

Investigation of Marinol (THC) Effects upon fMRI Activation During Active and Passive Driving Using Independent Component Analysis and SPM

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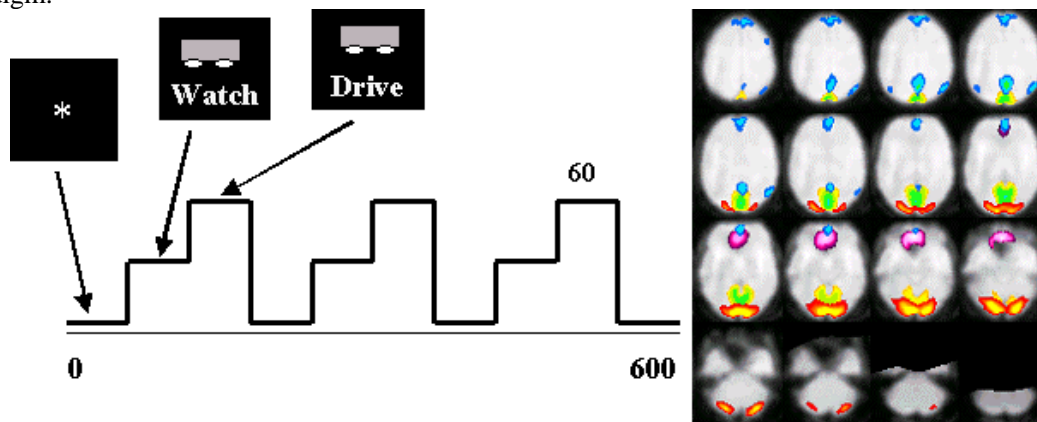
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Abstract

Introduction: Driving is a complex behavior involving multiple simultaneous cognitive elements including focused and divided attention, complex visuospatial interpretation and motor visual integration. A fMRI paradigm was developed to study the interrelation of the cognitive elements involved in “driving” as a whole. Here we show for the first time interrelated functional regions involved in simulated driving that we presume underlie capabilities including motor control, visuospatial integration and focused attention. Independent component analysis (ICA) was applied to the data set to extract components correlated with the paradigm either consistently or transiently. Results demonstrate drug-induced differences in cerebellar, frontal and orbitofrontal regions.

Methods: Using a Philips NT 1.5 T scanner, we acquired 600 functional scans (EPI, TR=1s, TE=39ms, fov=24cm, 64 x 64, st=5.5 mm, 18 slices). Thirteen subjects were scanned during two runs of a 10 min. paradigm (See Figure) consisting of 1-min. epochs of 1) a black screen, 2) watching a driving simulation (passive), or 3) driving. Subjects were trained to asymptote performance prior to scanning. We built a control device similar to a video game controller. After the first scan session subjects were removed from the scanner and given oral Marinol (10 mg) followed by another scan session involving two more runs of the driving paradigm.



Data Analysis: The images were corrected for timing differences between the slices (4,5), imported into SPM99, motion corrected, spatially smoothed and normalized into a Talairach template (6,7). A group ICA map was calculated for the entire experiment after reducing the data via principal component analysis. Data were also analyzed with SPM99 using linear contrasts between the three conditions.

Results: We obtained quantitative in-scanner behavioral measures of driving performance (e.g. crash ratio, lane deviation). Performance was consistent across subjects and deteriorated significantly following drug administration. Imaging results in the drug-free state indicated activation in cerebellum, primary visual, superior and inferior parietal, anterior cingulate (orbitofrontal), primary motor cortex, and supplemental motor areas. Following marinol, there was a decrease in the cerebellar activation during either passive or active driving (as compared with baseline) and a decrease in the change between the two conditions. Anterior cingulate regions showed the most striking difference with a very structured temporal pattern in non-drug subjects and a significantly different pattern following marinol. Finally, active driving specifically activated frontal regions but not following marinol.

Conclusion: We have demonstrated the feasibility of importing a quantifiable virtual driving paradigm into the fMRI environment and measured differential activation in such a paradigm following the administration of Marinol. Orbitofrontal regions probably related to attention were the most affected by the drug. Additionally cerebellar and frontal regions showed drug specific changes in activation.

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