

# The Psychopharmacological Effects of Khat

*Eleni Palazidou MD, PhD, MRCP, FRCPSYCH*

*Consultant Psychiatrist & Honorary Senior Lecturer  
East London Foundation NHS University Trust  
London E1 4DG, UK*

# 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

# Origins of Khat

- Native to Ethiopia
- 1<sup>st</sup> to 6<sup>th</sup> century AD –Yemen
- “Abyssinian tea” or “Tea of the Arabs” (as opposed to opium in Persians and Turks)
- Peter Forskal (1736-1763) –Catha Edulis Forsk (*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

# Khat alkaloid concentrations

- 100g fresh khat (22 khat samples)
- - 36 mg cathinone
- - 120mg cathine [(+)*norpseudoephedrine*]
- - 8 mg (-)norephedrine
- Cathinone transformed into cathine  
(*Schorna et al, 1982*)

# Cathinone

- **S(-)- $\alpha$ -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

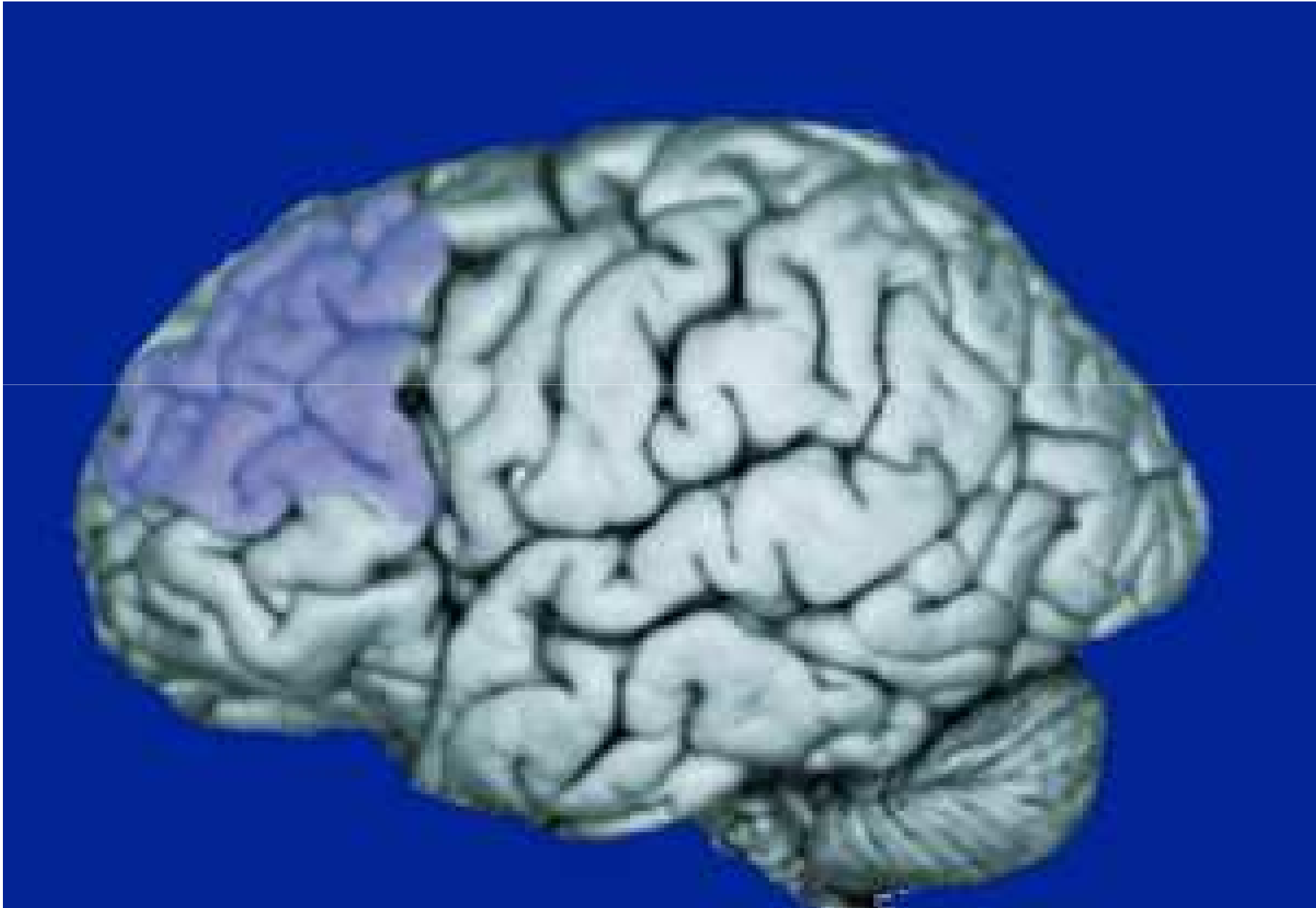
- **Transport into NAergic neurons (inhibited by desipramine)**
- **Promotes DA release from neuronal stores and NA (centrally and peripherally)**
- **Lipolytic action (dependent on functional integrity of sympathetic nerve endings)**

