Supplementary Materials for:

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

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Methods

Participants

Participants were required to be physically and neurologically healthy young adults (ages 18-30) with a documented intelligence quotient (IQ) ≥ 80, and to report regular marijuana use for the past 6 months. Two positive urine toxicology tests for Δ^9 - tetrahydrocannabinol (Δ^9-THC) metabolites during screening were required, as were negative pregnancy tests for females at each laboratory visit. No participant could be seeking treatment for marijuana use or report a serious adverse reaction to marijuana in the past. Participants could not meet DSM-IV criteria (First et al., 1995) for any current substance dependence other than marijuana, nor any lifetime psychotic or bipolar disorder, and could not be on any psychoactive medication other than antidepressants. All participants passed comprehensive psychological and physical exams prior to participation and provided written informed consent for the study. Participants in 1 group (n=6) met operationalized criteria for a clinical high-risk syndrome for psychotic disorders (CHR) while the other group (n=6) did not (controls), based on the Structured Interview/Schedule of Psychosis Risk Symptoms Version 4.0 (SIPS/SOPS; McGlashan et al., 2001).

CHR group. Five of the six CHR participants were recruited from the Center for Prevention and Evaluation (COPE), a research clinic for CHR patients at the New York State Psychiatric Institute (NYSPI). The sixth CHR participant was identified from research screening for the NYSPI Substance Use Research Center (SURC) due to his initial endorsement of psychotic-like symptoms on a screening questionnaire (Miller et al., 2004). All met criteria for the Attenuated Positive Symptom Syndrome (APS), which indicates recent onset of subthreshold positive psychotic symptoms (e.g., illusions and overvalued ideation). To qualify, APS symptoms could not be reported to occur exclusively during substance intoxication or be better explained by another Axis I disorder.

Control group. Eight control participants were recruited via word-of-mouth referral and newspaper advertisement in New York City. In addition to the above general criteria, they could not meet lifetime criteria for any of the CHR syndromes according to SIPS/SOPS assessment, and could not possess familial risk for any psychotic disorder. Six controls completed the minimum number (2) of sessions (see below).

Demographic, substance use and clinical characteristics. The CHR group had a mean age of 23.2 years (SD=4.0), reported a mean of 14.4 years of education (1.7), and had a mean Full Scale IQ (FSIQ) of 105.7 (10.9). The CHR group contained 5 males (3 Hispanic, 1 African-American, 1 Caucasian) and 1 female (Hispanic). The control group had a mean age of 24.3 years (3.0), reported a mean of 13.5 years of education (2.7), and had a mean FSIQ of 102.2 (13.9). The control group contained 4 males (2 Hispanic, 1 African-American, 1 Asian-American) and 2 females (1 Hispanic and 1 mixed Hispanic/African-American). The groups did not differ statistically ($p>0.05$) on any of the above demographic characteristics.

All participants reported current marijuana and alcohol use, except one control (who reported no alcohol use), and use characteristics for these substances did not differ between groups (Table S1). Other than occasional hallucinogen/stimulant use by two CHR participants, no current use of other illicit substances was reported (corroborated by multiple urine toxicology tests) by any participant during screening. Five CHR participants met criteria for one or more current DSM-IV Axis I psychiatric disorders (Anxiety Disorders [n=4]; Mood Disorders [n=2]). CHR participants' severity scores on measures of psychotic-like symptoms (McGlashan et al., 2001), depression (Beck et al., 1996) and anxiety (Beck et al., 1988) were also greater than controls (Table S1). The clinical scores of the CHR group fell within the range of those seen in larger samples of CHR participants (Addington et al., 2015; Cressman et al., 2015; DeVylder et al., 2014; Gill et al., 2013), indicating a representative sample. In sum, the CHR group exhibited greater levels of psychopathology than the control group, as expected.

