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Transition to psychosis in Cannabis abusers

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No conflict of interest

Transition to psychosis in Cannabis abusers

Cannabis and Psychosis

- 50-80%
- Ultra high risk candidates & Early psychosis
- Early phase or first episode schizophrenia
- Multifactorial along with Psychosocial factors
- Social determinants of health (SDH)
- Ethnic and geographical differences

Thomas H. A community survey of adverse effects of cannabis use. Drug Alcohol Depend 1996;42(3):201-7.
Manrique-Garcia E, Zammit S, Dalman C, Hemmingsson T, Andreasson S, Allebeck P. Cannabis, schizophrenia and other non-affective psychoses: 35 years of follow-up of a population-based cohort. Psychol Med 2011;1-8.
Stilo SA, Murray RM. The epidemiology of schizophrenia: replacing dogma with knowledge. Dialogues Clin Neurosci 2010;12(3):305-15.
van Os J, Kenis G, Rutten BP. The environment and schizophrenia. Nature 2010;468(7321):203-12.

Pathway to psychosis in cannabis abusers : understanding

- Consensus
- Controversies
- Hypothesis
- Causal relationship
- Important Considerations in this transition:
- Timeline, Severity, Candidate, & the Substance

van Os J, Kenis G, Rutten BP. The environment and schizophrenia. Nature 2010;468(7321):203-12.
Medical marijuana and the mind: More is known about the psychiatric risks than the benefits. Harv Ment Health Letter 2010;26(10):1-3. Received from: http://www.health.harvard.edu/newsletters/Harvard_Mental_Health_Letter/2010/April/medical-marijuana-and-the-mind.last accessed on 11.8.11.

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The question to question?

- Sequential multifactorial changes which can explain transition to psychosis across developmental period.
- Factors like: individual characteristics, environmental, and neurobiological.
- Determine therapeutic and preventive interventions

Welch KA, McIntosh AM, Job DE, Whalley HC, Moorhead TW, Hall J, et al. The impact of substance use on brain structure in people at high risk of developing schizophrenia. Schizophr Bull. 2010;37:1066–76Roser P, Vollenweider FX, Kawohl W. Potential antipsychotic properties of central cannabinoid (CB1) receptor antagonists. World J Biol Psychiatry 2010;11(2 Pt 2):208-19.

