Cannabis and Psychosis:
Is there an aspect of psychotic Illness that promotes cannabis use?

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Comorbidity of substance use and mental illness

Substance use can be very harmful and disruptive especially for people with mental illness

Improving our understanding of factors promoting this behaviour should lead to more effective treatments

Is substance use driven by similar factors in people with mental illness as in the general population?

Comorbidity of substance use and mental illness

Why do some individuals develop substance use problems while others do not?

It is well-established that people with mental illness, particularly psychotic disorders, have higher rates of substance-use problems

People with psychotic illness are not very responsive to some standard interventions for substance use

Is there an aspect of psychopathology that confers vulerability to substance use?

Models for the comorbidity of substance use and psychotic illness

Toxicity model

- Substance use is primary, causing psychopathology
- Particularly implicated in the case of cannabis and psychosis

Self-medication model

- Mental disorder is primary, leading individuals to consume substances to relieve symptoms or distress

Common factor model

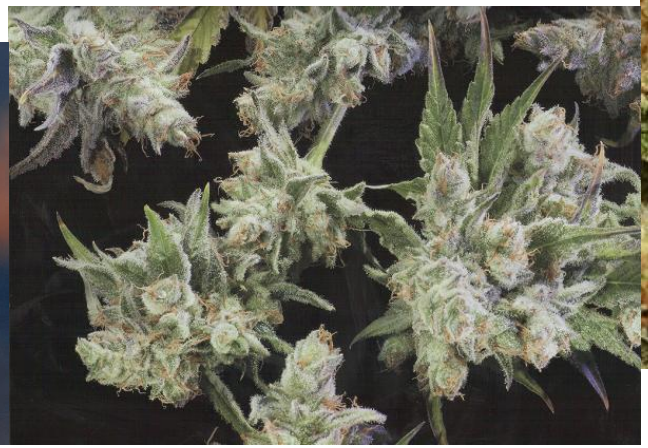
- Neither disorder causes the other
- There is another factor which confers risk of developing both psychotic illness and substance-use disorder

Cannabis

Reasons to focus on this substance

- High rates of use: relevance, convenience
- Negative consequences of use in context of psychotic illness

No *a priori* reason why our hypothesis should apply more to cannabis than other substances of abuse



Experimental strategy to identify common factors in cannabis use and psychosis

Ask psychosis patients why they use: **Study 1**

Find a characteristic that is:

(1) more highly present in psychosis patients than controls and
(2) associated with problematic cannabis use

Candidate common factors examined:

Reward processing deficits: **Study 2**

Childhood attention problems (Cassidy et al., 2011, *Schizophrenia Research*).

Experimental Sample

Studies were carried out on current and former FEP patients treated at PEPP-Montréal

Patients were between 3 months and 7 years from the onset of treatment of a FEP

Control subjects were recruited through online classifieds

Study 1:

Self-reported reasons for substance use

Step 1 in understanding substance use in psychosis—asking patients

Hypothesis-generating approach

Much existing research on this question, some have concluded similar reasons exist in patients and controls

Most studies could have been improved by:

- Emperical methods to categorize reasons for use
- Examining which reasons related to intensity of use
- Comparing reasons in patients to reasons in controls
- Looking at a specific substance

Reasons for substance use

Methods

Reasons for substance use in schizophrenia scale (ReSUS), new instrument, validated in schizophrenia for mixed substance use

38 items related to reasons for use scored on a 4-point scale

Factor analysed in schizophrenia to make 3 subscales:

- coping with distress
- social enhancement/intoxication
- individual enhancement

ReSUS was completed by young non-affective psychosis patients (n = 60) and controls (n = 73) who had used cannabis > 10 x in their life

Subjects simultaneously self-reported cannabis use over the past 6 months
Frequency of use (number of sessions/day * number of days of use)

10 most highly endorsed reasons for cannabis use in patients and controls

Reasons for using cannabis	Rank patient (n = 60)	Rank control (n = 73)	Mean score patient	Mean score control
to chill out or relax	1	2	3.0	2.9
to have a good time with friends	2	1	2.9	3.1
to pass the time when bored	3	7	2.9	2.4
to feel good/laugh/be happier	4	5	2.8	2.5
to feel high	5	3	2.6	2.9
When stressed	6	9	2.5	2.3
to feel more creative	7	6	2.5	2.4
When happy and content with life	8	4	2.4	2.6
to escape problems and worries	9	15	2.4	1.8
When I think about how good it tastes	10	11	2.2	1.9

What kind of reasons are related to heavy cannabis use?

