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Interface of Cannabis and Early Psychosis--Priorities in Research and Service Development

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INTERFACE OF CANNABIS AND EARLY PSYCHOSIS- PRIORITIES IN RESEARCH AND SERVICE DEVELOPMENT

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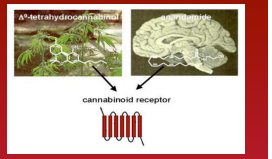

ABSTRACT

Introduction: cannabis continues to affect mental health. Its abuse is on rise globally. In Canada a rise by 30% in last ten years has been observed in high school students. Interrelationship of cannabis with psychosis and schizophrenia is a complex one. Cannabis is highly comorbid with psychosis, & related to functional disability and outcome. It poses several challenges in understanding causal relationship for comorbidity, underlying neurochemical basis and specifics of service development. Prevalence of Cannabis varies from 20 to 50% early psychosis. Objective of this paper is to review available literature to identify challenges for newer targets of research and preventive measures.
Method: Recent literature from electronic data base search identifies role and relationship of cannabis and psychosis.
Results. Cannabis is a risk factor for both psychosis and schizophrenia. & Appears to have causal relationship for early and later-age psychosis. Mood symptoms are also significant but less recognized. Understandings of the process and causes have significantly advanced with discovery of cannabinoid receptors and endogenous cannabinoids. It is clear that cannabis increases brain vulnerability, causes poorer outcome and more side effects. Cannabis causes cognitive dysfunction that perhaps works as a common denominator for the risk-vulnerability. It appears to have independent genetic component related to disruption in neurotransmission affecting neuronal plasticity. Much less attention has been paid in developing services targeted towards harm reduction and developing therapeutics.
Conclusion. Cannabis is potential risk factor for poorer outcome in psychosis. New biological and social service initiatives will add value to early psychosis programs

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INTRODUCTION

What do we know with 'Limited Evidence'?
- The brain changes seen by imaging
- Influence on brain development during adolescence
- Nature of most toxic metabolite which is psychosis-genic.
- Role of CB receptors in schizophrenia and psychosis
- The pathogenesis of risk.
- The 'Cannabis Phenotype of Psychosis'
- Validity of Diagnosis : 'Cannabis-Induced-Psychosis' Vs. 'Cannabi... Toxic-Psychotic State'
  - Adolescent mental health & Cannabis suggest long-term deleteri... outcomes in cognition, depressive symptoms, schizophrenia
    - neurodevelopmental effect,
    - predisposing genetic and/or environmental factors
    - Gender specific differences.
    - how cannabinoids influence neurodevelopment
  - development of therapeutic tools for a variety of neuropsychiatric ...

Adolescence | Drug abuse | Mood problems | Comorbidity Psychosis

40% to 70% of adolescents - at least one drug or alcohol problem.

With respect to sequencing, mood and other psychiatric disorders occur after the onset of drug-related problems. .This may not hold true for schizophrenia, however, which does frequently occur in adolescents., however the evidence is changing

METHODS AND MATERIALS

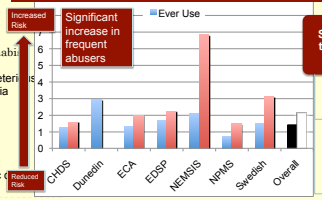
Explanation for close relationship between Psychosis & cannabis is still unclear.
Available evidence for 'causal relationship' suggests only possibilities

- There is a very strong epidemiological evidence for correlation/comorbidity.
- Cannabis is a risk factor for psychosis, for a variety of syndromes at later age.
- There seems to be no reliable biological explanation as to why exposure to cannabis should precipitate psychosis.
- THC causes brain effects and influences mental condition by causing abnormal transmission wi... dopamine
- There are regional changes in prefrontal corte... well as sub-cortical regions most of the behavio... effects are due to modulation of CB receptors.
- Cognitive impairment due to cannabis remains uncertain and unexplained

RESULTS

Risk of Psychosis & Cannabis

Adjusted odds ratio for any psychosis outcome according to ever use verses 'Frequent use' of Cannabis in individual studies at 95% CI



Theresa et al , Lancet, 2007

Strong Evidence that Cannabis is Risk for both

Psychosis

Schizophrenia

Physiological activity

- Cannabinoids & Neurogenesis
- Cannabis & Neuro-protection
- Cannabinoids & immunity/ Glioma
- Cannabinoids & Neurodegeneration
- Cannabis & Cognition

Huntington's disease | Parkinson's disease | Schizophrenia | Tremors

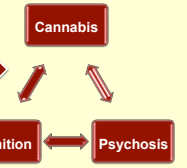
Potential therapeutic targets currently under investigation

cannabinoid Agonists and antagonists : interrupt - synthesis, uptake or metabolism of the endocannabinoids.