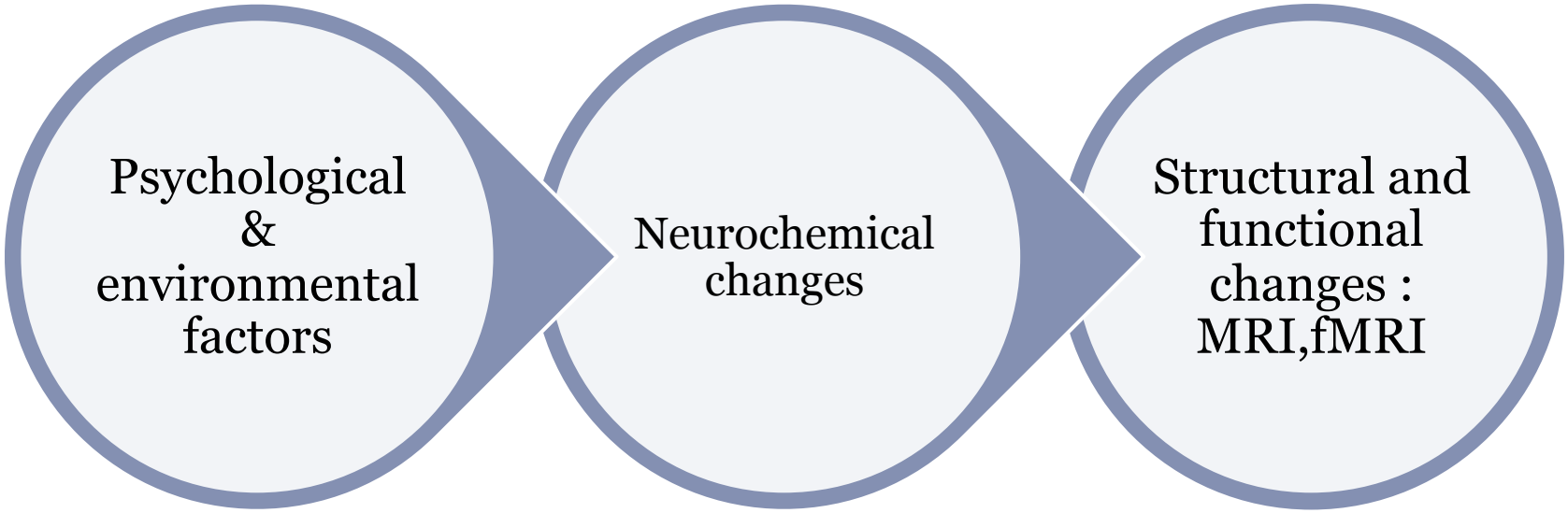
Proposed model

- Emphasizes the interaction between genetic and environmental variables, and their influence on neurodevelopment

Development of psychopathology

Verweij KJ, Zietsch BP, Lynskey MT, Medland SE, Neale MC, Martin NG, et al. Genetic and environmental influences on cannabis use initiation and problematic use: a meta-analysis of twin studies. Addiction. 2010;105(3):417-430.

Harley M, Kelleher I, Clarke M, Lynch F, Arseneault L, Connor D et al. Cannabis use and childhood trauma interact additively to increase the risk of psychotic symptoms in adolescence. Psychol Med 2010;40(10):1627-34.


Psychological & environmental factors
Neurochemical changes
Structural and functional changes : MRI,fMRI

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Main theme

It seems that neurobiological changes and the age at which these changes occur in cannabis related – psychosis are parallel or similar to those occurring in schizophrenia

Linszen D, van Amelsvoort T. Cannabis and psychosis: an update on course and biological plausible mechanisms. Curr Opin Psychiatry 2007; 20: 116-120.
D'Souza DC, Pittman B, Perry E, Simen A. Preliminary evidence of cannabinoid effects on brain-derived neurotropic factor (BDNF) levels in humans. Psychopharmacol 2009;202:569-578.

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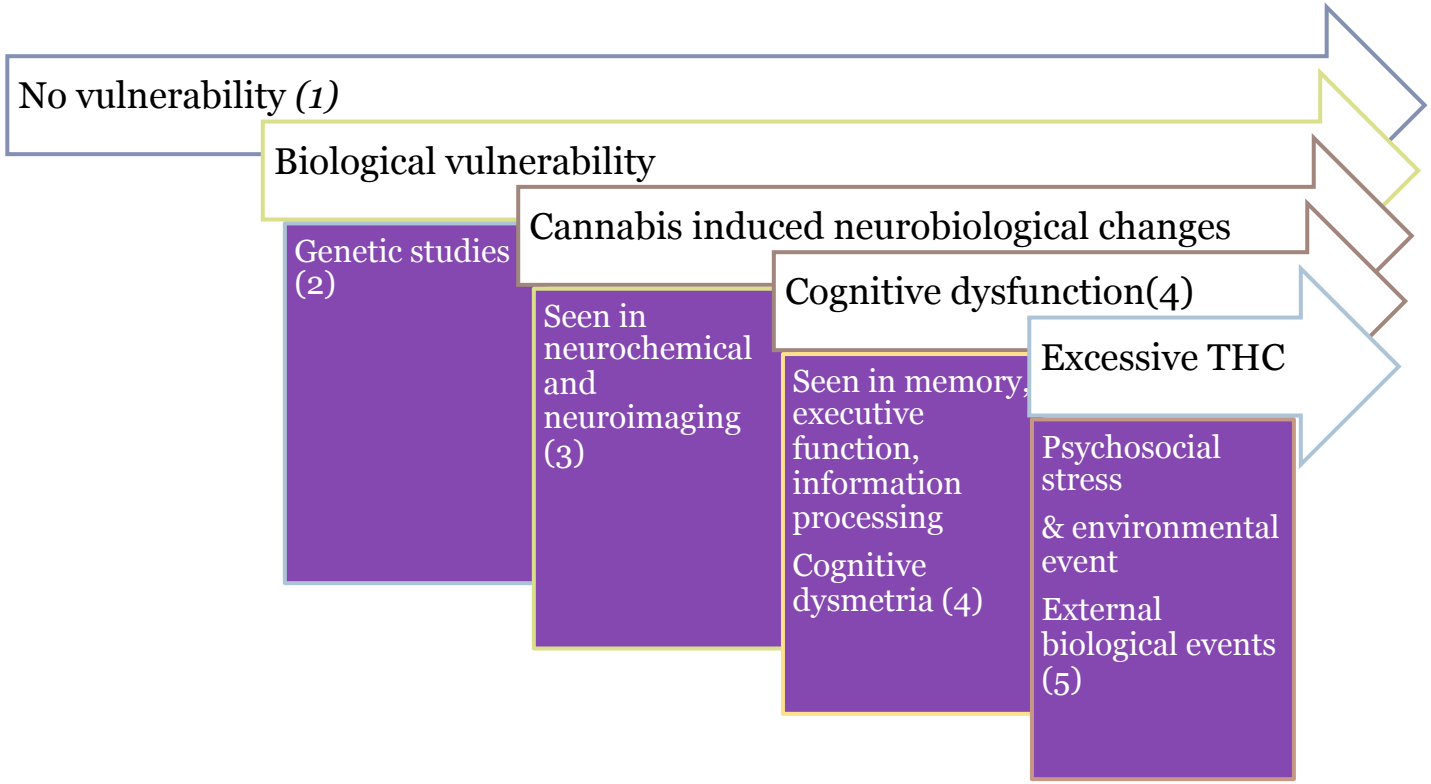
Abstract/ Summary



