Acute Neuropsychiatric Effects of Cannabis and Cannabinoids
Disclosure

• No financial or intellectual conflicts to report
Objectives

• Describe the structural changes that have occurred over time in synthetic cannabinoid receptor agonists (SCRAs)
• Relate those changes to possible behavioral abnormalities in users
• Explain the varied neuropsychiatric presentations and possible treatments
• Coordination with Amir Englund (next speaker)
Figure 1. Pharmacological actions of non-psychotropic cannabinoids (with the indication of the proposed mechanisms of action).

Abbreviations: Δ⁹-THC, Δ⁹-tetrahydrocannabinol; Δ⁸-THC, Δ⁸-tetrahydrocannabinol; CBN, cannabinol; CBD, cannabidiol; Δ⁹-THCV, Δ⁹-tetrahydrocannabinol; CBC, cannabichromene; CBG, cannabigerol; Δ⁸-THCA, Δ⁸-tetrahydrocannabinolic acid; CBDa, cannabidiolic acid; TRPV1, transient receptor potential vanilloid type 1; PPARγ, peroxisome proliferator-activated receptor γ; ROS, reactive oxygen species; 5-HT₁₅, 5-hydroxytryptamine receptor subtype 1A; FAAH, fatty acid amide hydrolase. (+), direct or indirect activation; ↓, increase; ↓, decrease.
<table>
<thead>
<tr>
<th></th>
<th>1960s</th>
<th>1970s</th>
<th>1990s</th>
</tr>
</thead>
<tbody>
<tr>
<td>$\Delta^9$-THC</td>
<td>Naturally occurring dibenzopyran</td>
<td>‘Classical’ cannabinoid (dibenzopyran)</td>
<td>Cyclohexylphenol</td>
</tr>
<tr>
<td></td>
<td>Tricyclic terpenoid derivative with a dibenzopyran ring</td>
<td>$\Delta^9$-THC analog</td>
<td>Naphthoylindole</td>
</tr>
<tr>
<td></td>
<td></td>
<td>AC-bicyclic cyclohexylphenol</td>
<td>1-alkyl-3-(1-naphthoyl) indole</td>
</tr>
</tbody>
</table>

![Chemical structures](image1.png)
AB-CHMINACA

XLR12

JWH-018 8-quinolinyl carboxamide

FUB-144

5F-AKB-48
My Favorite Indole (Serotonin) is a Tryptamine

\[ \text{HO} \quad \text{N} \quad \text{NH}_2 \]
Speculation

Psilocybin

Bufotenine

LSD
Clinical Toxicity

- Chemical(s)
- Plant(s)
- Solvent(s)

Users of synthetic drug filling emergency rooms

Substances sold as "synthetic marijuana" are linked to seizures, heart, and kidney problems.
Characteristics of novel psychoactive substance exposures reported to New York City Poison Center, 2011–2014  

Joseph J. Palamar, PhD, MPH, Mark K. Su, and Robert S. Hoffman
K2, a Potent Drug, Casts a Shadow Over an East Harlem Block

By NICHOLAS CASEY  SEPTE. 2, 2015
**Visit Summary**

<table>
<thead>
<tr>
<th>ED Triage Note</th>
<th>10/24/15 1856</th>
<th>complete</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sat, 24Oct 1856 ED Triage Note Status: complete</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Last ED Visit</td>
<td>:06/23/14 2227</td>
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<tr>
<td>Life Saving</td>
<td>:Complete Full Triage Note</td>
<td></td>
</tr>
<tr>
<td>Communication Method</td>
<td>:Direct Communication in English</td>
<td></td>
</tr>
<tr>
<td>Restraints</td>
<td>:No restraints or handcuffs on patient upon arrival to ED.</td>
<td></td>
</tr>
<tr>
<td>Mode of Arrival</td>
<td>:other ambulance</td>
<td></td>
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<tr>
<td>Chief Complaint</td>
<td>:Vomiting after walking in street and a rat and snake have both crawled up his rectum,</td>
<td></td>
</tr>
<tr>
<td>Assessment</td>
<td>:denies drugs and etoh</td>
<td></td>
</tr>
<tr>
<td>Past Medical/Surgical Hx</td>
<td>:schizophrenia, broken nose</td>
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<tr>
<td>Medications on Arrival</td>
<td>:Pt states they are non-compliant with Medications.</td>
<td></td>
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<tr>
<td>Allergies - Medications</td>
<td>:no known drug allergies</td>
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</tr>
<tr>
<td>Allergies - Other</td>
<td>:no known allergens</td>
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</tr>
<tr>
<td>Domestic Violence</td>
<td>:Domestic Violence: no</td>
<td></td>
</tr>
<tr>
<td>Blood Pressure</td>
<td>:137/84</td>
<td></td>
</tr>
<tr>
<td>Pulse</td>
<td>:86</td>
<td></td>
</tr>
<tr>
<td>Respirations</td>
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<td></td>
</tr>
<tr>
<td>Temperature</td>
<td>:97.3 F (36.3 C)</td>
<td></td>
</tr>
<tr>
<td>Temperature Method</td>
<td>:Tympanic</td>
<td></td>
</tr>
<tr>
<td>O2 Saturation</td>
<td>:98 %</td>
<td></td>
</tr>
<tr>
<td>Glucose</td>
<td>:121 mg/dL</td>
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<tr>
<td>Suspected Infection?</td>
<td>:no</td>
<td></td>
</tr>
<tr>
<td>Alteration of Mental Status</td>
<td>:no</td>
<td></td>
</tr>
<tr>
<td>Pain Screen</td>
<td>:pt denies pain at this time</td>
<td></td>
</tr>
<tr>
<td>Per Invasive</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

