Demystifying Marijuana Dependence in Youth

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Royal Ottawa Foundation for Mental Health		✓		

Learning Objectives

1. Describe cannabis dependence and vulnerability in youth
2. Distinguish between cannabis myths and facts
3. Recognize cannabis related problems and association with mental disorders
4. Evaluate the need and direct treatment for cannabis dependence in youth

Legend

Substance Use Disorders = SUD

Cannabis Use Disorders = CUD

Marijuana is no big problem – everyone uses it

EPIDEMIOLOGY

- Substance use has moved into the mainstream adolescent population and to younger age groups.

- Cannabis is the most common substance of daily use by adolescents (5-6% of senior high school students vs. alcohol at 2.5-3%).

EPIDEMIOLOGY

U.S. National Comorbidity Survey-Adolescent Supplement (2010):

- 20-25% of adolescents met criteria for a lifetime mental disorder with severe impairment
- Comorbidity was common (40%) in adolescents with mental disorders
- Median age of onset for *SUD~ 15 years with steep increase thereafter*

EPIDEMIOLOGY

- Lifetime Prevalence:
  - Substance Use Disorders 11.4%
    - Drug abuse/dependence 8.9%
    - Alcohol abuse/dependence 6.4%

- Somewhat more prevalent in males 12.5% than females 10.2%

EPIDEMIOLOGY

- Prevalence of use increases with grade level
- Perceived risk has declined over time
- Cannabis is the most common substance of dependence in youth

EPIDEMIOLOGY

In comparison to disorders with severe impairment:

- Depressive Disorders 8.7%
- Anxiety Disorders 8.3%
- ADHD 4.3%

EPIDEMIOLOGY

- Gradual but notable increase of CUD in young adults (ages 18-25) over the last decade
- CUD ~ 4% in those 12 years or older (US)
- Onset after 30 is rare

ETIOLOGY

- Adolescence from a developmental perspective may be a unique period of heightened susceptibility for SUD.

- Convergence of major psychosocial challenges (stresses) and maturational neurodevelopmental brain changes in adolescence may enhance their vulnerability to the effects of substance use.

DEVELOPMENT AND COURSE

- Adolescence is a period of major risk for the onset of SUD.
- In general peak age of onset for SUD is between ages 18-20.
- However, the peak age of onset for CUD is 16-18 years.

DEVELOPMENT AND COURSE

- Marijuana has been identified as a gateway drug.
- Early initiation of substance use (≤15y.o.) has been shown to increase the risk for:
  - Continued use and subsequent daily use.
  - Other SUD in adulthood apart from cannabis.

DEVELOPMENT AND COURSE

- Weekly cannabis use marks a threshold for increased risk of later dependence.

- Youth who report positive reactions or preference to early use of cannabis are at increased risk of later cannabis dependence.

DEVELOPMENT AND COURSE

- Negative consequences of CUD in youth are well established and include:
  - Disruption of adolescent developmental tasks
  - Education and employment
  - Family and community role responsibilities