DeRosse P, Kaplan A, Burdick KE, Lencz T, Malhotra AK. Cannabis use disorders in schizophrenia: effects on cognition and symptoms. Schizophr.Res. 2010;120(1-3):95-100.
Battisti RA, Roodenrys S, Johnstone SJ, Respondek C, Hermens DF, Solowij N. Chronic use of cannabis and poor neural efficiency in verbal memory ability. Psychopharmacology (Berl) 2010.
Ashtari M, Cervellione K, Cottone J, Ardekani BA, Kumra S. Diffusion abnormalities in adolescents and young adults with a history of heavy cannabis use. J Psychiatr Res 2009;43:189-204.

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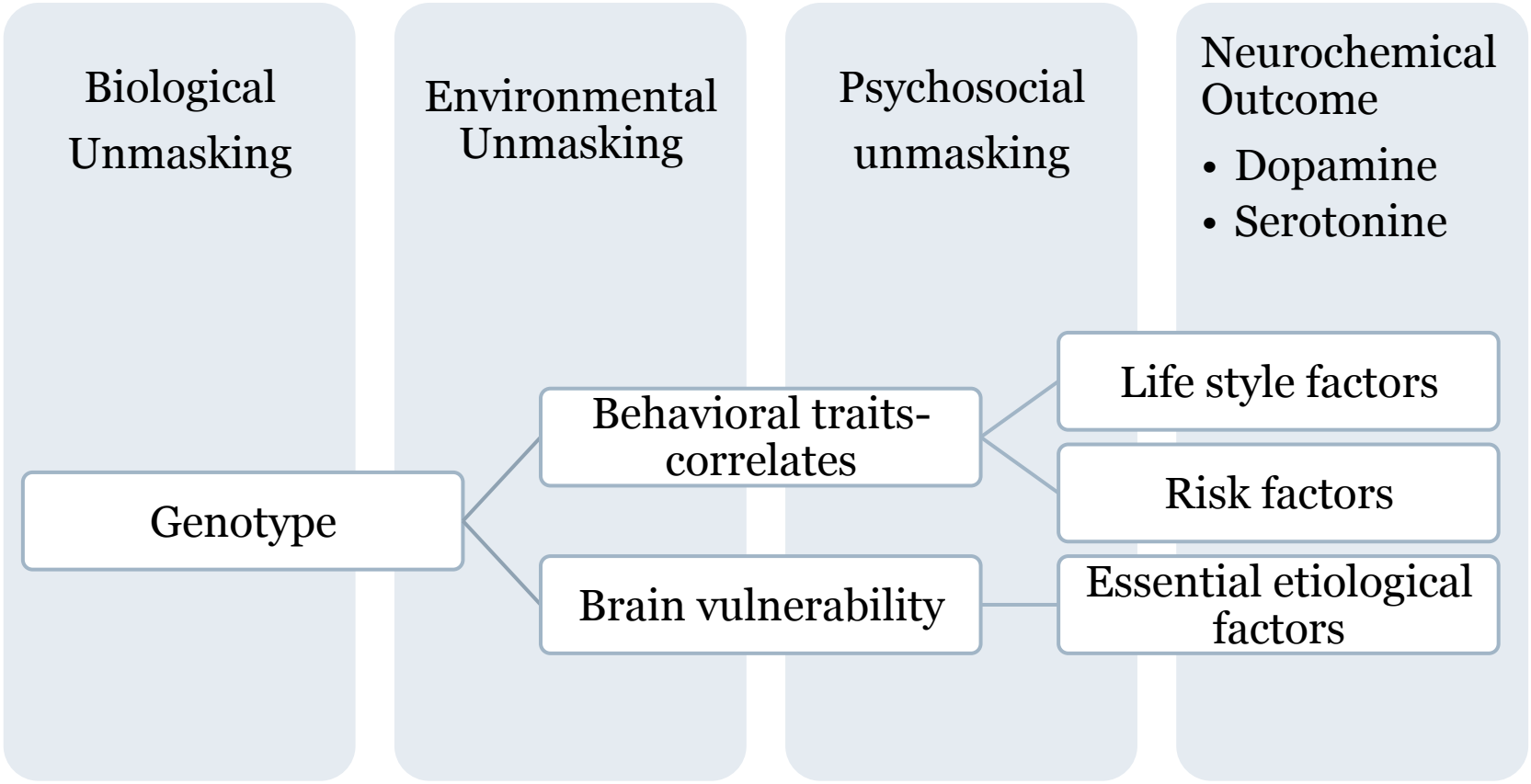
Risk factors and Psychopathology Vulnerability: biological and psychosocial



