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Acute effects of smoked marijuana in marijuana smokers at clinical high-risk for psychosis: A preliminary study

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Abstract

Marijuana use is associated with psychosis, but its effects are understudied in individuals with preexisting risk for psychotic disorders. This preliminary study examined the acute psychological and physiological effects of smoked marijuana (0.0% or 5.5% Δ^9-THC) in marijuana users at clinical high-risk (CHR; n = 6) to develop a psychotic disorder, and those not at risk (n = 6), under controlled laboratory conditions. CHR marijuana users exhibited temporary increases in psychotic-like states and decreases in neurocognitive performance during marijuana intoxication but control marijuana smokers did not. These findings, if replicated, may support a psychotogenic role for marijuana in CHR individuals.

Keywords

Cannabis; Prodromal psychosis; Ultra high-risk

1. Introduction

The association between marijuana smoking and the development of psychotic disorders (Gage et al., 2016) is concerning, but the cause-and-effect relationship between marijuana use and psychosis is not well-established (Auther et al., 2015; Haney and Evins, 2016). This impedes the development of clinical recommendations and interventions. Marijuana use and use disorder are common (Auther et al., 2015) in those at clinical high-risk (CHR) for a psychotic disorder (i.e., adolescents or young adults who exhibit attenuated psychotic symptoms and/or familial predisposition, with recent psychosocial decline or chronic low functioning; McGlashan et al., 2001). In this population, increases in reported marijuana use

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All authors declare that they have no conflicts of interest.

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Appendix A. Supplementary material

Supplementary data associated with this article can be found in the online version at http://dx.doi.org/10.1016/j.psychres.2017.07.070.

are associated with exacerbations of psychotic-like symptoms (Corcoran et al., 2008), both of which are predictive of psychosis onset (McHugh et al., 2016; Valmaggia et al., 2014).

In laboratory studies, administration of marijuana or its primary psychoactive component (Δ^9-THC) may acutely produce psychotic-like and neurocognitive effects, with its most robust effects in participants with psychotic disorders (Sherif et al., 2016). However, to our knowledge no laboratory study has directly examined marijuana effects in CHR individuals, who have a distinct and appreciable risk to develop a psychotic disorder (Fusar-Poli et al., 2012). Further, existing laboratory studies in the psychosis spectrum may be limited in terms of ecological relevance and/or nonstandard measurement of marijuana effects (e.g., D'Souza et al., 2004). Therefore, in this preliminary study, we characterize the psychological and cardiovascular effects of active and placebo marijuana cigarettes (containing 5.5% and 0.0% Δ^9-THC, respectively) in CHR and control marijuana users, under controlled laboratory conditions.

2. Methods[1]

This study was approved by the NYS Psychiatric Institute IRB and the NYS Office of Mental Health, and all participants provided written informed consent.

2.1. Participants

Participants were an ethnically-diverse sample (n = 12) of physically-healthy weekly marijuana users with minimal use of other illicit substances (verified by urine toxicology). They reported no prior serious adverse reactions to marijuana and denied seeking treatment for marijuana use. Half (n = 6; 5 M, 1 F) were a clinical sample that met operationalized criteria for a CHR syndrome (McGlashan et al., 2001), while the rest (n = 6; 4 M, 2 F) did not (controls). The groups were similar in demographic characteristics and marijuana/alcohol use patterns ($p > 0.05$), but not psychopathology ($p < 0.05$; see Supplemental [S] Table 1).

2.2. Procedures

During each laboratory session, participants completed a battery of subjective (e.g., visual analogue scale), neurocognitive (Keilp et al., 2014) and cardiovascular measures, smoked 50% of an active or placebo marijuana cigarette (provided by NIDA) according to a standardized procedure (e.g., Haney et al., 2016), and repeated the measures (Table S2). The strength of marijuana tested was randomized and double-blinded.

2.3. Statistical analyses

Due to the limited sample size, acute effects were examined for each group independently. Repeated measures ANOVA assessed the main effects of drug condition (active vs. placebo) and the drug condition × time (baseline vs. post-marijuana) interactions on dependent measures, with t-tests to probe significant interactions. Alpha was set at 0.05.

