Abstract Rationale: Many previous studies have reported that alcohol and cannabis produce additive psychomotor effects in acute combination, but few have explicitly tested whether chronic exposure to cannabis, in the absence of acute administration, alters the effects of alcohol on psychomotor performance. Objectives: To test whether long-term cannabis use modulates the effects of alcohol on psychomotor skills and self-reported mood and sensation. Methods: Regular cannabis users (minimum: daily use for at least 3 years) and infrequent users (maximum: once-monthly use for at most 3 years) were matched for sex, age, alcohol intake and other drug use (14 participants in each group). Participants received alcohol (females 0.35 g/kg; males 0.45 g/kg) and placebo drinks. By urinalysis, only regular users tested positive for metabolites of ∆9-tetrahydrocannabinol; breath alcohol levels were similar between groups. Participants were tested on a computerised tracking task that has been used to screen drugs for adverse effects on driving. The task involved tracking a moving target on a computer screen while simultaneously responding to occasional presentations of stimuli in the periphery of the screen. Results: Tracking accuracy was similar for both groups after placebo, but alcohol caused a significant deterioration in performance among infrequent cannabis users relative to regular users. These changes were mirrored by significant changes in self-reported scores for dizziness, measured by visual analogue scales. Alcohol slowed reaction times, but not differentially between groups. Conclusions: For psychomotor skills relevant to driving, chronic cannabis use (in the absence of acute administration) does not potentiate the effects of alcohol. In fact, the superior tracking accuracy of regular users relative to infrequent users after alcohol, and their lower scores for dizziness, suggest that chronic cannabis use may instead confer cross-tolerance to specific effects of alcohol on behaviour.

Keywords Cannabis · Alcohol · Psychomotor performance · Driving · Cross-tolerance

Introduction

The performance effects of alcohol and cannabis are frequently reported to be similar in several respects, although qualitative differences between the effects of the two drugs have also been identified (Bech et al. 1973; Rafaelson et al. 1973a, 1973b; Hansteen et al. 1976; Belgrave et al. 1979; Bird et al. 1980; Chait and Perry 1994; Heishman et al. 1997; Robbe 1998). In acute combination, alcohol and cannabis tend to produce additive effects (Manno et al. 1971; Cheshet al. 1976, 1977; Belgrave et al. 1979; Bird et al. 1980; Chait and Perry 1994). Less common are reports of synergistic effects following conjoint administration (MacAvoy and Marks 1975; Sutton 1983; Perez-Reyez et al. 1988; Robbe 1998). Of the many studies that have compared the effects of the two drugs alone and/or in combination, nearly all have tested participants who are experienced cannabis users. An exception is the study by Marks and MacAvoy (1989), who tested the effects of cannabis and alcohol in experienced cannabis users and also in non-users matched for levels of alcohol use. The task was a test of divided attention and involved two types of visual detection: responding to changes in the flash rate of a light in the central visual field and simultaneously responding to light flashes in the peripheral visual field. Surprisingly, they found that the experienced users were significantly less impaired than the non-users at detecting the peripheral stimuli after alcohol. Although no other advantage of users over non-users was found on any of several other measures, neither was there any tendency for the users to demonstrate poorer performance than the non-users after either cannabis or alcohol. These results were consistent with those from
previous studies that failed to control for levels of alcohol use between groups (MacAvoy and Marks 1975) or lacked other appropriate controls (Jones and Stone 1970). Therefore, long-term cannabis use, and/or residual effects from last use, do not appear to enhance a person’s susceptibility to the detrimental effects of alcohol. Indeed, chronic cannabis use might protect against certain deleterious effects of alcohol.

The present study compared regular cannabis users with infrequent cannabis users on a test of psychomotor performance, both in the presence and absence of alcohol. The psychomotor test employed was a compensatory tracking task (CTT) that measures component skills of divided attention and tracking. The task has been established as an effective analogue of car driving and is sensitive to drug effects (Hindmarch 1983; Kerr et al. 1991). At moderate-to-high doses alcohol can be very detrimental to tracking accuracy and reaction time performance (Klein and Jex 1975; Hansteen et al. 1976; Moskowitz et al. 1985; Heishman et al. 1989). Since it was anticipated that relatively subtle between-group differences would be found in this study, an alcohol dose was required that would be high enough to degrade performance but low enough to avoid a ceiling effect. The target peak breath alcohol concentration (BrAC) was between 35 µg/100 ml and 22 µg/100 ml (between the current limits for legal driving in the UK and several other European countries, respectively). Given the results of Marks and MacAvoy (1989), who used a task that was also intended to test component skills relevant to driving, it might be expected that regular cannabis users would demonstrate some resistance to the effects of alcohol on performance.