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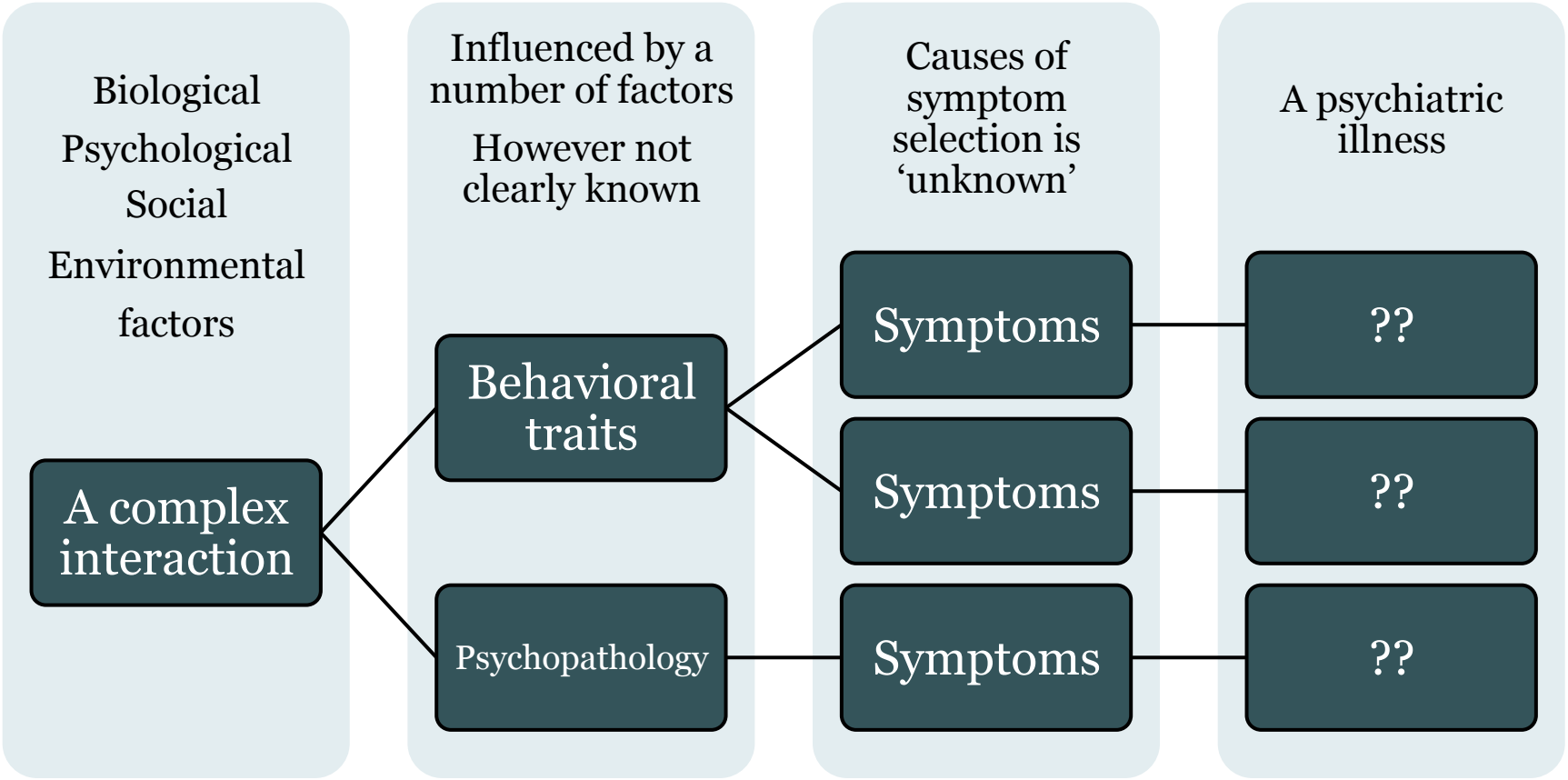
Transition to psychopathology



