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**Acute Effects of Smoked and Vaporized Cannabis in Healthy Adults Who Infrequently Use CannabisA Crossover Trial**

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**Question**  How does smoked and vaporized cannabis acutely influence subjective drug effects, cognitive and psychomotor performance, and cardiovascular measures in healthy adults who infrequently use cannabis (>30 days since last use)?

**Findings**  In a crossover trial of 17 healthy adults, inhalation of smoked and vaporized cannabis containing 10 mg of Δ9-tetrahydrocannabinol (THC) produced discriminative drug effects and modest impairment of cognitive functioning, while inhalation of a 25-mg dose of THC was associated with pronounced drug effects, increased incidence of adverse effects, and significant impairment of cognitive and psychomotor ability. Vaporized cannabis produced greater pharmacodynamic effects and higher concentrations of THC in blood compared with equal doses of smoked cannabis.

**Meaning**  Significant, sometimes adverse, drug effects can occur at relatively low THC doses in infrequent cannabis users, and accordingly these data should be considered with regard to regulation of retail cannabis products and education for individuals initiating cannabis use.

Abstract

**Importance**  Vaporization is an increasingly popular method for cannabis administration, and policy changes have increased adult access to cannabis drastically. Controlled examinations of cannabis vaporization among adults with infrequent current cannabis use patterns (>30 days since last use) are needed.

**Objective**  To evaluate the acute dose effects of smoked and vaporized cannabis using controlled administration methods.

**Design, Setting, and Participants**  This within-participant, double-blind, crossover study was conducted from June 2016 to January 2017 at the Behavioral Pharmacology Research Unit, Johns Hopkins University School of Medicine, and included 17 healthy adults. Six smoked and vaporized outpatient experimental sessions (1-week washout between sessions) were completed in clusters (order counterbalanced across participants); dose order was randomized within each cluster.

**Interventions**  Cannabis containing Δ9-tetrahydrocannabinol (THC) doses of 0 mg, 10 mg, and 25 mg was vaporized and smoked by each participant.

**Main Outcomes and Measures**  Change from baseline scores for subjective drug effects, cognitive and psychomotor performance, vital signs, and blood THC concentration.

**Results**  The sample included 17 healthy adults (mean [SD] age, 27.3 [5.7] years; 9 men and 8 women) with no cannabis use in the prior month (mean [SD] days since last cannabis use, 398 [437] days). Inhalation of cannabis containing 10 mg of THC produced discriminative drug effects (mean [SD] ratings on a 100-point visual analog scale, smoked: 46 [26]; vaporized: 69 [26]) and modest impairment of cognitive functioning. The 25-mg dose produced significant drug effects (mean [SD] ratings, smoked: 66 [29]; vaporized: 78 [24]), increased incidence of adverse effects, and pronounced impairment of cognitive and psychomotor ability (eg, significant decreased task performance compared with placebo in vaporized conditions). Vaporized cannabis resulted in qualitatively stronger drug effects for most pharmacodynamic outcomes and higher peak concentrations of THC in blood, compared with equal doses of smoked cannabis (25-mg dose: smoked, 10.2 ng/mL; vaporized, 14.4 ng/mL). Blood THC concentrations and heart rate peaked within 30 minutes after cannabis administration and returned to baseline within 3 to 4 hours. Several subjective drug effects and observed cognitive and psychomotor impairments persisted for up to 6 hours on average.

**Conclusions and Relevance**  Vaporized and smoked cannabis produced dose-orderly drug effects, which were stronger when vaporized. These data can inform regulatory and clinical decisions surrounding the use of cannabis among adults with little or no prior cannabis exposure.

**Trial Registration**  ClinicalTrials.gov Identifier: NCT03676166.