Medical Marijuana: Impact for Psychiatry

Brian Bonfardin M.D.
Brianbonf@aol.com
ETSU, Clinical Professor, Department of Psychiatry
Frontier and Helen Ross McNabb

DISCLAIMER
NEITHER THE PUBLISHER NOR THE AUTHORS ASSUME ANY LIABILITY FOR ANY INJURY AND OR DAMAGE TO PERSONS OR PROPERTY ARISING FROM THIS WEBSITE AND ITS CONTENT.

Objectives
1. Be familiar with the neurochemical impacts of marijuana.
2. Be able to appreciate the cultural factors of marijuana being seen as healing.
3. Understand the research findings of medical marijuana.

History of Marijuana
• Grass or Weed used to make hemp fiber for clothing, rope, paper.
• 4000 BC seeds used as food and oils for calories.
• 3000 BC oils, seeds, crushed buds used for medical treatments.
Intoxicant

- 1500 BC breeding produced less cellulose more THC.
- Found in Middle East burial sites and ceremonial rituals used as intoxicant.
- Muslim forbids alcohol and breeding/use as intoxicant increases.

Expansion

- Cannabis moves medicinal markets in Asia.
- Transported to US/Mexico as hemp fabric.
- Late 1800's budding breeds brought to US.
- After opiate epidemic in 1920's prohibition US makes cannabis illegal.
- Mexican growers export to US market.

Legalization

- After 1960's purported benefits of cannabis begins.
- US government confronts high numbers of use with discussions of legalization.
- 2003 Canada legalizes medical marijuana.
- California starts medical use legalization.

US Medical Marijuana

- Alaska, California, Colorado, Hawaii, Maine, Maryland, Michigan, Montana, Nevada, New Mexico, Oregon, Rhode Island, Vermont and Washington all legalize consumption for medical purposes.
- Marijuana card required.
Studies

• *Marijuana and Medicine; Assessing the Science Base*, Joy, Watson, and Benson, 1999 study reviewed all published data.
• Used for AIDS, MS, chronic pain, anxiety and depression.

Endocannabinoid

• Diffuse regulatory system in brain, gut, heart, genitals, immune system.
• Modulates K+, Ca+ signaling, neurochemicals, cAMP, Adenylyl cyclase.
• A cluster of four effects analgesia, hypothermia, immobility and catalepsy seen in mice.

Membrane Stabilizer

• G protein-coupled receptors, Childers and Breivogel.
• CB1 is in axon of cells in brain, gut, heart, reproductive system.
• CB2 is spleen immune system.
• CB1 is most common G protein receptor system in brain.
• Low signal ratio, attenuates slowly.

Roles

• Endocannabinoid mediated short-term depression (eCB-STD). Taber and Hurley 2009
• ACH, Dopa, NE, Glutamate activity ECB.
• Modulate tone of hypothalamic-pituitary-adrenal (HPA) axis, hippocampus, cortisol system, appetite centers.
Anandamine

- Arachidonyl-ethanolamine, anandamide, phospholipid metabolite.
- Precursor is Arachidonic acid related to eicosanoids and prostaglandins.
- AEA regulates neural tone, inflammation and cellular response rates.

2-Arachidonoylglycerol

- 2-AG is intermediate in lipid metabolism.
- Monoglyceride binds to CB1 receptor modulates Ca+.
- Most potent CB1 agonist.
- Non stored and on immediate demand based on membrane activity.

Regulating

- Two cellular activities regulate.
- Fatty acid amide hydrolase (FAAH) and the monoacylglyceride lipase (MAGL) breakdown EDC. 
- Cellular reuptake inactivates EDC.
Cannabinoid receptor agonists.

Cannabinol CBN
- Non psychoactive cannabis by product.
- Diffuse blocker of P450 systems.
- Increase brain levels of THC by blocking breakdown.
- Repeated exposure increase P450 activity.

Cannabidiol CBD
- Represents a bulk by product of cannabis
- CBD partial antagonizes G protein-coupled receptor 55 (GPR55) in the putamen caudate.
- Sativex is a mouth spray containing THC and CBD for MS and studied for cancer.

Low Coupling Ratio
- Decreases risk for withdrawal.
- Increased exposure has mild effect on tolerance.
- Low dose exposure pushes system and high dose pulls system in over stimulation.
- Biphasic distribution, “push/pull.”
### Cannabis
- Delta 9 THC is CB1 partial agonist.
- Effectiveness determined by ratio of THC/CBD/CBN.
- 4 hour half life.
- Storage and delivery alter THC amounts.

### Marijuana Abuse
- Alcohol, nicotine use and psychiatric disorders predict abuse.
- Intensity of use is predictive of gateway use.
- Mild withdrawal syndrome documented.

### Psychotic disorders
- Cannabis use increases frequency of psychotic episodes in Schizophrenic patients. [Parolari, 2010](#).
- Linked to earlier onset of psychosis and longer psychotic episodes. [Lange, 2010](#).

### Anxiety/Mood
- Cannabis smoking improves and worsens anxiety/mood.
- Genetic variants of gene AKT1 influences differential sensitivity. [van Winkle, 2010](#).
- Children who regularly smoked had elevated risks for depression anxiety as adults. [Rey, 2002](#).
## Dronabinol Marinol

- Dronabinol is synthetic delta-9-THC.
- 1985 FDA approved for nausea, vomiting and anorexia associated with AIDS.
- No evidence of effectiveness in psychiatric disorders.
- Nabilone is marketed for nausea.

## Rimonabant

- CB1 antagonist for treatment of obesity.
- Marketed by Sanofi in 2006, Acomplia.
- 2008 Off market due to depression and anxiety side effects.

## Future

- APA urged federal government to stop interfering with research in states where medical marijuana is legal.
- Pharmaceuticals continue to synthesize differing combinations of active ingredients.
- Potential for compounds for anxiety, depression, and psychotic disorders looks promising.