Delta9-tetrahydrocannabinol (THC) impairs working memory system capacity: a pharmacological MRI study

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- No potential conflict of interest

Introduction

How does THC affect memory-related brain function?
- Cannabis use increases the risk for developing schizophrenia.
- Both in schizophrenia and after cannabis administration working memory (WM) is impaired.
- WM system is thought to be compromised in schizophrenia due to inefficient brain function; what is the role of the endocannabinoid system in WM brain function?
- The effect of an acute challenge with the cannabinoid agonist ∆9-THC on WM performance and brain function was assessed in healthy volunteers.

Methods

- Double-blind, randomized, placebo-controlled, crossover pharmacological MRI study
- Nineteen healthy male subjects scanned during two functional MRI sessions separated by two weeks
- Incidental cannabis users: mild cannabis use for at least one year (≤1/week and ≥4/year)
- Inhalation of either 6 mg THC or placebo using a Volcano® vaporizer (Storz-Bickel, Tuttlingen, Germany)
- Parametric Sternberg item-recognition task consisting of letter sets with increasing memory load
- Brain activation during placebo and THC challenge assessed with repeated measures GLM analysis in SPM5
- Regions of interest defined based on pooled group activation maps for load 7 – load 1 contrast

Results

THC did not affect reaction times

THC induced an earlier decline in performance than placebo

THC decreased activation in left middle frontal gyrus and inferior frontal gyrus for higher WM loads

THC tended to enhance brain activation in left inferior parietal gyrus

Conclusions

THC reduces working memory system capacity

- THC affected the response to increasing WM load in terms of performance and activity in frontal regions critically involved in WM-related processes such as maintenance of information.
- These results suggest that THC reduces WM system capacity.
- This is in line with reports on WM deficits in schizophrenia which state that either efficiency or capacity of the WM system is reduced.
- Would a cannabinoid antagonist alleviate WM symptoms in schizophrenia patients?

Introduction

Working memory task (load 7 – load 1) activated a commonly found WM network of brain regions

Conclusions

Working memory task used to determine brain activation