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Candidate who develops psychosis

- Vulnerable and Non-vulnerable
- Multiple groups of Endophenotype,
  - Epidemiological,
  - Biological,
  - Cognitive
- There are people with different genetic background –
  - COMT and other genetic markers
  - Twin study –
  - Family history

Pelayo-Terán JM, Pérez-Iglesias R, Mata I, Carrasco-Marín E, Vázquez-Barquero JL, Crespo-Facorro B. Catechol-O-Methyltransferase (COMT) Val158Met variations and cannabis use in first-episode non-affective psychosis: clinical-onset implications. Psychiatry Res 2010;179(3):291-6.

Barrigon ML, Gurpegui M, Ruiz-Veguilla M, Diaz FJ, Anguita M, Sarramea F, et al. Temporal relationship of first-episode non-affective psychosis with cannabis use: a clinical verification of an epidemiological hypothesis. J Psychiatr Res 2010;44(7):413-420.

Time line

- Consumption at which age leads to psychosis?
- Consumption and development of symptoms:
  - early age consumption and early psychosis,
  - early age consumption and later onset psychosis,
  - later age consumption and psychosis,
  - later age consumption and no psychosis
- Prenatal consumption and Psychosis
-

Martín-Santos R, Fagundo AB, Crippa JA, Atakan Z, Bhattacharyya S, Allen P et al Neuroimaging in cannabis use: a systematic review of the literature. Psychol Med 2010;40(3):383-98.

Substance

- High potency
- Dose
- Duration
- Nature of plant
- Nature of metabolite

Wilson N, Cadet JL. Comorbid mood, psychosis, and marijuana abuse disorders: a theoretical review. J Addict Dis 2009;28(4): 309-319.

