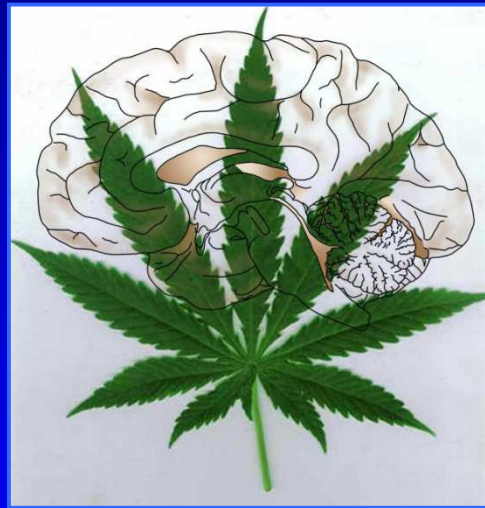


# Acute psychotropic effects of $\Delta^9$ -tetrahydrocannabinol (THC) associated with resting state brain function in the human insula: a pharmacological MRI study



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# Disclosures

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- Nothing to disclose



# Outline

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- Acute effects of cannabis
- Assessment of:
  - Subjective effects of THC
  - Impact of THC on resting state perfusion
  - Correlations between subjective and perfusion effects
- Summary & conclusions



# Acute effects of cannabis

Cannabis produces a broad range of acute psychotropic effects, mainly induced by  $\Delta^9$ -tetrahydrocannabinol (THC)

Euphoria  
Relaxation  
Laughter  
Increased appetite  
Increased creativity  
Perceptual changes  
(music, time, space)

Increased heart rate  
Reddening eyes  
Dry mouth

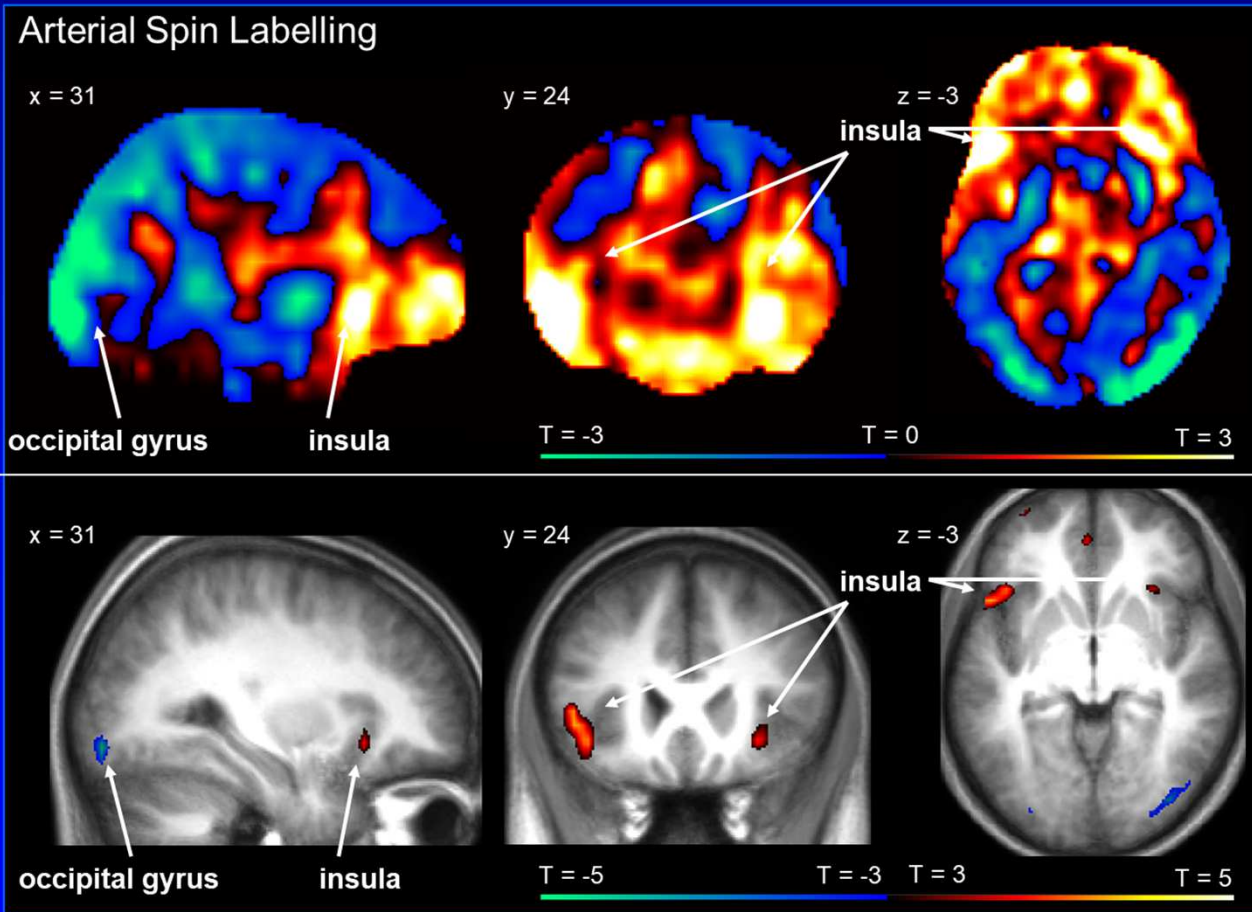
Impaired learning and memory  
Acute hallucinations  
Anxiety or panic attacks