**Materials and methods**

**Participants**

A group of 14 regular cannabis users (minimum use: daily for at least 3 years) and a group of 14 infrequent cannabis users (maximum use: once-monthly for at most 3 years) were matched for gender, age, weight, employment status, histories of other drug use and weekly levels of alcohol intake (factor group, Table 1). All cannabis use was by smoking. Participants were professional workers, students in tertiary education or unemployed. By self-report, all participants were in good health, were not on any medication and had no history of mental illness. The study was approved by the intramural ethics committee, and written informed consent was provided by all participants. No payment was given for participation; only travelling expenses were reimbursed.

**Experimental design**

Each participant was tested in two drug conditions (with alcohol and with placebo: factor alcohol) in a single-blind design. Test orders for factors alcohol and group (regular versus infrequent cannabis users) were counterbalanced. Before each session, participants were asked by telephone to abstain from alcohol for 24 h, caffeine for 4 h and nicotine for 1 h. The cannabis users were asked to refrain from using the drug from midnight before each session; all testing was between 1000 hours and 1200 hours. By self-report, all regular cannabis users reported last use of the drug no less than 12 h before testing.

**Alcohol administration**

Alcohol drinks contained 75% Schweppes Indian tonic water, 25% Safeway vodka (37.5% alcohol) and 1.5% Angostura bitters (Glaudier et al. 1992). Placebo alcohol drinks replaced vodka with tonic water and 0.25 ml vodka was floated on the drink surface and around the rim of the glass. To achieve the intended BrAC level (between 22 µg/100 ml and 35 µg/100 ml breath, 50–80 mg/100 ml blood), alcohol was administered at 0.45 g/kg and 0.35 g/kg (1.49 ml/kg and 1.15 ml/kg) body weight to males and females respectively. Pilot tests confirmed that the doses achieved the desired BrAC level.

**Compensatory tracking task**

Participants were required to track a moving target circle presented on a video display unit using a mouse-driven cursor. At the same time a white disc (2.5 cm diameter) was presented at a random interval within a given 10 s trial in one of the four corners of the screen. Responses to the onset of the peripheral stimulus were made by clicking the mouse button, after which the stimulus disappeared. Reaction times (RTs) were measured in milliseconds (ms) to 72 stimuli over a 12-min period (72×10 s trials) following a 3-min practice trial (18 peripheral stimuli; pilot tests had indicated that practice effects were negligible). Mean accuracy was calculated as the mean deviation from the centre of the target circle over the same number of trials.

**Procedure**

Food intake before each of the two morning test sessions was controlled by giving a fixed meal of two slices of buttered toast; prior food intake was not restricted, but no participants reported eating during the preceding 12-h period. Each participant completed a visual analogue scale (VAS), assessing (broadly) mood and sensations (items: friendly, cheerful, confident, clearheaded, anxious, nauseous, dizzy, irritable). For each item, participants were required to place a mark on a 100-mm line, extending from ‘not at all’ to ‘extremely’, according to how they currently felt. Before starting, a urine sample was collected to test for the presence of Δ⁹-tetrahydrocannabinol (THC) metabolites (primarily 11-nor-Δ⁹-THC-9-carboxylic acid) using enzyme immunoassay (Diacheck Diagnostics Inc., Boston, Mass.), and a BrAC reading was taken (Lion alcolmeter breathalyser, model S-D2; Lion Industries, Barry, Wales). All BrAC measures were zero pre-test. Alcohol and placebo test sessions were counterbalanced. Alcohol or placebo alcohol drinks were consumed over 20 min. After a 20-min interval to allow for absorption, a second BrAC reading was taken, and physical symptoms and mood scales were again completed. The CTT was then performed over 15 min, and a final BrAC reading was taken afterwards.