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**NYU School of Medicine**

NYU Langone Medical Center
Acute Mental Disturbance Caused by Synthetic Cannabinoid: a Potential Emerging Substance of Abuse in Hong Kong  

Psychosis and Severe Rhabdomyolysis Associated with Synthetic Cannabinoid Use: A Case Report

Clin Schizophr Relat Psychoses. 2015;8:205-8
Psychosis Associated With Synthetic Cannabino
doid Agonists: A Case Series

To the Editor: Recreational use of synthetic cannabi
daoid agonist-containing compounds, commonly known as
“Spice,” has become increasingly popular. These products
consist of nonpsychoactive plant material coated with vary-
ing combinations of synthetic cannabinoid agonists (1). Very
little is known about the toxicology and psychiatric effects of
these drugs. We present a case report in which the smoking
of synthetic cannabinoid agonists precipitated new-onset
psychosis.

Case Report

Ten otherwise healthy men were admitted with new-
onset psychosis to the psychiatry ward at the Naval Medi-
cal Center San Diego between August and December 2010.
The patients were between 21 and 25 years old and had
K2 Toxicity: Fatal case of psychiatric complications following AM-2201 exposure

Amy L. Patton, B.S.¹, Krishna C. Chimalakonda, M.S.², Cindy L. Moran, B.S.³, Keith R. McCain, PharmD.⁴, Anna Radominska-Pandya, Ph.D.², Laura P. James, M.D.⁵, Charles Kokes, M.D.³, and Jeffery H. Moran, Ph.D.¹,²
There was a significant association between a previous history of mental illness and more severe outcome.

Intensive care admission or death

OR = 4.4; 95% CI = 1.4–14.2
15 patients with serious mental illness in New Zealand

69% of users experienced or exhibited symptoms consistent with psychotic relapse

None reported becoming physically unwell
Human Laboratory Studies on Cannabinoids and Psychosis

Mohamed Sherif, Rajiv Radhakrishnan, Deepak Cyril D’Souza, and Mohini Ranganathan

Biological Psychiatry April 1, 2016; 79:526–538

- Almost all data from THC studies
- Some cases with dronabinol and nabilone
- No SCRA data
Comparison With THC Cases

- NYC PCC data
- THC cases from 1/1/2000 (n~2200)
- SCRA cases from same time period but none reported before 2010 (n~1400)

Preliminary analysis

- Agitation
  - THC 16.7%
  - SCRA 19.1%
  - $p = \text{NS}$
Zaurova M, Hoffman RS, Vlahov D, Manini AM: Clinical effects of synthetic cannabinoid receptor agonists compared with marijuana in emergency department patients with acute drug overdose

- 17 patients with SCRAs vs 70 with THC
- Groups not different with regard to age, gender, race/ethnicity, intent or vital signs
- Agitation significantly more likely in SCRA subgroup (OR 3.8, CI 1.2-11.9)
Treatment

- No easy answers
- Largely symptom related
  - Sedation for agitation
    - Ideal choice of sedatives unclear
    - Personal experience – No data
      - Success with midazolam
      - Failure with ketamine
      - Benefits of antipsychotics in patients with underlying psychiatric disease
- Often require long admissions
FUTURE DIRECTIONS
Antiobesity drug rimonabant linked to anxiety and depression

BMJ 2007;335:1070
doi:10.1136/bmj.39402.625544.BE
THANK YOU AND QUESTIONS