# THC and resting brain function

A limited number of neuroimaging studies examined the acute impact of cannabis on resting state brain function, thereby mapping its effects



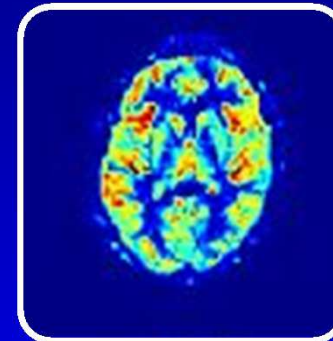
N=20,  $T > 3.6$ ,  $p < 0.001$  uncorrected

Van Hell et al. (2011) - Int J Neuropsychopharmacology



# Research question & design

How does cannabis produce its acute psychotropic effects in the human brain?



39 healthy participants

Double-blind, randomised, placebo-controlled cross-over pharmacological MRI study with THC administration

Test day 1

At least two weeks

Test day 2



# Administration & subjective effects

THC (6 mg) and placebo were administered with a Volcano vaporizer



Subjective effects were assessed with composite visual analogue scales

## Perception

Thoughts

Tranquil

High

Time

## Relaxation

Mentally slow

Dreamy

Drowsy

Muzzy

## Dysphoria

Suspicious

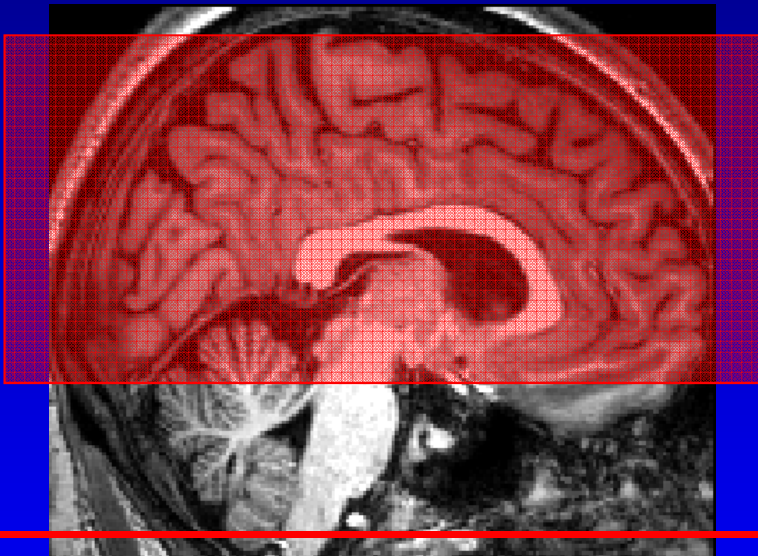
Meaning

Voices



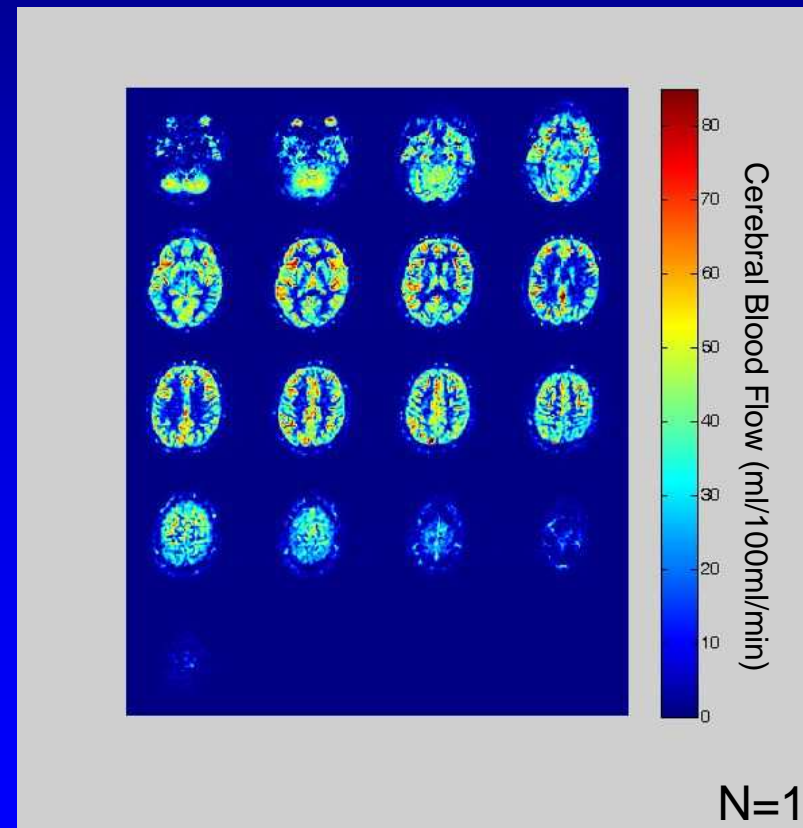
# Arterial Spin Labelling

THC effects on resting brain function measured with Arterial Spin Labelling (ASL), which provides a quantitative measure of perfusion