You can’t get hooked on marijuana

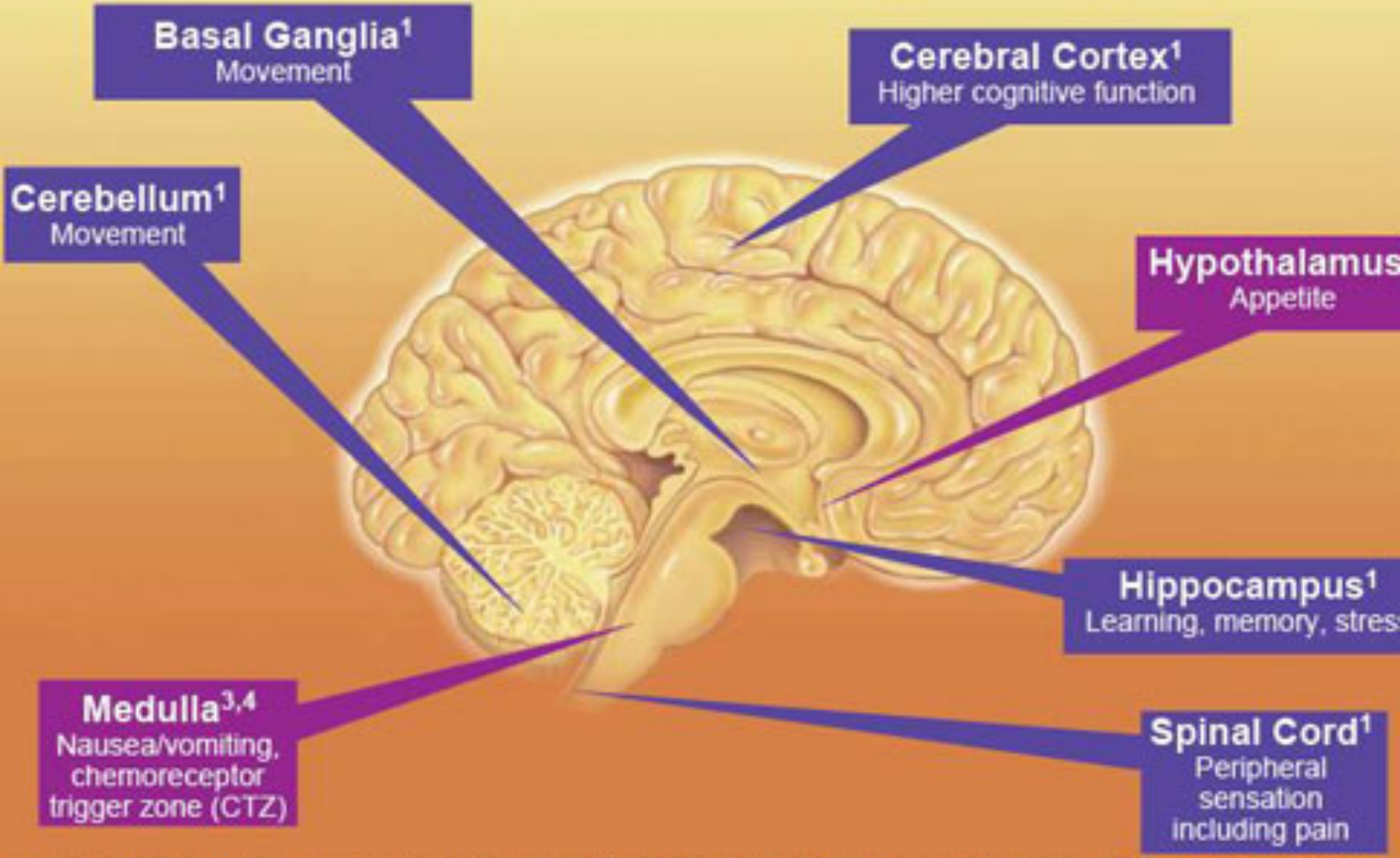
CANNABIS DEPENDENCE

- Chronic heavy use of cannabis may be associated with both psychological and physiological dependence as indicated by drug craving, compulsive use, tolerance and withdrawal.

NEUROBIOLOGY

- CB1 receptors have been identified in the brain
- Presence of endogenous ligands or Endocanabinols has been established
- Active ingredient/metabolite of marijuana is THC
  - There are many derivatives of THC
  - CB1 receptor distribution mirrors effects of THC