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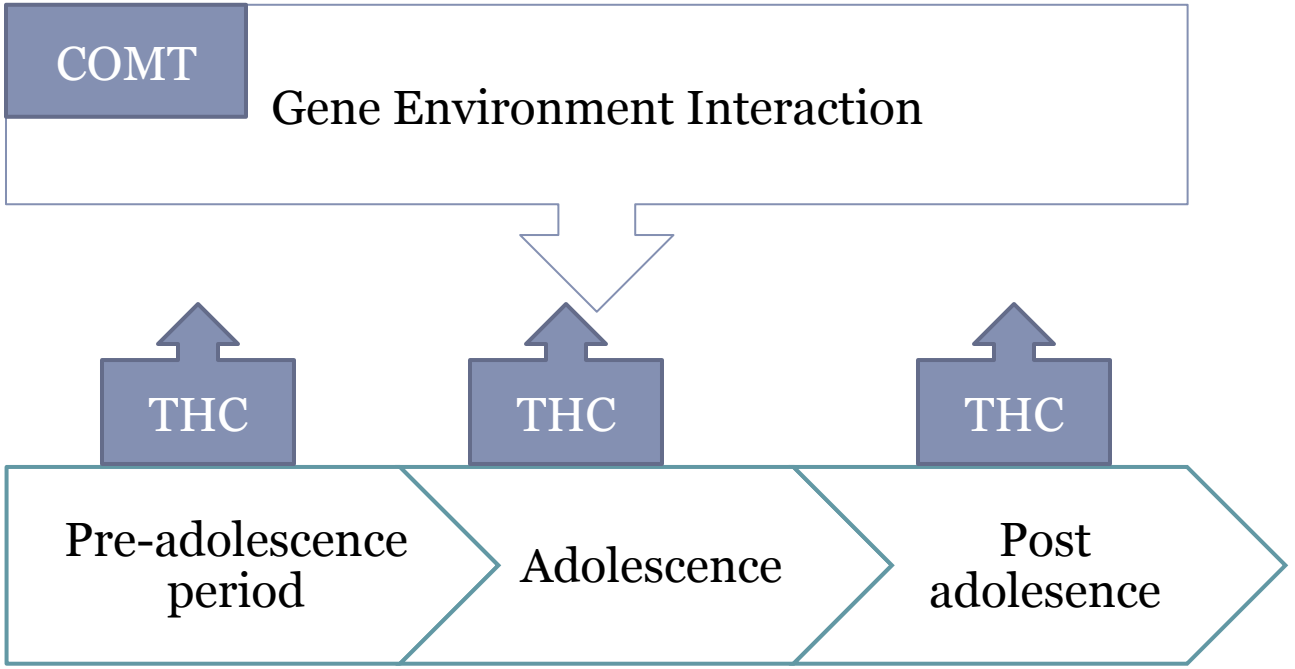
Age spectrum up to 22-25 years remains vulnerable/ sensitive



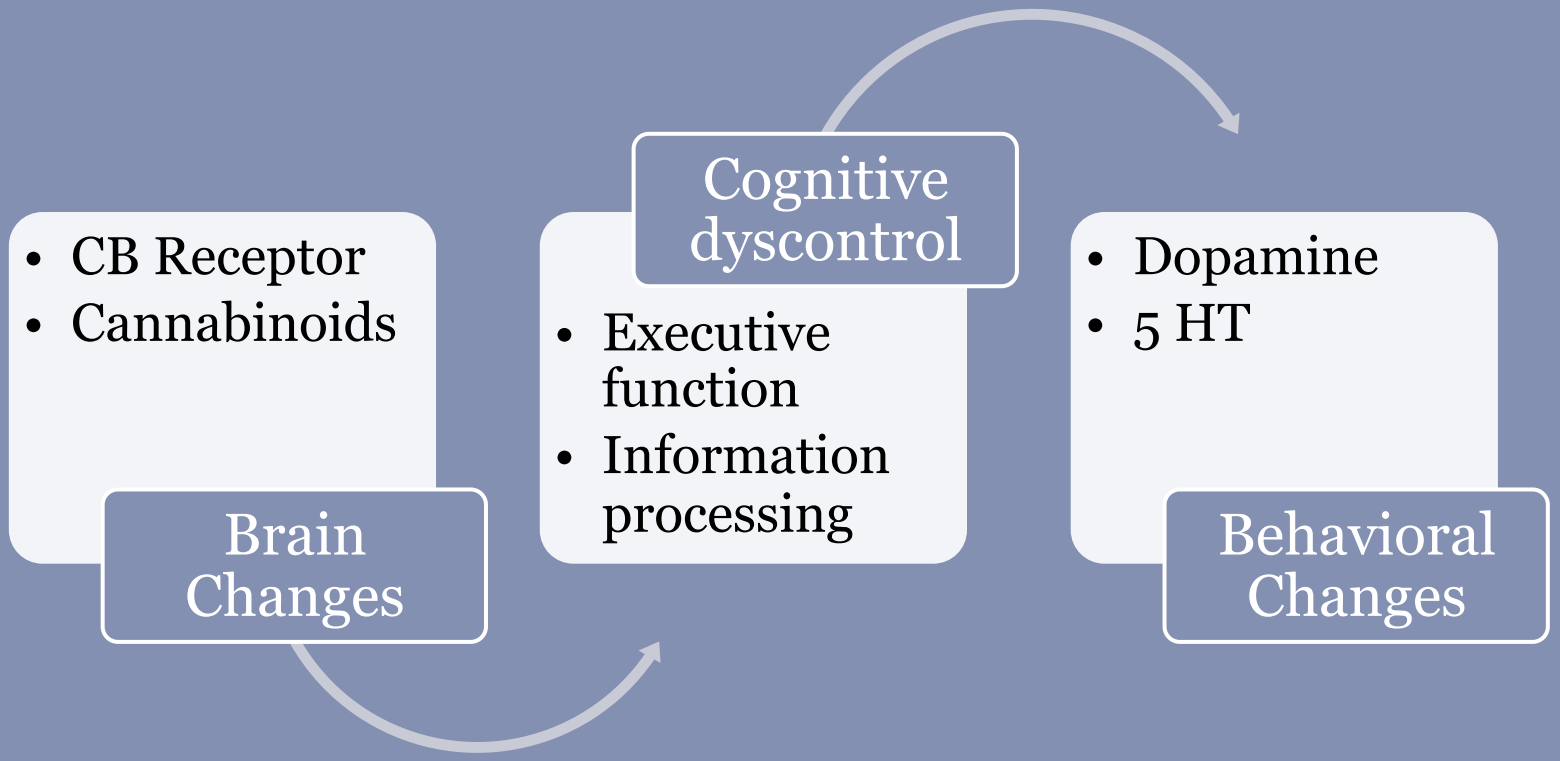
Novel hypotheses role of cannabinoids on Neurodevelopmental - being studied