tag

- Scans obtained 1.5 sec after tagging
- Cerebral Blood Flow = tagged – control

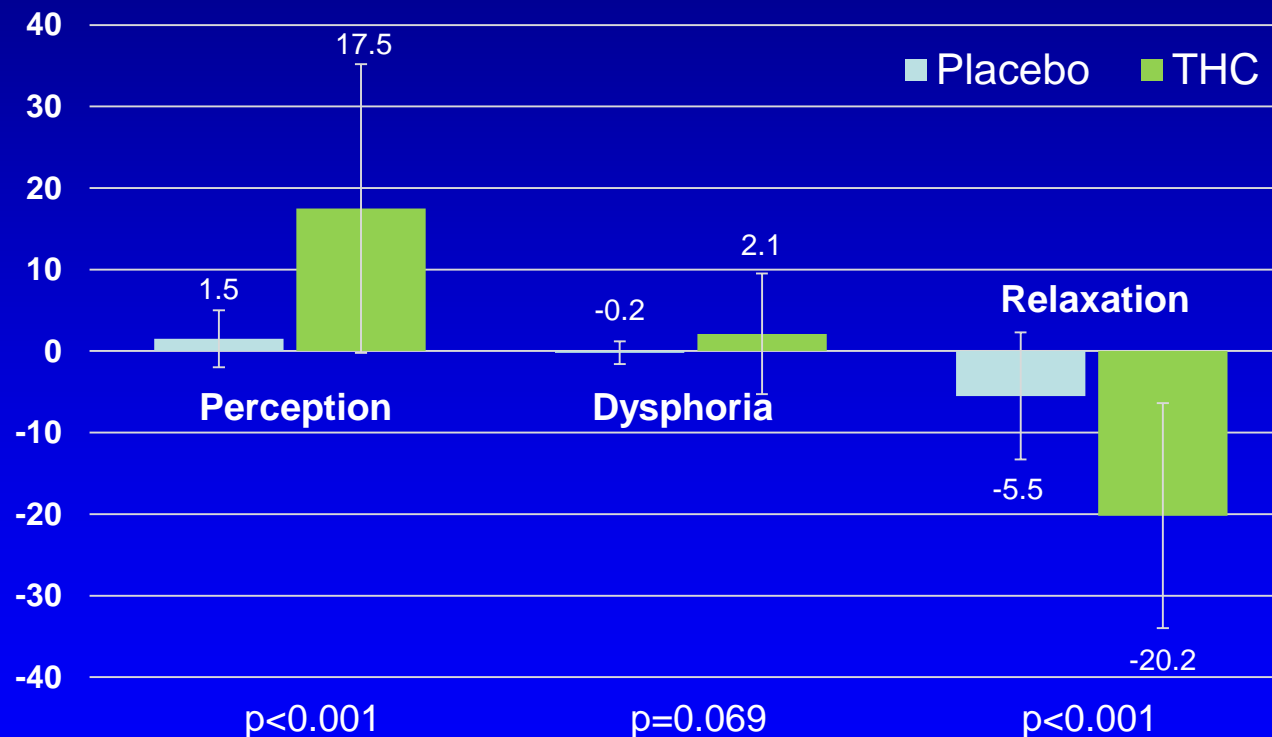






# Results: subjective THC effects

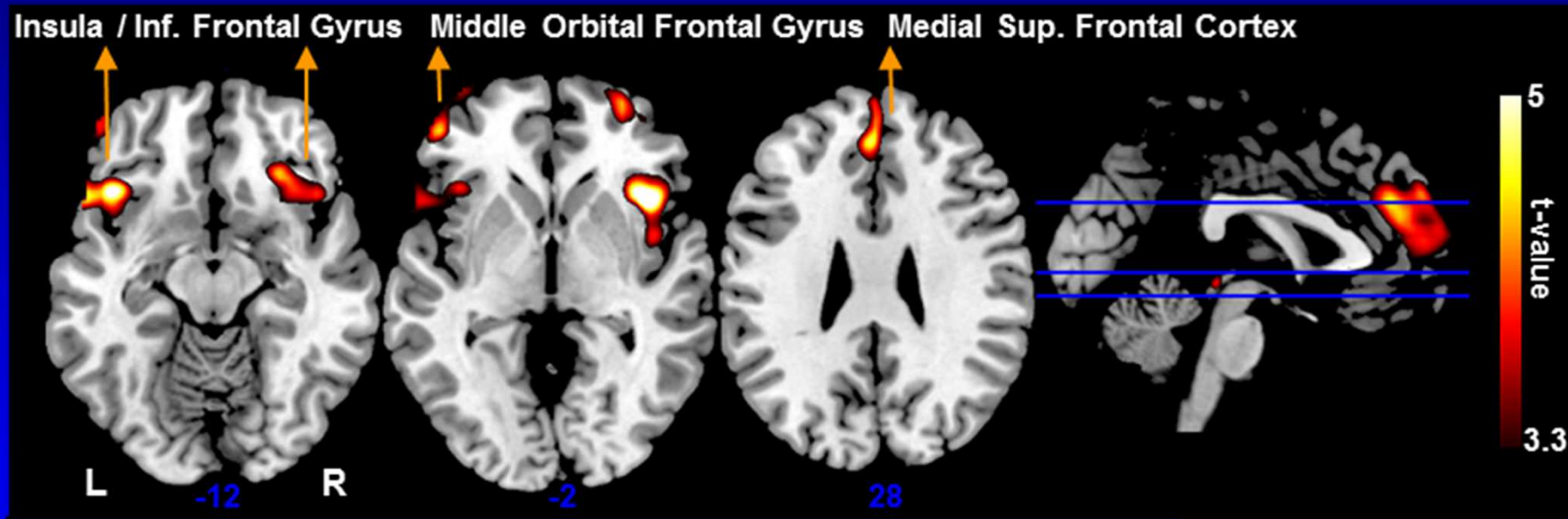
THC induced a significant increase in the subjective rating of 'perception' and a significant reduction in 'relaxation'





# Results: effects on perfusion

THC significantly increased perfusion in both left and right insula, medial superior frontal cortex, and left middle orbital frontal gyrus