Concentrations of CB_1 receptors



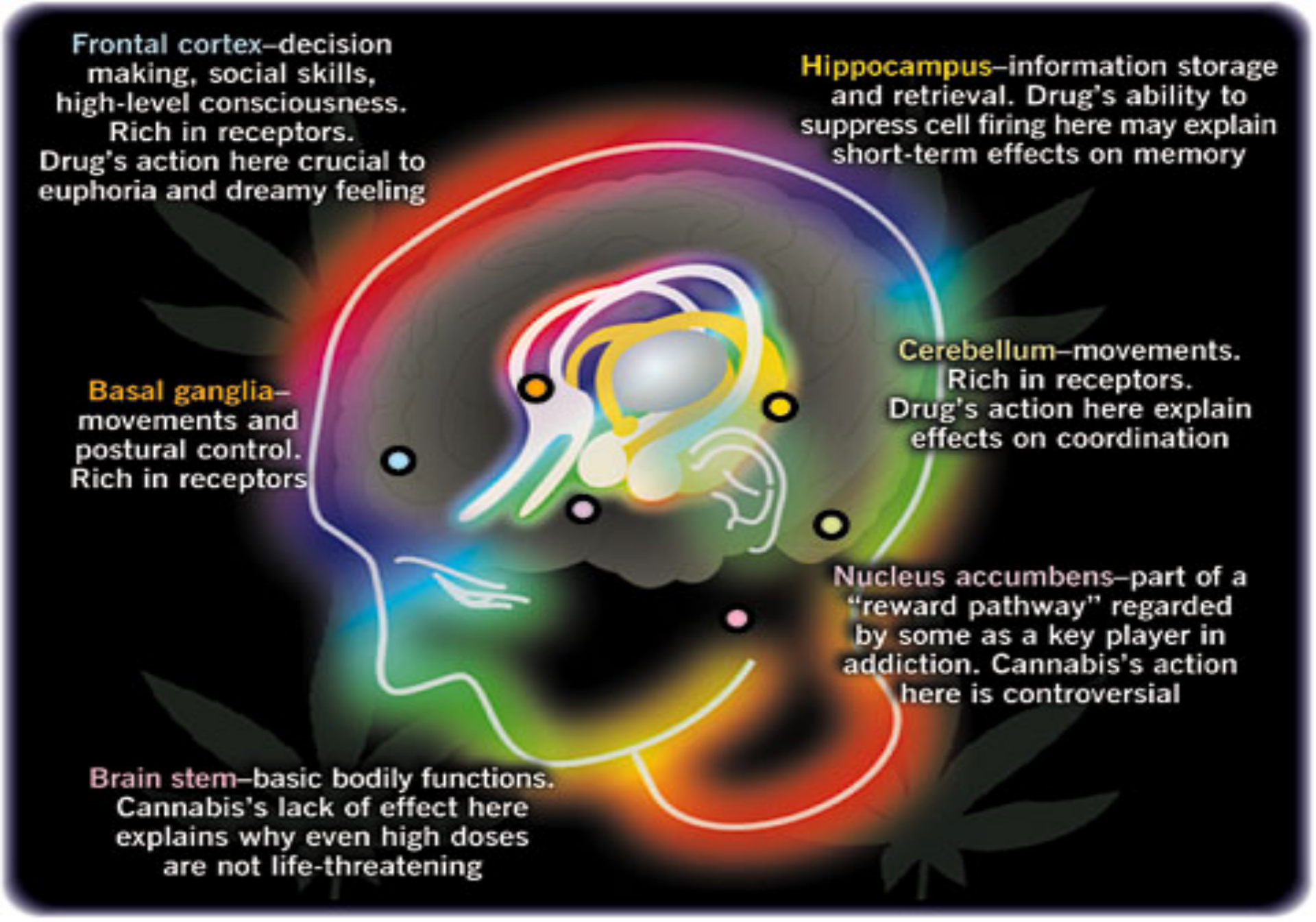
1. Joy JE, et al, eds. *Marijuana and Medicine: Assessing the Science Base*. Washington, DC: National Academy Press; 1999:33-81. 2. Martin BR, et al. *J Support Oncol*. 2004;2(4):305-316. 3. Grotenhermen F. *Curr Drug Targets CNS Neurol Disord*. 2005;4(5):507-530. 4. Navari RM, et al. *Expert Opin Emerg Drugs*. 2006;11(1):137-151.

NEUROBIOLOGY

- Cannabis modulates mood and possesses euphoric properties, mediated by its effect on CB1 receptors.

- Evidence suggests that marijuana interacts with the endogenous opioid system in the brain.

How cannabis gets to work on our brains



NEUROBIOLOGICAL HIGHER DOSE ADVERSE EFFECTS

- Acute panic reactions or mild paranoia have been observed.

- May also lead to an acute toxic psychosis accompanied by loss of insight.
  - Cannabis-induced psychotic disorder (CIPD) is an infrequent event estimated at 2.7 per 100,000 person-years.

NEUROPSYCHOLOGICAL ADVERSE EFFECTS

- Heavy and frequent marijuana use (daily use in past 30 days) is associated with significantly greater impairment than light use (1-9 days of use in past 30 days) on attentional and executive functions.

- Short-term/working memory impairment may persist for some time on neuropsychological testing (up to 3 months).

