The Psychopharmacological Effects of Khat

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The Psychopharmacological Effects of Khat

Objectives:

- Brief overview of pharmacology and its relevance to the pathogenesis of mental disorders
- Brief mention of clinical evidence
- Can khat abuse cause mental health problems
Khat bush
The Psychopharmacological Effects of Khat

- Khat
- Chat – Ethiopia
- Mirraa – Kenya
- Qaat or jaad – Somalia
- Qat – Yemen
Native to Ethiopia

1\textsuperscript{st} to 6\textsuperscript{th} century AD – Yemen

“Abyssinian tea” or “\textit{Tea of the Arabs}” (as opposed to opium in Persians and Turks)

Peter Forskal (1736-1763) – Catha Edulis Forsk \textit{(Niebuhr 1775)}
Mode of ingestion

- Infusion
- Smoking
- Chewing! – brownish discoloration of mouth
Use of Khat (in the past)

- Religious – facilitate praying
- Social – ceremonial approach
- Work performance – awake
- Suppress hunger - food shortage
- Medicinal – depression *(Arabic medical manuscript 1332)*

- Now – recreational!
Psychoactive properties

- Described in Arabic medical literature centuries ago
- Nor-pseudoephedrine (*Wolfes, 1930s*)
- Cathinone – 1975 (*UN Narcotics laboratory*)
Khat chemistry

Trace elements, ascorbic acid, tannins etc

Alkaloids
- 62 cathedulins (Kite et al, 2003)
- Phenylalkylamine
- cathinone
- cathine [(+)norpseudoephedrine]
- (-)norephedrine
100g fresh khat (22 khat samples)
- 36 mg cathinone
- 120mg cathine [(+)norpseudoephedrine]
- 8 mg (-)norephedrine
Cathinone transformed into cathine
(Schorna et al, 1982)
S(-)-α-aminopropiophenone- structure almost identical to amphetamine

Amphetamine-like pharmacological, behavioural and physiological effects

Animals conditioned to recognize amphetamines fail to distinguish from cathinone
Pharmacokinetics

Oral cathinone
30-90 minutes – disappears at 7.5hrs

Khat single dose 0.8mg/kg stimulant effect in 2hrs (magnitude of effect = 0.5mg/kg cathinone)
(Widler et al, 1994)
Pharmacology of cathinone

- Transport into NAergic neurons (inhibited by desipramine)
- Promotes DA release from neuronal stores and NA (centrally and peripherally)
- Lipolytic action (dependent on functional integrity of sympathetic nerve endings)
Cathine/norephedrine effects

Sympathomimetic effects
– chronotropic and inotropic

Increase BP and heart rate
Vasoconstriction
Central Nervous System - Khat

- Cathinone psychostimulant effects probably mediated via the meso-striato-cortico limbic DAergic pathway

- Cathinone prevents haloperidol-induced catalepsy in rats
Intermittent administration of cathinone or khat extract showed progressive augmentation of behavioural sensitisation in animal models (locomotor sensitisation and prepulse inhibition deficit – animal models of psychosis) as with amphetamine and cocaine (Banjaw et al, 2005)
Chronic amphetamine use in animals reduces brain neurotrophins (BDNF) in selected brain areas relevant to schizophrenia and mood disorders (Angelucci et al, 2007)
**Khat - Behavioural effects**

*(Kalix, 1996)*

- Sociable, communicative, loquacious
- Increased self-esteem and sense of well-being
- Increased energy
- "Grandiosity characterised by unrealistic projects"
- Subjectively increased ability to concentrate
WHAT MATTERS MOST
IS HOW YOU SEE YOURSELF.
Khat – cognitive effects

- Objectively decreased concentration and slowed thinking
- Memory function (visuo-perceptual) and decision speed impaired compared to normal subjects (Khattab & Amer, 1995)
Khat behavioural effects

cont.

• Nervousness, agitation, irritability, restlessness, aggressiveness

• Stimulant effect (lasts 3hrs) followed by “depressive phase” – “feelings of depletion”, mental fatigue
<table>
<thead>
<tr>
<th>Symptoms</th>
<th>Mild (%)</th>
<th>Moderate (%)</th>
<th>Severe (%)</th>
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</thead>
<tbody>
<tr>
<td>Insomnia</td>
<td>39</td>
<td>29</td>
<td>32</td>
</tr>
<tr>
<td>Weight loss</td>
<td>55</td>
<td>36</td>
<td>9</td>
</tr>
<tr>
<td>Feeling paranoid</td>
<td>47</td>
<td>30</td>
<td>23</td>
</tr>
<tr>
<td>Feeling depressed</td>
<td>50</td>
<td>37</td>
<td>13</td>
</tr>
<tr>
<td>Mood swings</td>
<td>56</td>
<td>33</td>
<td>12</td>
</tr>
<tr>
<td>Feeling anxious</td>
<td>47</td>
<td>43</td>
<td>11</td>
</tr>
<tr>
<td>Feeling irritable</td>
<td>70</td>
<td>17</td>
<td>13</td>
</tr>
<tr>
<td>Hallucinations</td>
<td>65</td>
<td>22</td>
<td>13</td>
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</tbody>
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What is mental disorder?

A change that occurs in an individual in the way he or she feels, thinks, experiences the environment or behaves and is thought to cause distress or poor functioning.
Khat-induced mental illness

Case reports:
- Paranoid psychosis - with/without first rank symptoms with clear consciousness and intense fear
- Manic illness
- Suicidality during cessation – “withdrawal state” dysphoric/depressed state

(Pantelis et al, 1989; Yousef et al, 1995; Rasool et al, 2000)
Effects on mental health

- Case report series (Pantelis et al, 1989)
- Only 2 of 12 cases had past history of mental illness
- Only 2 of 6 cases had family history of mental illness
- All cases developed psychosis after recent heavy or increased khat use
- Episode resolved within 1-2 weeks off khat
- Psychosis recurred on reinstating khat
Khat and Psychosis – epidemiological studies

Case controlled studies

- Odenwald et al, 2005 (Somaliland) (*WHO CIDI  PNSS*)
- Dhadphale & Omolo, 1988 (Kenya) (*SPQ, ICD-9*)
Khat and Psychosis – epidemiological studies

- Khat use (from an early age and excessive use) was a risk factor for psychosis (Odenwald et al, 2005)

- No significant difference between chewers and non-chewers

  BUT!

  High quantities of chewing associated with increased incidence of psychiatric morbidity (Dhaphale & Omolo, 1988)
Psychosocial

- Khat is associated with concomitant alcohol use and smoking (Alem et al, 1999; Rasool et al, 2000)
- Khat is associated with being Muslim and low income (Awas et al, 1995)
- Stress of recent conflict or migration etc

Mental illness is multifactorial!
Khat

Affects physical, mental and cognitive function

- Good pharmacological evidence showing cathinone’s/khat’s effects on the brain
- Good quality epidemiological evidence supports this
- Ample clinical experience
Conclusion

- Khat can cause serious mental health problems particularly when used frequently and in larger amounts.
- Should be seriously concerned about its increasing use in very young people.
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Thank you for your attention