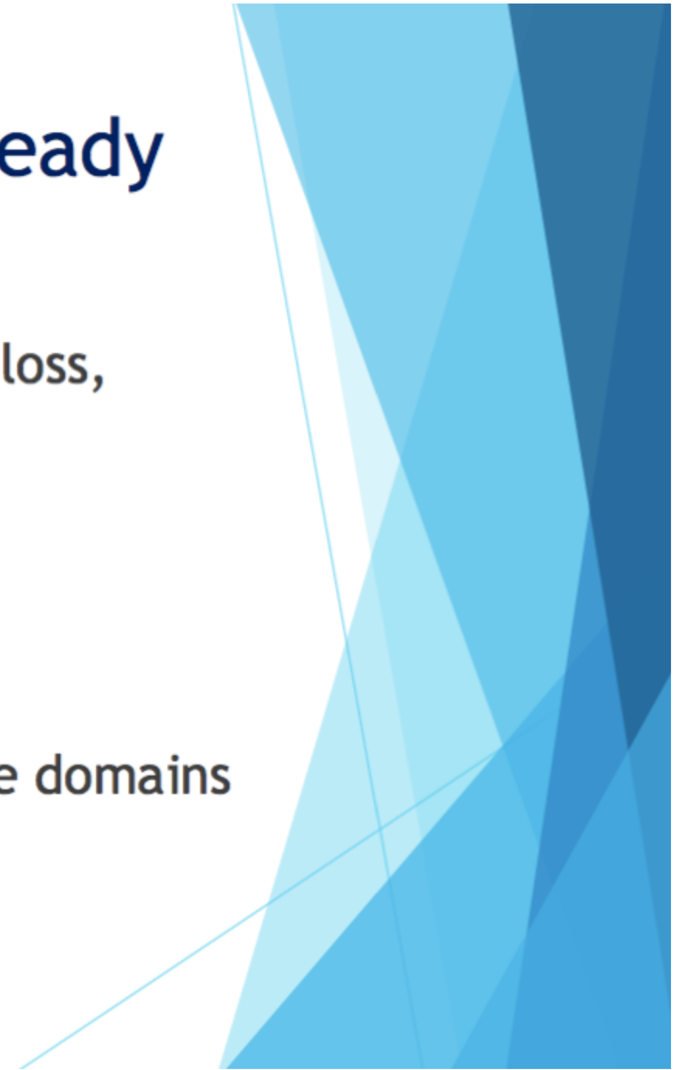
Gage et al. 2016. *Biological Psychiatry* Volume79(Issue7) p.549To-556
Di Forti et al. 2015. *Lancet Psychiatry* 2: 233-238
O'Donoghue et al. 2016. *Schizophrenia Res.* 168 p 106-112

Cannabis use among individuals already diagnosed with schizophrenia

- Associated with accelerated grey matter volume loss, more refractory symptoms and poorer outcomes

Cannabis use among youth without a psychotic disorder

- Associated with transient deficits across cognitive domains similar to those found in schizophrenia



Notes…

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- *Global Burden of Disease Study 2013 Collaborators**: Global, regional, and national incidence, prevalence, and years lived with disability for 301 acute and chronic diseases and injuries in 188 countries, 1990–2013: a systematic analysis for the Global Burden of Disease Study 2013. *Lancet 2015; 386: 743–800.*
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Additional comments, questions, etc.

Contact:

Dr. Richardson .O. Tachere

Email: rtachere@cmhaww.ca

The End