NEUROPSYCHOLOGICAL ADVERSE EFFECTS

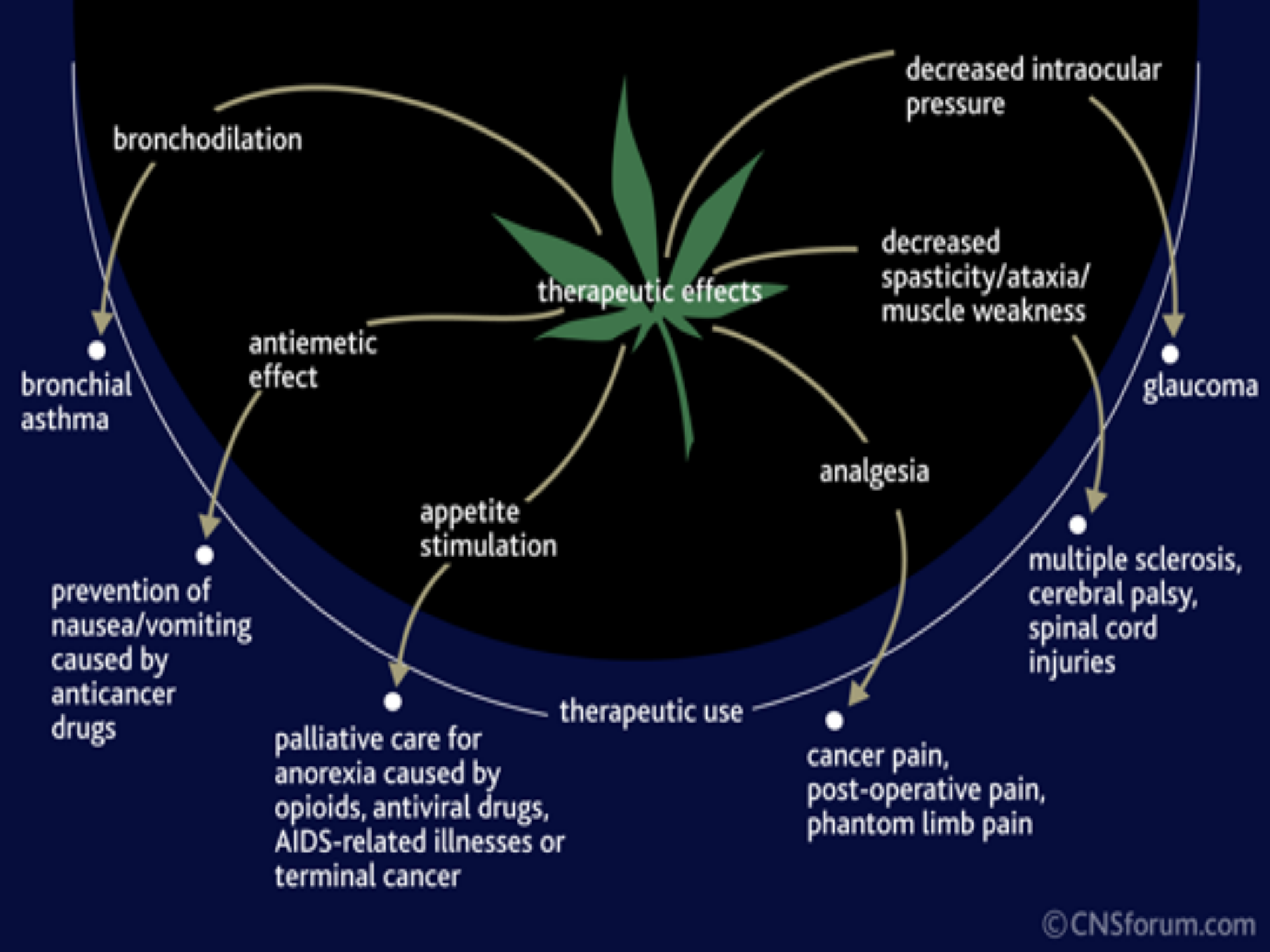
- Solid evidence that persistent regular cannabis use (4 day/week) and/or dependence in adolescence is associated with broad based neuropsychological decline in adulthood.
  - Greater the duration of use the greater the decline

NEUROPSYCHOLOGICAL ADVERSE EFFECTS

Cont'd

- Negative impact on functioning
- Cessation of cannabis did not fully restore neuropsychological profile
- Even after controlling for years of education

Meier et al, 2012


bronchodilation
decreased intraocular pressure
therapeutic effects
decreased spasticity/ataxia/ muscle weakness
antiemetic effect
bronchial asthma
glaucoma
analgesia
appetite stimulation
multiple sclerosis, cerebral palsy, spinal cord injuries
prevention of nausea/vomiting caused by anticancer drugs
therapeutic use
palliative care for anorexia caused by opioids, antiviral drugs, AIDS-related illnesses or terminal cancer
cancer pain, post-operative pain, phantom limb pain
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PHARMACOLOGY OF CANNABIS

- The cannabis used today has a significantly higher THC content and is much more potent than the cannabis used in the late 1960's and 70's.