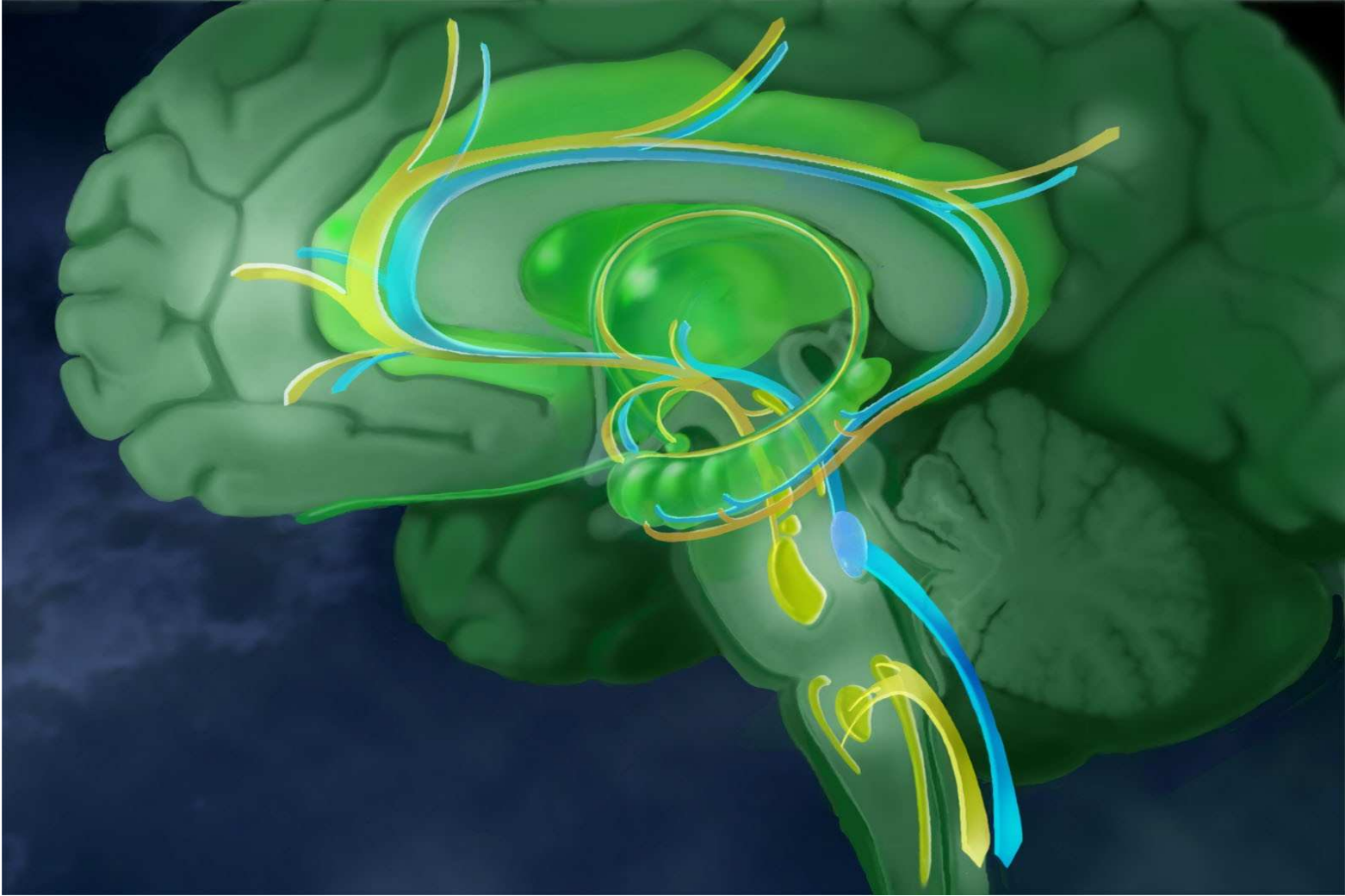
# Cathine/norephedrine effects

**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

# Central Nervous System - Khat

- 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)

# Khat Psychopharmacology

- **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**

# Khat and mental health (adapted from Griffiths et al, 1997)

Symptoms	Mild (%)	Moderate (%)	Severe (%)
Insomnia	39	29	32
Weight loss	55	36	9
Feeling paranoid	47	30	23
Feeling depressed	50	37	13
Mood swings	56	33	12
Feeling anxious	47	43	11
Feeling irritable	70	17	13
Hallucinations	65	22	13



# 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*)
- Ahmed & Salib, 1998 (UK) (*GHQ-28*)

# **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!**

# Summary

## 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

- **What 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*