Endocannabinoid involvement in brain reward processing in nicotine addiction

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Introduction

• Addiction is a disabling disease in which reward processing is affected.
• In animal studies, the endocannabinoid (eCB) system has been implicated in both reward processing and in the pathophysiology of addiction, but results in humans are less clear.
• The present pharmacological fMRI study investigated whether eCB receptor activation affects the response of the reward system in nicotine addicts.
• We used the CB1 agonist Δ⁹-tetrahydrocannabinol (THC) to challenge the eCB system, and a monetary incentive delay task to activate the reward system.

Aim

To assess the role of the endocannabinoid system in reward processing in nicotine addiction

Methods

• Thirteen healthy males (age 21.1 ± 2.6) and ten nicotine addicts (age 25.6 ± 6.7; 17.2 ± 5.1 cigarettes per day) participated in a randomized, placebo controlled, double-blind, cross-over pharmacological MRI study. Subjects had a history of mild cannabis use (≤ once a week).
• Two functional MRI sessions, separated by two weeks, with THC administration (6 mg) or placebo using a Volcano® vaporizer.
• Activation of the brain reward system with a monetary reward paradigm (see left figure). Performance measures were speed of response (reaction times).
• Functional imaging data analysis with SPM5.
• GLM with factors representing event-related changes time-locked to anticipation and feedback of neutral (0 euro), and reward (0.10 or 5 euro), and loss (-5 euro) trials (hits and misses modeled separately) and trend correction factors (frequencies lower then 0.007 Hz).
• Nucleus accumbens used as Region of Interest (ROI) for anticipation of reward in nucleus accumbens and striatum.

Results

Behavioral effects
THC administration increased heart rate (F = 36.0, p < 0.001) and subjective scores of ‘feeling high’ (F = 24.4, p < 0.001) and external perception (F = 7.8, p = 0.01). THC decreased ‘alertness’ (F = 27.2, p < 0.001), ‘contentedness’ (F = 18.8, p < 0.001) and ‘calmness’ (F = 10.1, p < 0.005).

Performance
Reaction times showed a linear effect of condition (F = 53.4, p < 0.001). THC increased reaction times in both groups (F = 10.5, p < 0.005). No differences between groups were found.

Brain activity
• In healthy controls we found a near significant effect of condition (F = 4.2, p = 0.06) during placebo, and this effect was significant during THC (F = 10.4, p = 0.01). No significant drug by condition interaction effect was found (F = 0.2, p = 0.7).
• In subjects with a nicotine addiction, we found a significant effect of condition after placebo administration (F = 7.0, p < 0.05), but after THC this effect was eliminated (F = 1.2, p = 0.3). In addition, a linear drug by condition interaction effect (F = 10.3, p < 0.05) indicated that nicotine users showed blunted nucleus accumbens brain activation after THC compared to placebo.

Conclusion

• THC induced significant behavior effects as reflected in increased heart rate, increased feeling high, and decreased alertness.
• THC administration reduced the brain response to anticipation of a monetary reward in the nucleus accumbens in nicotine addicts, but not in healthy controls.
• This indicates that the reward system in nicotine addiction is overly sensitive to an eCB challenge.
• These results may have implications for prevention of addiction, as well as treatment possibilities through pharmacological challenging of the eCB system.

Notes

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Monetary incentive delay task used to determine brain activation.