- Currently a good quality marijuana cigarette contains 10-15% THC (active metabolite).

CANNABIS DEPENDENCE

- Both American and Australian studies have concluded that approximately 9% of those people who ever used marijuana will qualify for a lifetime diagnosis of marijuana dependence.

- The risk of developing cannabis dependence may be as high as 20-30% among those people who used marijuana more than a few times.

CANNABIS DEPENDENCE

- In adults, patterns of use have been found to be stable with a high rate of dependence but few recognized that they had a cannabis problem.

- Mean duration of cannabis:
  - Abuse 35 months
  - Dependence 44.3 months

CANNABIS DEPENDENCE

- Rates of cannabis dependence in the U.S. among those who used cannabis within the last year have been found to be greater in adolescents than adults.

- Rates being similar for females and males in adolescence and significantly higher for males than females in adulthood.

CANNABIS WITHDRAWAL IN ADOLESCENTS

- Cannabis withdrawal is common showing a similar time course and symptoms
- Cannabis withdrawal increases risk of relapse
- Cannabis withdrawal appears to be an indicator of dependence severity and predictor of a more chronic course

Marijuana helps me cope

COMORBIDITY

- Weekly or more frequent use of marijuana doubles an adolescent's risk of depression and anxiety

- Marijuana use is associated with and may worsen depression in adolescents

COMORBIDITY

- Depressed adolescents are 2X more likely to abuse or become dependent on marijuana

- Frequent cannabis use in adolescence increases the risk for depression and anxiety, especially in young women.

COMORBIDITY

- Substance use (1° marijuana) has a negative impact on treatment response in adolescent MDD

- SUD significantly adds to the burden of youth mental disorders with evidence of poor treatment response and clinical outcomes

CUD AND PSYCHOSIS

- Growing body of evidence to support cannabis use increases risk of psychotic outcome and clinically relevant psychotic disorders controlling for confounding factors.

- Increased risk of psychosis:
  - 40% for ever used cannabis
  - 50-200% for used cannabis most frequently

CUD AND PSYCHOSIS

- Similar significant relationship for cannabis use as an independent risk factor for development of schizophrenia in adulthood

- 2-3 X greater risk of developing schizophrenia

CUD AND PSYCHOSIS

- Risk for psychotic outcomes/disorders increases in dose dependent manner (severity) and greater with onset of use in adolescence (duration)

- Preliminary findings suggest a link between higher potency cannabis and development of first episode psychosis

CUD AND PSYCHOSIS

- Evidence, however, to date doesn't support a causal link between cannabis use and schizophrenia

- Nonetheless there is now sufficient evidence to warn young people that cannabis use may increase their risk for developing a psychotic disorder in adulthood

CUD AND PSYCHOSIS

- Converging epidemiological and clinical evidence to show:
  - CIPD not a random event or benign condition.
  - Drug induced psychotic disorder represents a cogent vulnerability marker for development of schizophrenia.

- Clinical follow-up of CIPD is warranted.

I can stop whenever I want to

TREATMENT

- Majority of individuals with CUD have not received treatment
- However the number of adolescents and adults receiving treatment for CUD almost doubled in the last decade
- CUD is the most common reason for which adolescents seek SUD treatment

TREATMENT

- There have been significant advances in evidence based psychosocial treatments specific for adolescent SUD.

- These include developmentally appropriate:
  - Family Therapy Modalities
  - Cognitive Behavioural Therapy (CBT)

TREATMENT

- Motivational Enhancement Therapy (MET) has been incorporated into psychosocial treatments for SUD.

- The addition of contingency management have shown promise in the treatment of CUD in youth.