	Correlation to frequency of cannabis use	
	Control (n = 46)	Patient (n = 31)
Coping with distress	.55***	.04
Social enhancement/ intoxication	.63***	.51**
Individual enhancement	.28*	.28

Reasons correlated to frequency of cannabis use (ranked by R)

	Spearman R non-affective patients, (n = 30)	Rank of R (patient)	Spearman R control, (n = 46)	Rank of R (control)
When I am feeling happy and content with my life	.44	1	.23	23
When drinking/intoxicated	.37	2	.18	24
When I think about how good it tastes	.35	3	.64	1
To have a good time with friends	.33	4	.37	15
When feeling excited	.32	5	.47	8
To feel motivated	.31	6	.32	20
To be awake/alert/energetic	.31	7	.03	27

In controls 6 of 7 top-ranked reasons load on ‘Coping with Distress’

Reasons for substance use

Conclusions

Looking in more detail at the evidence reveals that there may be important differences in factors driving heavy cannabis use in psychosis patients vs controls, contrary to some previous findings

Evidence suggests heavy use in patients may be an attempt more to enhance positive feelings than to escape negative feelings

Investigating reward processing in cannabis-psychosis comorbidity may be fruitful

Study 2:
Physiological response to cannabis cues and natural rewards in young non-affective psychosis patients

Objectives:

To examine response to natural rewards and drug-associated rewards in cannabis-using schizohprenia-spectrum patients and controls

To see if these measures predict subsequent cannabis self-administration

Principal response measure was the **late positive potential (LPP)** a component of the event-related potential (ERP) response

Well-established measure
robust response to emotional images
reflects ability to sustain **motivated attention** toward salient stimuli
related to **memory encoding**

Also looked at other physiological and subjective responses to stimuli

Physiological response to cannabis cues and natural rewards in young non-affective psychosis patients

Evidence of a deficit in sustained attention to pleasant stimuli in schizophrenia as measured with the LPP (Horan et al., 2010)

2 studies found severity of future substance use (nicotine, opiates) was predicted by decreased sustained attention to pleasant images as measured with ERP

Our hypothesis:

- Patients will show blunted response to pleasant images
- Patients will show robust response to cannabis images
- Blunted response to pleasant images will predict greater subsequent cannabis use

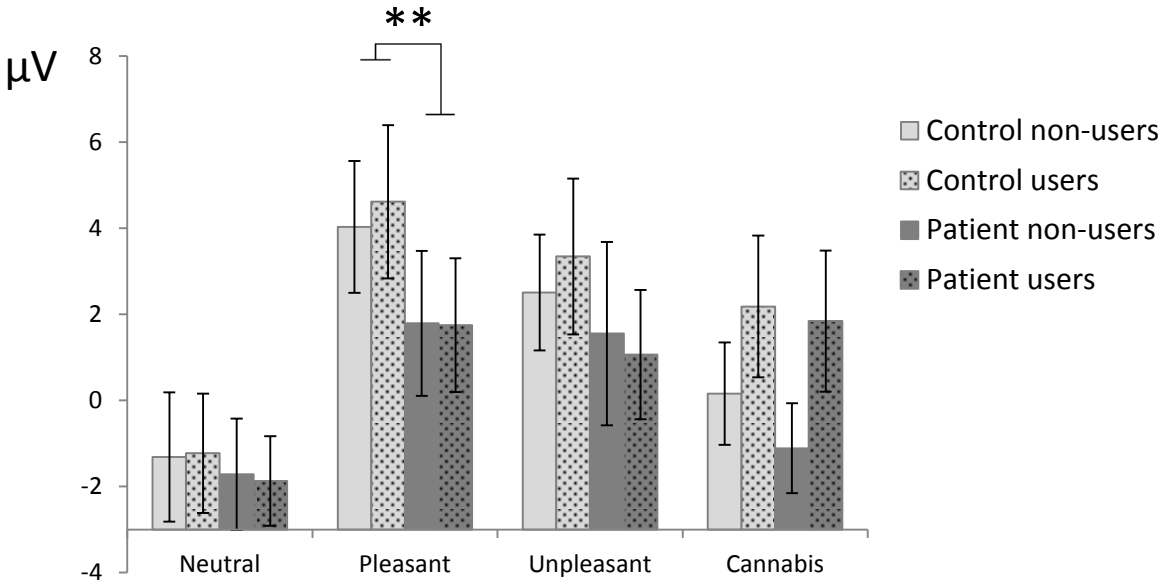
Experimental procedure

4 groups, 35 scz-spectrum patients and 35 controls, divided into those with current regular cannabis use and those with little lifetime substance use

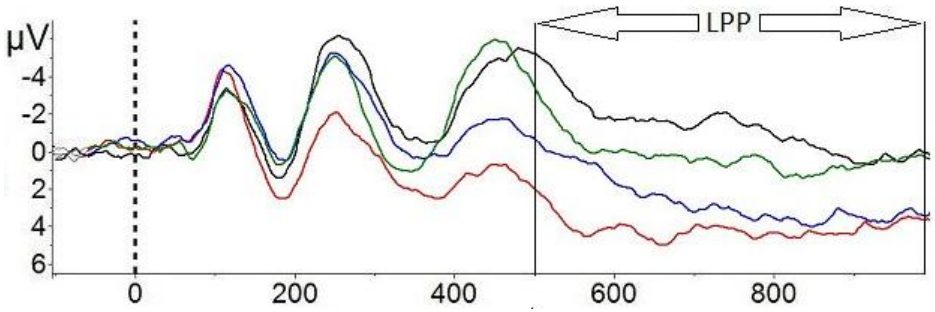
All subjects passively watched a 30 minute slideshow of emotional images (pleasant, unpleasant, cannabis, neutral) while physiological measurements were recorded (ERP, fEMG, GSR)

