Effects of cannabis use on cognitive brain function in adolescents: short-term memory, long-term consequences?

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Objectives

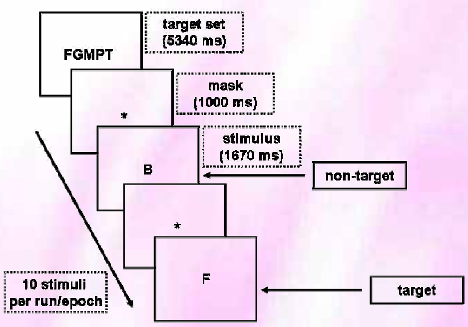
This functional MRI study investigated the sustained effects of teenage cannabis use on working memory brain function.

Use of cannabis is common among school-going youth[1]. As brain maturation continues during adolescence, the long-term consequences of early onset cannabis use for cognitive brain function may be different from and more severe than in adult users. Here, we focussed on working memory (WM) which is dependent on prefrontal brain function. The prefrontal cortex is among the areas in the brain that mature relatively late[2].

Methods

- This study was a joint venture of the University Medical Center Utrecht (NL) and the University of Iowa (US).

- Twenty-one cannabis using boys (age; 15 – 19, average number of joints in the year preceding the study; 740 (SD ± 772, range 200 – 3500) were compared with twenty-three non-using age-matched peers. All subjects abstained from cannabis and alcohol for at least 1 week before examination. The WM system was assessed with a modified Sternberg paradigm (STERN)[3]



- STERN assesses the WM system before and following rule-based learning (automatization). Subjects were instructed to memorize a set of five letters and subsequently respond to matching probes (targets). A novel (NT) and a practiced task (PT) were administered. In PT a fixed set was used repeatedly, on which subjects were trained before scanning to induce automatization. In NT the composition of the target-set was changed after every epoch. An additional reaction time control task (CT) was included, as well as rest periods of equal epoch duration.

- Scanner: Clinical 3.0 T MRI scanner (Philips Achieva (NL) or Siemens Magneton Trio (US)). Sequence: FE-EPI, TE/TR 35/2000 ms, FOV read 256, voxelsize 4 mm isotropic, number of scans = 384, registered and spatially smoothed (FWHM: 8 mm) using a Gaussian filter in SPM5.

Analyses

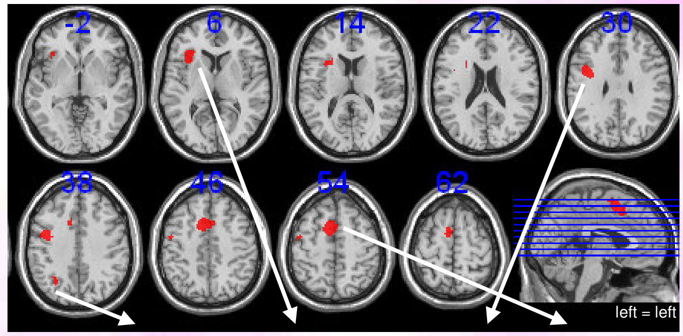
- GLM repeated-measures analysis on task performance with task as within- and group as between-subjects factors. Age was included as covariate to adjust for normal developmental effects.

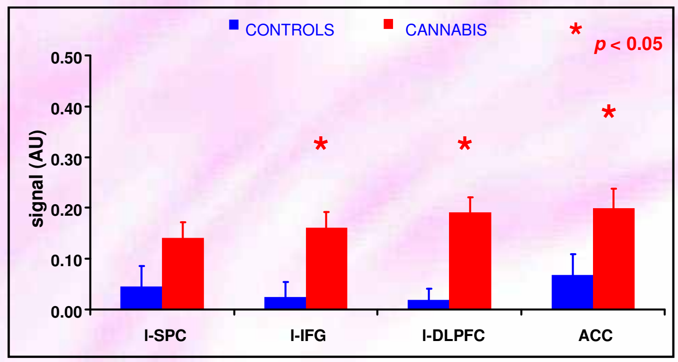
- Multiple regression with factors modeling task (novel, practiced, control) in SPM5. Activity during NT and PT reflected WM-activity before and following rule-based learning (automatization).

- Whole-brain group-analysis of activity during PT and NT at p<0.05 (corrected for multiple comparisons), adjusted for effects of normal development (age) and potential differences in MRI equipment across countries.

- Regions of interest (ROI) were derived from a group t-map of all subjects combined (threshold z = 4.0) and yielded four activated regions in the left superior parietal cortex (l-SPC), the left inferior frontal gyrus (l-IFG), the left dorsolateral prefrontal (l-DLPFC), the anterior cingulate (ACC) and the left superior parietal cortex (l-SPC). A mean activity score (b-values) was obtained for NT and PT and entered into repeated measurements GLM analysis.

Results





Upper figure shows regions-of-interest, i.e. the left superior parietal (l-SPC), the left inferior frontal (l-IFG), the left dorsolateral prefrontal (l-DLPFC) and the anterior cingulate cortex (ACC), projected on a T1-single subject MNI template. Numbers above the slices indicate MNI z-coordinates. Lower graph shows contrast values (in arbitrary units), i.e. activity during NT minus activity during PT.

On average cannabis users had lower IQ-scores (p<0.01) than controls, and reported more frequent alcohol use (p<0.01) and tobacco smoking (p<0.001). Nine out of twenty-one cannabis users fulfilled criteria for conduct disorder, but no other psychopathology was present.

Cannabis users performed equally fast and accurate as their non-using peers.

A whole brain voxel-by-voxel analysis yielded no group differences. Subsequent ROI-analysis revealed that the WM system tended to be overactive before learning in cannabis users (p=0.10). They showed significant larger differences in activity before and following automatization in the l-IFG (p<0.01), the l-DLPFC (p<0.001) and the ACC (p<0.05). As automatization reduced activity in the WM system to the same level in both groups, this indicates that excessive effort was required in cannabis users to achieve normal performance when a task is novel. Adjustment for group differences in IQ and use of alcohol and tobacco did somewhat attenuate the main findings without making them disappear.

Discussion

In adolescent cannabis users the WM system was overactive during a novel task, whereas automatization reduced activity to the same level in users and controls. This pattern is similar to what we observed in schizophrenic patients[3]. Inefficient WM recruitment is not related to a failure in automatization, but becomes evident when processing continuously changing information in WM. This suggests that teenage cannabis use may reduce the ability to process information requiring frequent updating. Whether these effects will persist over longer periods of abstinence, as well as their clinical relevance in terms of cognitive dysfunction remain to be determined.

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