[1]Full details on methodology, results and safety can be found in the online supplement.

3. Results

In the CHR group, active marijuana (relative to placebo) increased ($p < 0.05$) subjective ratings of paranoia (Fig. 1A), anxiety (1B), slowed time perception, visual illusions, feelings of strangeness and inattention (Table S3a), and decreased ($p < 0.05$) objective performance on tasks of working memory and response inhibition (Table S4a). These effects were not observed ($p > 0.05$) in the control group (Fig. 1A–B, Tables S3b–4b). In both groups, active marijuana increased ($p < 0.05$) measures of intoxication ("*High*") and arousal (heart rate, "*Stimulated*"), relative to placebo (Fig. 1C and Table S3, respectively). Active marijuana did not significantly affect ($p > 0.05$) subjective ratings of auditory or visual hallucinations, extra-sensory perception, depression, loneliness, or quickened time perception (data not shown), or objective measures of sustained attention or complex reaction time (Table S4), in either group. The marijuana was relatively well tolerated, with only 1 temporary adverse reaction (e.g., dizziness, nausea) in each group.

4. Discussion

The results of this preliminary study are the first demonstration, to our knowledge, of marijuana producing some psychotic-like and neurocognitive effects under controlled conditions selectively in CHR individuals. These effects are consistent with the results of laboratory and naturalistic studies in samples of other populations within the broad psychosis spectrum (Mason et al., 2009; Sherif et al., 2016; Verdoux et al., 2003), and extend the laboratory results to those who are at heightened and imminent risk for psychotic disorders. The clinical relevance of the psychotic-like effects is demonstrated by a larger study (McHugh et al., 2016) that found that those CHR patients who endorsed experiencing marijuana-induced psychotic-like effects in the natural environment were almost 5 times more likely to develop a subsequent psychotic disorder than those who did not. Convergently, in the current study we observed apparently stronger marijuana effects (including psychotic-like) in the two CHR individuals who eventually developed a psychotic disorder than those who did not (see Fig. S1). Further, the neurocognitive functions affected by marijuana in this study were relatively higher-order functions that are considered uniquely relevant to psychosis development (Lewis et al., 2004; Vadhan et al., 2009).

The lack of psychotic-like and neurocognitive effects in the controls contrasts with other results (e.g., Bhattacharyya et al., 2012), but these earlier studies employed nonsmoking routes of drug administration and/or participants with minimal or varied prior experience with marijuana, which may impact its acute effects (D'Souza et al., 2008; Ramaekers et al., 2009). These factors were accounted for in the current study by employing smoked marijuana administration in experienced users. The seemingly aversive effects of marijuana in the CHR participants raise questions about their motivation for regular marijuana use. Marijuana's robust intoxication and arousing effects and its potential interaction with altered dopamine function (Kuepper et al., 2013; Mizrahi et al., 2014) in this population, suggest that coping with anhedonia should be examined as a possible motivation (Cressman et al., 2015; Gill et al., 2015).

