Marijuana: Modern Medical Chimaera

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chultes (left), internationally known botanist spe-

Chimaera

- Greek mythology: creature with lion’s head, goat’s body, & serpent’s tail capable of vomiting flames.
- Chimerical properties: imaginary, fanciful, or fantastic
Cannabinoids as Therapeutic Tools

- Oscar Prospero-Garcia et al.
- Marijuana affects series of brain receptors: CB1R, CB2R, etc.
- What we know so far:
- **Endocannabinoids** modulate behaviors: food intake, sleep-wake cycle, learning & memory, motivation, pain perception, motor control, & more
Brief History

- 1964, Mechoulam discovered THC
- 1988, Howlett receptors in brain (CB1R)
- 1992, Devane isolated anandamide in pig’s brain; CB2R discovered
- 1994, 2-AG in dogs; oleamide in cats
- So far at least 8 endogenous cannabinoids discovered, 8 synthetic cannabinoids, & 4 therapeutic compounds developed
MARIJUANA EFFECTS

1. **Hypothalamus**: increased appetite
2. **Brain stem**: nausea relief; lowered BP; drowsiness; lowered: pain, spasticity, & tremor
3. **Cerebral cortex**: altered consciousness; perceptual distortions; memory impairment; delusions; hallucinations
4. **Hippocampus**: memory impairment
5. **Cerebellum**: loss of coordination
6. **Amygdala**: changes in anxiety; panic attacks; lowered traumatic memories; decreased hostility
Theoretical Uses of Cannabinoids

- Facilitation or blockade
- **Food Intake**: increase calories from sweet snacks
- CB1 antagonism for anorectic effect, Rimonabant (depression/anxiety)
- **Sleep**: cannabis induces drowsiness; Rimonabant for wakefulness?
Learning + Memory: negative effect on short-term memory

Extinction of fear memories & maladaptive behaviors: PTSD, OCD?

Therapeutic Properties:

Inflammation, pain, muscle spasticity, anxiety, depression, fatigue, insomnia, digestive disorders, etc.
Review of the Literature

- Review of research literature related to medical applications of various forms of cannabis.

- Benefits of medical use examined, as well as, potential risks associated with medical & recreational use.
Drug Delivery

- **Marinol** (dronabinol): synthetic version of delta-9 tetrahydrocannabinol (THC) in sesame oil capsule
- **Cesamet** (nabilone): better absorbed version of dronabinol
- **Sativex**: THC + cannabidiol, natural liquid marijuana extract sprayed into mouth—not approved in U.S.
Review of literature from past 40 years

- 164 serious adverse events among patients receiving cannabis therapy as compared to 60 such events in controls
- Adverse events included primarily respiratory & nervous system disorders
- “short term use of existing medical cannabinoids appeared to increase the risk of nonserious adverse events”
  - Wang et al. 2008
Meta-Analysis of Double-blind Randomized Controlled Trials

- Medical marijuana for pain
- Reviewed 93 studies (18 in final analysis)
- Authors concluded that cannabis use in the treatment of pain presented more risks than benefits

-Martin-Sanchez et al., 2009
First Study of Sativex for Intractable Pain

- Diabetic neuropathy, 38 patients
- No more efficacious than placebo
- Need for more research

-Salvarajah et al., 2010
Cannabis for Palliative Care

- Review of all literature from 1996-2010
- Authors noted “systematic reviews on the efficacy of cannabis in pain control for humans suggests that there is as yet inconclusive evidence that cannabis has any major therapeutic role in pain management.”

-Green & DeVries, 2010, p. 2457
Positive Findings from Green & DeVries

- Literature suggestive of improvements in Quality of Life (QOL) outcomes such as improvements in sleep and abatement of depressive symptoms.

Also, reports on opioid-sparing effects-
synergistic effects of opioid/cannabinoid preparations
More Positive Potential

- Cesamet & Sativex potentially efficacious as *adjuvant therapies* for secondary treatment of chronic illness
- Maybe subjective improvement from patient’s perception for chronic pain
- Patients may not perceive benefits of oral administration

- Peat, 2010
Sativex for Overactive Bladder with MS

- 135 patients, 10 week double-blind randomized, placebo-controlled trial

- Concluded Sativex did provide some improvements in QOL indicators but results did not reach statistical significance.

-Kavia et al., 2010
Sativex for MS related Spasticity

- Meta-analysis of 3 randomized, placebo-controlled, double-blind studies
- 666 patients with MS-related spasticity
- Large numbers of subjects experienced at least one adverse event
- Sativex did reduce spasticity & was well tolerated overall

-Wade et al., 2010
“no solid conclusive data have emerged that would justify the use of cannabis as an alternative to the currently marketed and accepted therapeutic analgesic arsenal.”

-Martin-Sanchez et al. 2009, p. 1354
Risks Associated with Chronic Marijuana Use
Marijuana Abstinence Syndrome
(>48 hrs-2 weeks)

1. irritability/anger/agitation
2. anorexia
3. Insomnia/vivid dreams
4. depression
5. anxiety
6. headaches
7. muscle tension

-Lamarine & Sbarbaro. 1996
Lung Damage/Heart Disease

- Threefold increase of inhaled tar compared to tobacco
- Fivefold increase in CO (carboxyhemoglobin) from smoked marijuana → heart disease
- Depth of inhalation, volume of smoke inhaled, duration of breath holding
- Evidence of obstructive lung disease
- Concurrent use with tobacco may produce synergistic effects and increase risk for COPD
Cancer

- Inhaled smoke loaded with carcinogens
- Increased risk for a wide variety of cancers in smoker and child if smoker is pregnant
Anxiety

- Consistent relationship between frequent marijuana use & higher anxiety levels but NOT with anxiety disorders

- Anxiety also related to withdrawal syndrome

-Crippa et al., 2009
PSYCHOSIS

*risk for psychosis in general population <1%
marijuana users have 40% increase
heavy users 200% increase
six major studies in five countries targeting adolescents & young adults
link only for psychosis, not anxiety, depression, or other mental health problems
mabe pre-existing problems may lead to BOTH pot use + psychosis??

Also poor outcomes in schizophrenic users
<table>
<thead>
<tr>
<th>Drug</th>
<th>Addiction Rate</th>
</tr>
</thead>
<tbody>
<tr>
<td>Marijuana</td>
<td>9%</td>
</tr>
<tr>
<td>Alcohol</td>
<td>15%</td>
</tr>
<tr>
<td>Heroin</td>
<td>23%</td>
</tr>
<tr>
<td>Tobacco</td>
<td>32%</td>
</tr>
</tbody>
</table>
Conclusions

1. Risk/benefit outcomes inconclusive
2. Smoking as a delivery mechanism has significant health risks & concerns regarding dosage administration
3. Clinical trials have not presented clear evidence of significant efficacy
4. Synergistic opioid-sparing effect appears promising
4. Risks with “medical” use appear to be minor but not insignificant
5. Does long-term marijuana use increase risk for psychosis?
6. Anxiety risks appear to be dose-related & of short-term duration
7. Moving cannabis to Schedule II would facilitate more research
Chinese characters:

大 = TA (pronounce da). Literally this means a man, and by extension signify great or tall.

麻 = MA. It represents fiber plant, literally a plant ( 林 ), growing in dwelling ( 广 ). Hence two symbols together “the tall fiber plant,” which everywhere in China signifies canna.
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