K54 Neurocognitive Performance in Occasional and Frequent Smokers Following Controlled Smoked, Vaporized, and Oral Cannabis Administration

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After attending this presentation, attendees will be able to describe cannabis' effect on neurocognitive performance after smoked, vaporized, and oral cannabis administration to occasional and frequent cannabis smokers.

This presentation will impact the forensic science community by aiding in the interpretation of neurocognitive performance after three different administration routes in two groups of cannabis smokers.

The objective of this study was to evaluate cannabis' neurocognitive effects in occasional and frequent smokers after three different administration routes. Cannabis remains the most commonly used illicit substance in the world and was the most prevalent illicit drug detected in 12.6% of nighttime drivers in the 2013-2014 National Roadside Survey. Cannabis smoking is associated with poor driving performance and approximately doubles the risk of involvement in a motor vehicle accident. Although smoking is the most common cannabis administration route, oral consumption and cannabis vaporization are also popular; however, data on the impact of delivery mode and intake frequency on cannabis' pharmacodynamic effects remain limited.

Eight frequent (≥5x/week) and eight occasional (≥2x/month but <3x/week) adult cannabis smokers were recruited to participate in this National Institute on Drug Abuse Institutional Review Board, Food and Drug Administration (FDA), and Drug Enforcement Administration (DEA) -approved study; all participants provided written informed consent. Participants entered the secure research unit approximately 19h prior to dosing to preclude acute intoxication. Sessions followed a double-blind, double-dummy, randomized, crossover, placebo-controlled design. Over the course of four dosing sessions, participants consumed a placebo or active oral (baked in a brownie) cannabis dose (6.9% THC), followed by either placebo or active smoked or vaporized cannabis. Only one route of administration had active THC in each session. Smoking, inhaling, and eating were each performed *ad libitum* for 10min. Participants were trained before study sessions to achieve stable task performance. Neurocognitive tasks were performed at -1.5h (baseline), 0.5h, and 2.5h relative to the start of dosing. The Stop Signal Task (SST) measures motor impulsivity, or the inability to inhibit a pre-cued response. The Tower of London (TOL) task is a decision-making task measuring executive function and planning. Friedman's Analysis of Variance (ANOVA) and Wilcoxon tests were utilized to examine within-group effects while Mann-Whitney tests were executed to examine between-group effects. Statistical significance was attributed at $p<0.05$, with trends attributed at $p<0.1$.

In the SST, there was a significant group effect between frequent and occasional smokers for all administration routes, indicating poorer performance in frequent smokers. Frequent smokers demonstrated significantly lower total accuracy ($p=0.0180$) than occasional smokers 2.5h after vaporization with a trend at 0.5h ($p=0.0512$). A trend also was observed ($p=0.0512$) for frequent smokers' lower total accuracy compared to occasional smokers 2.5h after smoking. Trends in longer reaction times in no-stop trials at 0.5h ($p=0.0939$) and 2.5h ($p=0.0721$) after oral administration in occasional smokers were observed. For frequent smokers, the SST was sensitive to cannabis' impairing effects as indicated by lower accuracies after smoking and vaporization. For occasional smokers, the SST was sensitive to oral cannabis' impairing effects as indicated by longer reaction times in no-stop trials.

For TOL, there were no significant effects in frequent cannabis smokers on total score or task completion time after smoked or oral cannabis administration. Frequent smokers had no significant change in total score, but completed the task significantly faster ($p=0.0371$) 0.5h after vaporization compared to baseline with a trend observed between baseline and 2.5h ($p=0.0645$). A significant ($p=0.0375$) overall time effect was observed for occasional smokers' decrease in completion time after smoking. Other factors, such as consumed *ad libitum* dose, tolerance, and baseline neurocognitive function may play a role in task performance. These data have implications for driving under the influence of cannabis, as reaction time and motor impulsivity impact driving performance.

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Cannabis, Administration Route, Neurocognitive Impairment

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