Central theme: Interrelationship & determinants of ' damage-control'

Most users don't develop Psychosis;
95% of 18 year; 90% of 15 years old; Did not develop at age 26 – Capsi et al

E-CB - endocannabinoids provides Explanation For Cognitive deficits



Two main questions

Why Cognition is significant to psychosis?

What impact can cannabis cause on Cognition?

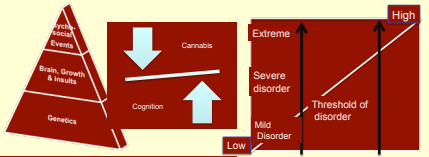
Neurobiology of cognition is one of the most challenging in research.

RESULTS

The RISK – Absolute or Relative

Cannon M, Clarke MC.
Risk for schizophrenia--broadening the concepts, pushing back the boundaries. Schizophr Res. 2005 Nov 1;79(1):5-13.

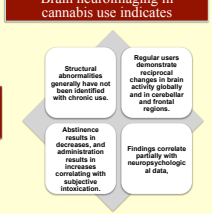
forms the theoretical context of Risk-



Early age use , Polydrug abuse, Personality type-nonspecific-predisposed social anxiety and dysphoria, good evidence for comorbidity ASPD-83% ***Enhance vulnerability*** { with OD 29.6, ***Life Time Prevalence for cannabis dependence was 14.7%*** }

Brain effects of Cannabis

Brain neuroimaging in cannabis use indicates



Extensive areas of the cortex (especially in the frontal and temporal cortex)

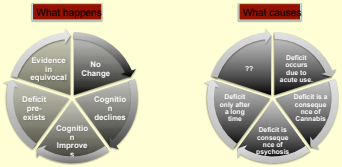
Subcortex (Amygdala, Hippocampus & Insular cortex) Basal regions (striatum)

These alterations are associated with abnormal patterns of activation during cognitive memory tasks, inhibition & decision-making

J Neuropsychiatry Clin Neurosci. 2006 Summer;18(3):318-32

Rev Neurol. 2007 Apr 1-15;44(7):432-9

Cognition in Psychosis due to Cannabis Use: The Evidence



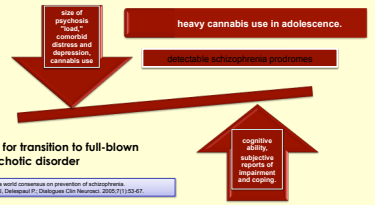
How does the cognitive dysfunction arise?

Knowledge of neurochemical correlates & exact neuronal mechanism of cognitive dysfunction continues to be a major limitation in understanding the deficit and developing therapeutics

DISCUSSION

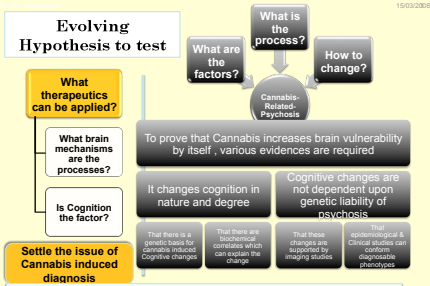
Towards a world consensus on prevention of schizophrenia.

Cannabis Research: An Evidence and Argument for Schizophrenia Prevention



Toward a world consensus on prevention of schizophrenia
Van Os J, Delespaul P, Dialogues Clin Neurosci. 2005;7(1):53-67.

Evolving Hypothesis to test



Objectives: To address this hypothesis :
Most interesting fields are :

- Establish the pattern of cannabis usage in a cohort of schizophrenia.
- Establish the clinical pathway and correlates, determinants and risk factors for cannabis-associated psychosis.
- Investigate the correlation of neuro-cognitive status in cannabis exposure
- Investigate the correlation of neurocognitive status and time line for onset of psychosis.

CONCLUSIONS

- Predominant questions & Limitations of available research data
- Is cannabis involved in memory impairment?
- Do Cognitive effects (arising from Cannabis) form a 'risk –factor' for psychosis?
- What are the biochemical correlates of these cognitive changes?
- Will cognitive enhancement reduce the risk for psychosis in abusers? Will it be possible to develop such cognitive enhancers?
  - Limited data-still needs more political push & more group initiatives in research of Cannabis and Mental Health.
  - However there are sufficient pointers to suggest the possibilities and need for more aggressive research.