CANNABIS YOUTH TREATMENT (CYT) STUDY
Dennis et al, 2004

- RCT of treatment modalities
- Multisite 1 year study
- N=600 with CUD
- Comorbid sample: 33% Internalizing & 60% Externalizing disorders

CYT STUDY 2004

Trial 1:

- MET/CBT 5 sessions
- MET/CBT 12 sessions
- FSN: Family Support Network includes MET/ CBT 12 + engagement type case management, family support groups and aftercare

CYT STUDY 2004

Trial 2:

- MET/CBT 5
- ACRA: Adolescent Community Reinforcement Approach
  - ***10 individual sessions***
  - ***4 sessions with caregivers***
  - ***Focus to rearrange environmental contingencies***
- MDFT: Multidimensional Family Therapy
  - ***12 weeks (12-15 sessions)***

CYT STUDY 2004

- **Promising findings**
  - Treatment improvements
    i. in days of abstinence
    ii. percent in recovery/remission (range 17 to 34%)
  - No clear advantage to any of the 5 treatments

CYT STUDY 2004

- **Promising findings**
  - Although treatments were effective and treatment effect was sustained at follow-up
    i. 2/3 of the CYT youths were still reporting substance use related problems at 1 year post-treatment
    ii. Relapse rates were high

TREATMENT

Pharmacotherapy, Gray et al 2012

- RCT (N=116) of N-acetylcysteine (NAC) in youth (ages 15-21) with cannabis dependence
- NAC 1200mg bid
- Contingency management & brief weekly cessation counselling

TREATMENT

Results

- NAC group 2X more likely of having negative urine cannabinoid results during treatment (primary outcome measure)
- Findings suggest NAC may be an effective complement to psychosocial treatment for Cannabis Dependence in adolescents

MARIJUANA AS MEDICINE

Position Paper of American Psychiatric Association (Dec 2013)

Key Clinical Points

- No current scientific evidence that marijuana is beneficial for the treatment of any psychiatric disorder
- Current evidence supports a strong association of cannabis use with the onset of psychiatric disorders
- Adolescents are particularly vulnerable to harm
- Further research needed

A FEW SELECTED REFERENCES

- Dennis M, Godley SH, Diamond G, Tims FM, Babor T, Donaldson J, Liddle H, Titus JC, Kaminer Y, Webb C, Hamilton N, Funk R. (2004) The Cannabis Youth Treatment (CYT) study: Main findings from two randomized trials. Journal of Substance Abuse Treatment, 27:197-213.

- Duffy A, Horrocks J, Milin R, Doucette S, Persson G, Grof P. Adolescent substance use disorder during the early stages of bipolar disorder: A prospective high-risk study. Journal of Affective Disorders (2012), http://dx.doi.org/10.1016/j.jad.2012.04.010

- Gray KM, Carpenter MJ, Baker NL, DeSantis SM, Kryway E, Hartwell KJ, McRae-Clark AL, Brady KT. A double-blind randomized controlled trial of N-Acetylcysteine in cannabis-dependent adolescents. Am J Psychiatry, 2012, online.

A FEW SELECTED REFERENCES

- Meier MH, Caspi A, Ambler A, Harrington H, Houts R, Keefe RS, McDonald K, Ward A, Poulton R, Moffitt TE. Persistent cannabis users show neuropsychological decline from childhood to midlife. Proc Nat Acad Sci USA, 2012, online.

- Milin R., Manion I., Dare G. and Walker S. (2008) Prospective study of cannabis withdrawal in adolescents with cannabis dependence: A pilot Study. Journal of the American Academy of Child and Adolescent Psychiatry, 47(2):174-179.

REVIEW REFERENCES

- Milin R, Walker S. Adolescent Substance Abuse. Lowinson & Ruiz's Substance Abuse: A Comprehensive Textbook, Fifth Edition, Pedro Ruiz and Eric Strain (eds), Lippincott Williams & Wilkins, 2011.

- Milin, R., Walker, S., Duffy, A. Assessment and Treatment of Comorbid Psychotic Disorders and Bipolar Disorder. Clinical Manual of Adolescent Substance Abuse Treatment, Yifrah Kaminer and Ken Winters (eds), APPI, 2011.

- Office of National Drug Control Policy, Executive Office of the President. (2008) Teen marijuana use worsens depression: An analysis of recent data shows "self-medicating" could actually make things worse.