Brain region	BA	mm <sup>3</sup>	p value	x	y	z	Max T
Insula / Inferior Frontal Gyrus R	47	8344	<0.001	40	20	-2	6.06
Insula / Inferior Frontal Gyrus L	38	5224	0.003	-44	22	-12	5.21
Medial Superior Frontal Cortex	32	4440	0.005	-2	44	28	4.77
Middle Orbital Frontal Gyrus L	46	2664	0.026	-48	48	-2	4.56

There were no brain areas showing a significant decrease in perfusion after THC administration

N=33, FDR-corrected at cluster level, p<0.05

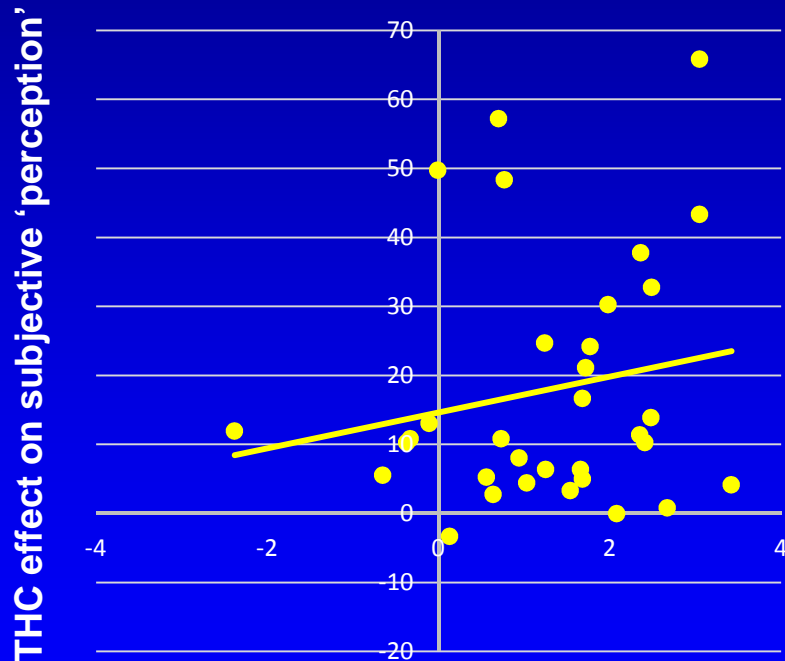
Bossong et al. (2019) - European Neuropsychopharmacology