Van Os J, Bak M, Hanssen M, Bijl RV, de Graaf R, Verdoux H. Cannabis and psychosis: a longitudinal population-based study. Am J Epidemiol 2002;156:319-327.

What changes occur?

- Brain development
- Genetic – COMT
- Neurochemical changes
- Functional and structural changes
- Cognitive changes
- Dopamine
- Neuroplasticity
- THC, Cannabinoid legends & receptor

D'Souza DC, Abi-Saab WM, Madonick S, Forselius-Bielen K, Doersch A, Braley G, et al. Delta-9-tetrahydrocannabinol effects in schizophrenia: implications for cognition, psychosis, and addiction. Biol Psychiatry 2005;57(6):594-608.
Delisi LE, Bertisch HC, Szulc KU, Majcher M, Brown K, Bappal A, Ardekani BA. A preliminary DTI study showing no brain structural change associated with adolescent cannabis use. Harm Reduct J 2006;3:17.
McLaren JA, Silins E, Hutchinson D, Mattick RP, Hall W. Assessing evidence for a causal link between cannabis and psychosis: a review of cohort studies. Int J Drug Policy 2010;21(1):10-19.
Arnone D, Barrick TR, Chengappa S, Mackay CE, Clark CA, Abou-Saleh MT. Corpus callosum damage in heavy marijuana use: preliminary evidence from diffusion tensor tractography and tract-based spatial statistics. Neuroimage 2008;41(3):1067-74.
Di Forti M, Morgan C, Dazzan P, Pariante C, Mondelli V, Marques TR, et al. High-potency cannabis and the risk of psychosis. Br J Psychiatry 2009;195(6):488-491.
Ostentin J. Neuropsychopharmacology of delta-9-tetrahydrocannabinol. Ann Pharm Fr 2008;66(4):219-231.