These conclusions are limited by the sample size, which was constrained by the difficulty in recruiting eligible CHR marijuana smokers (i.e., regular users that were nontreatment-seeking and physically healthy), and the employment of multiple parametric comparisons. Although these methodological characteristics are consistent with other investigations involving acute administration of Δ^9-THC to participants on the psychosis spectrum (e.g., D'Souza et al., 2005; Kuepper et al., 2013), the findings still should be viewed as preliminary. In sum, these results indicate the feasibility of marijuana administration research in the CHR population, and the possibility that the psychotic-like effects of marijuana may relate to an individual's preexisting level of risk for psychotic disorders. Replication research on this topic may be warranted.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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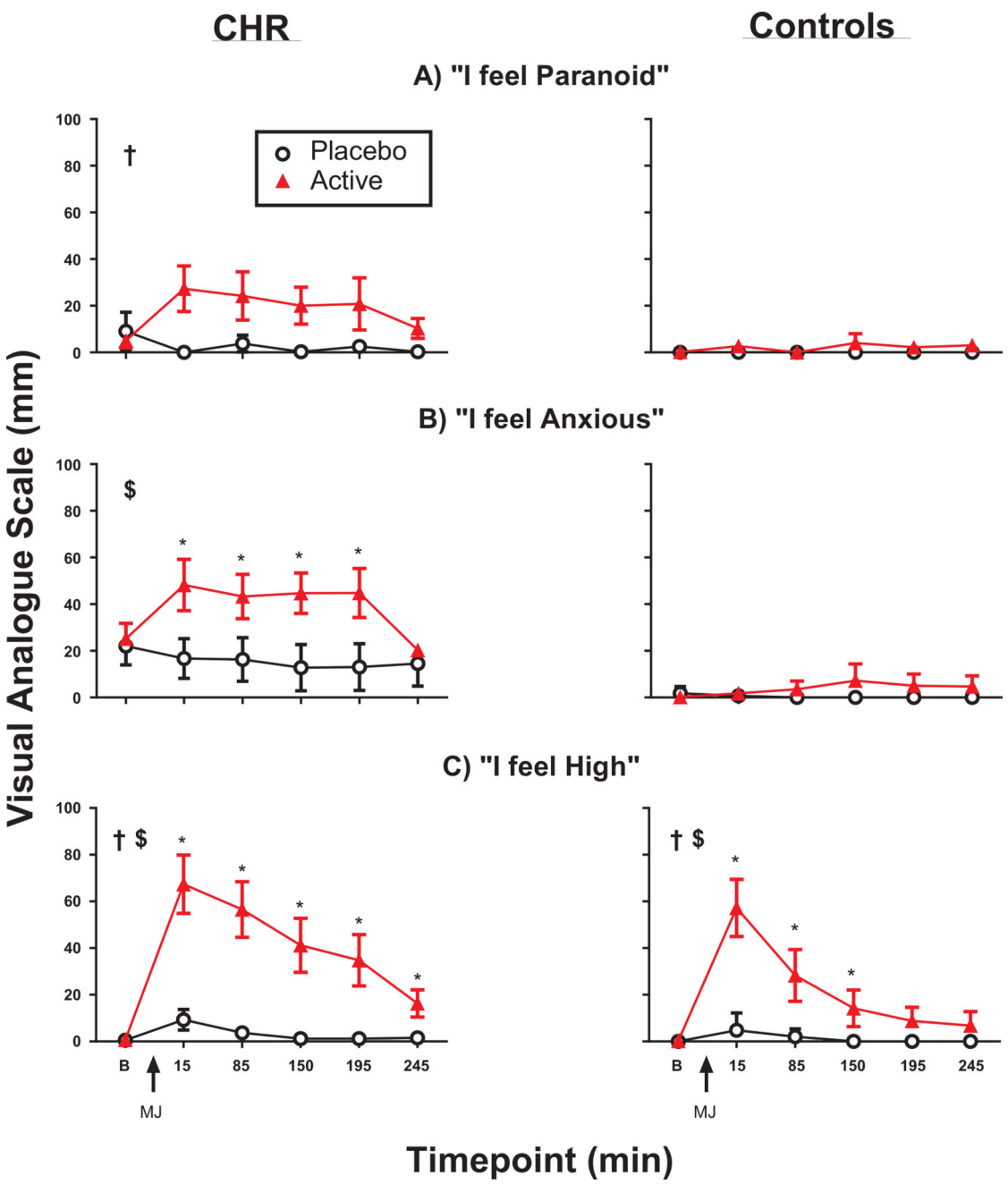

Fig. 1.

Selected subjective ratings before and after marijuana administration as a function of group (Clinical High-Risk [CHR], left side; Controls, right side). On x-axis: B = baseline; MJ = marijuana administration. Error bars reflect SEM. †main effect of drug condition; $^{\$}$drug condition × time interaction; *active (5.5% THC) differs from placebo (0.0% THC); $p < 0.05$. Full ANOVA results in Table S2.