Event-related potential (ERP) main measure of interest (9 electrodes)

LPP response to stimuli



Error bars represent 95% Confidence interval
**p < .01



Prediction of future cannabis use based on LPP response

	Correlations with frequency of cannabis use over the month post-testing		Regressions on use-frequency controlling for baseline THC exposure	
	Controls n = 20	Patients n = 20	Combined n = 40	
			R^2 for model	β
LPP at Cz for pleasant images	-.30	-.50*	.58	-.24*
LPP at Cz for unpleasant images	-.35	-.49*	.62	-.30**

Summary

As hypothesized:

blunted motivated attention toward pleasant images was related to both psychotic illness and frequency of cannabis use

Motivated attention to cannabis images was preserved in cannabis-using psychosis patients

Conclusions

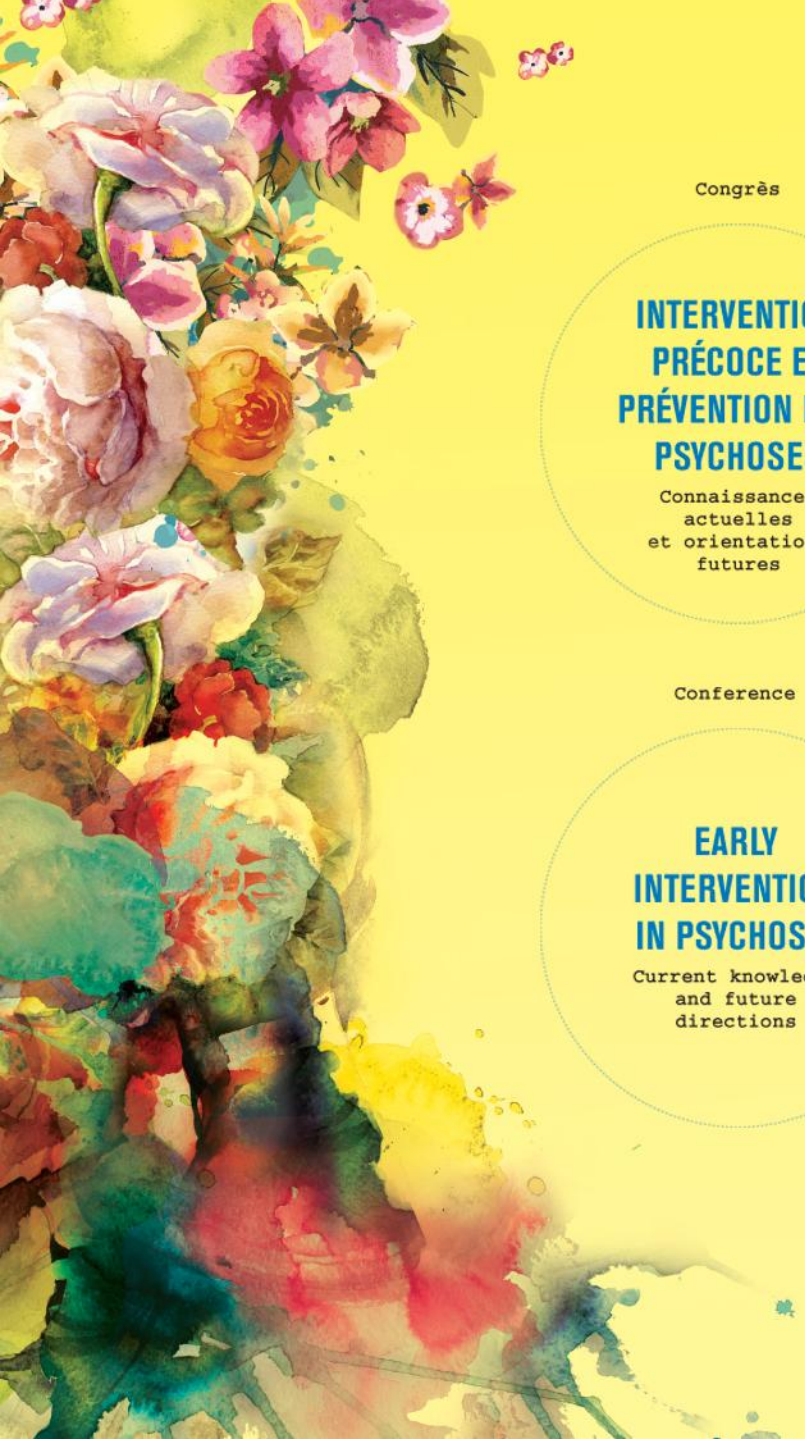
Psychosis patients with substance use comorbidity can be challenging to work with (vicious circle)

Risk of blaming patient for their mental illness (caused by substance use?)

A component of psychotic illness or its many comorbidities may deprive individuals of some of the resources necessary to fight addiction

Treatments for substance use in psychotic illness should be tested in this population

Improving reward processing in psychotic disorders may lead to better substance-use outcomes



Thank You!

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