# Results: correlations

Subjective ratings of 'perception' and 'relaxation' were significantly related to THC effects on perfusion in the left insula

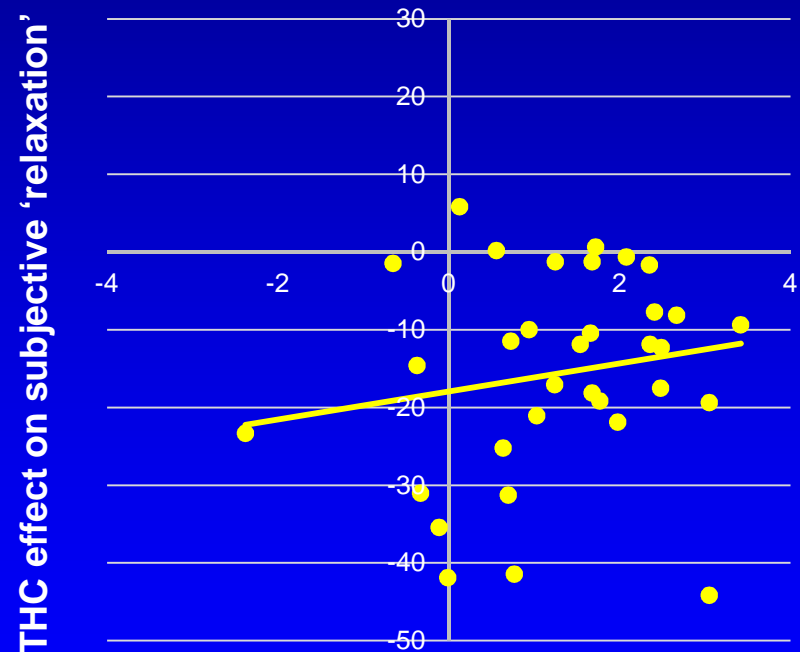
perception



THC effect on perfusion in left insula

$\beta=0.629, p=0.014$

relaxation



THC effect on perfusion in left insula

$\beta=0.540, p=0.020$



# Conclusions

**How does cannabis produce its acute psychotropic effects in the human brain?**

**THC significantly increased perfusion in insula and medial superior frontal cortex, indicating elevated neural activity in salience network**

**Findings in line with previous resting state studies, suggesting a THC-induced increase in awareness and anticipation of salient information**

**Consistent with description of typical THC effects, such as perceptual alterations, time distortion and intensification of ordinary experiences**

**Correlations between THC effects on perfusion and subjective measures further suggest that the main acute psychotropic effects of THC are mediated through recruitment of the salience network**



# Conclusions

## Acute effects of $\Delta^9$ -tetrahydrocannabinol (THC) on resting state brain function and their modulation by COMT genotype

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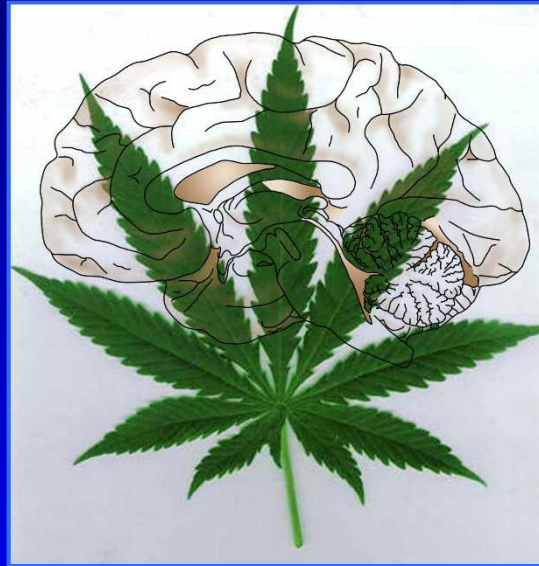
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# Questions?



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