Brain Changes
• CB Receptor
• Cannabinoids
Cognitive dyscontrol
• Executive function
• Information processing
Behavioral Changes
• Dopamine
• 5 HT

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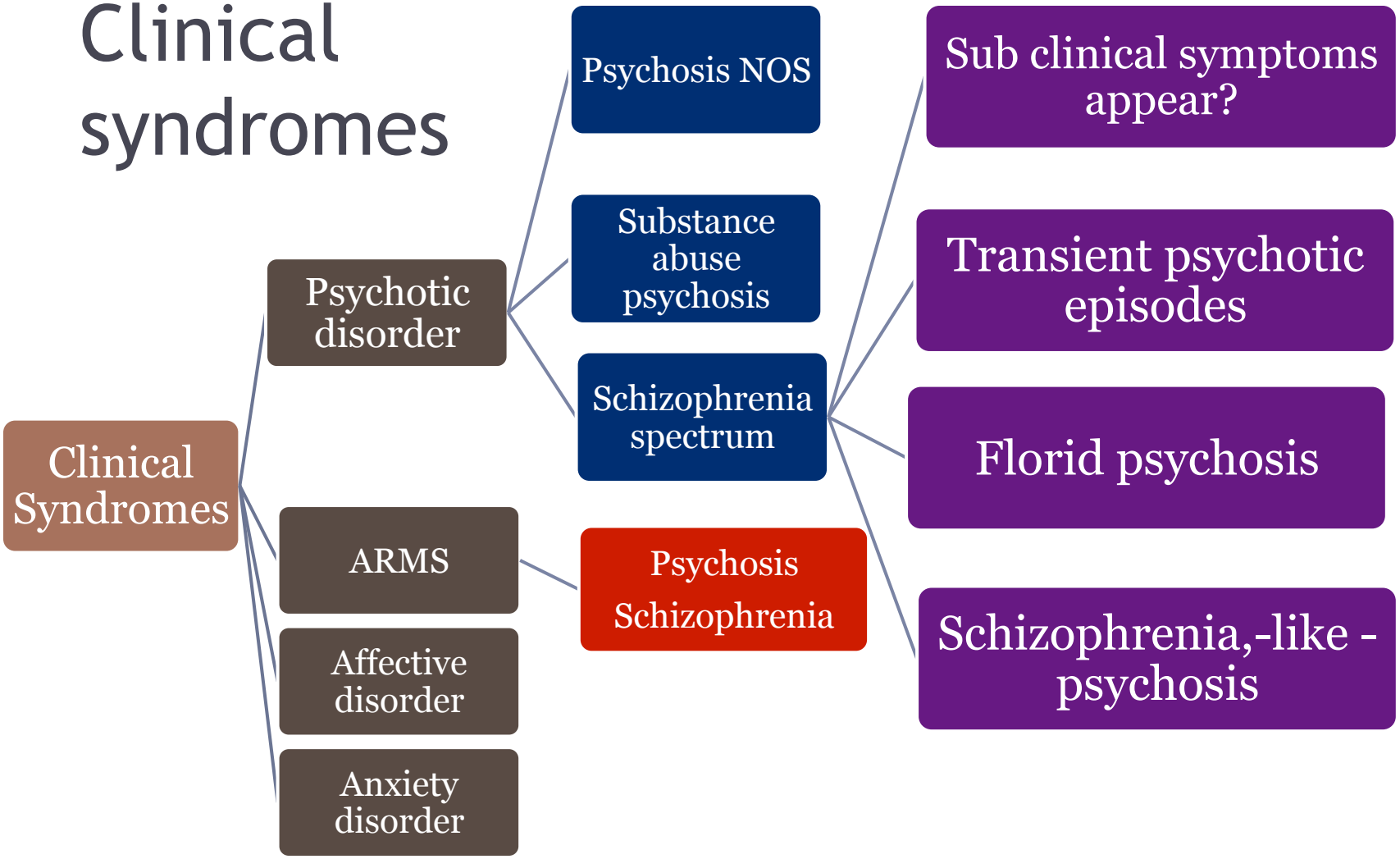
Clinical syndromes



Severity of psychopathology:

- Neurobiological changes are likely to be independent to severity of psychopathology

- No proportionate relationship with brain changes or any other factor

Final statement

- Overall maximum possibility is that 'in a select group, consumption of low or high potency cannabis, mostly at an early age while neurodevelopment is going on increases propensity of psychiatric symptoms which would mostly start at a later-age under-influence of specific or nonspecific psychosocial stressful conditions.

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Shrivastava A, Johnston M, Tsuang M.
Indian J Psychiatry. 2011 Jul;53(3):187-91. doi: 10.4103/0019-5545.86796

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