	CHR		Controls		Test value	P value
Demographics	M	SD	M	SD		
Age (years)	23.2	4.0	24.3	13.5	t(10) = 0.57	0.58
Education (years)	14.4	1.7	13.5	2.7	t(10) = -0.68	0.51
Marijuana use						
Age of first use (years)	15.8	3.0	16.5	3.0	t(10) = 0.44	0.67
DSM-IV Marijuana Use Disorder	n=5		n=4		Fisher's exact = 1.0	
Past 30 days						
Frequency (days/week)	4.1	2.0	4.2	1.4	t(10) = 0.08	0.94
Amount ($/week)	39.2	32.0	47.5	50.8	t(10) = 0.34	0.74
Alcohol use						
Frequency (days/week)	1.6	0.9	1.9	0.9	t(9) = 0.58	0.58
Amount (SDUs/week)	4.3	2.8	3.3	1.4	t(7.5) = 0.80	0.45
Schedule of Psychosis Risk Symptoms (SOPS)						
Positive Symptoms*	**12.0**	**4.4**	**0.8**	**0.8**	**t(5.3) = 6.2**	**0.001**
Negative Symptoms*	**10.7**	**5.3**	**0.5**	**0.8**	**t(5.3) = 4.6**	**0.005**
Disorganized Symptoms*	**8.0**	**3.2**	**0.3**	**0.5**	**t(5.3) = 5.9**	**0.002**
Beck Depression Inventory - Second Edition (BDI-II)*	**9.7**	**4.0**	**0.2**	**0.4**	**t(5.1) = 5.8**	**0.002**
Beck Anxiety Inventory (BAI)*	**12.2**	**8.4**	**0.0**	**0.0**	**t(5.0) = 3.5**	**0.02**

Table S1. Demographic, substance use and clinical characteristics. ***** indicates a significant group difference ($p<0.05$).

Procedures

Measures. Subjective effects of marijuana were measured with a computerized Visual Analogue task (VAS; (Haney et al., 2016) that consisted of a 100-mm line anchored by "not at all" and "extremely." Phrases appeared one at a time and participants responded by mouse click along the line. The scale included typical drug states (e.g., "I feel High") and psychotic-like and nonpsychotic-like psychiatric states (e.g., “I feel Paranoid”, “I feel Anxious”); the psychotic-like items were adapted from standard psychosis symptom measures (Kay et al., 1987; McGlashan et al., 2001) to the visual analogue format for measurement of acute drug effects. Heart rate was measured by a heart rate monitor (Sentry II, Model 6100 automated vital sign monitor; NBS Medical, Costa Mesa, CA).

Neurocognitive performance was measured with tasks of four distinct functions relevant to both psychosis and marijuana use; a comprehensive description of this battery can be found in Keilp et al. (2005). Task names, functions measured, number of trials and primary outcomes were as follows: 1) The A, Not B, Logical Reasoning task (working memory, 16 trials, reaction time [RT] to “simple” and correct negations); 2) Stroop task (selective attention and response inhibition, 90 trials, RT for incongruently-colored words); 3) the Choice Reaction Time (CRT) task (motor response speed, 60 trials, RT on all responses); and 4) the Continuous Performance Test (CPT) (sustained attention, 150 trials, signal detection index d’). All tasks were adapted for repeated administration by use of alternate forms or random presentation of task stimuli, and responses were all by keypress.

Task training and clinical measures. At study outset, participants were given instructions for the marijuana administration sessions, and were administered all tasks 1-2 times to ensure familiarity. Self-report clinical measures were also administered.

Marijuana administration sessions. Participants completed three outpatient sessions separated from each other by at least 72 hrs. During the sessions (see Table S2), each participant was administered half of an active or placebo marijuana cigarettes (provided by the National Institute on Drug Abuse) containing one of three Δ^9 -THC concentrations: 0.0%, 2.02%, or 5.5% (all cigarettes contained <0.5% cannabidiol). Half cigarettes were administered to ensure that all participants smoked a precise amount of marijuana in the prescribed time, and would not exceed their natural pattern of use (for safety reasons). Two CHR participants did not receive the 2.02% session (see below); thus only data from the 0.0% (placebo) and 5.5% (active) sessions are reported here. All cigarettes were administered in a double-blind fashion and a random sequence of Δ^9 -THC concentration sessions across participants was generated (same sequence for each group).

Time	Event	Time	Event
-75	Substance use tests (Biological) Meal Field sobriety test Heart Rate Visual Analogue Scale Neurocognitive battery	150	Heart Rate Visual Analogue Scale Meal
		195	Heart Rate Visual Analogue Scale
0-15	Marijuana administration	245	Heart Rate Visual Analogue Scale
15	Heart Rate Visual Analogue Scale Neurocognitive battery		End session
85	Heart Rate Visual Analogue Scale		

Table S2. Session timeline.

Participants were instructed to refrain from using marijuana or any other psychoactive drugs, with the exception of usual caffeine, nicotine and prescribed medication (for CHR participants), on the morning of each session (from midnight on). If self-report, or breath-alcohol, breath-CO or urine samples indicated noncompliance, the session was rescheduled. Two pre-selected meals were served during each session. After the first meal, participants completed all tasks once, smoked half of the marijuana cigarette according to a paced puffing procedure (e.g., Haney et al., 2016), and completed the tasks again. For the puffing procedure, participants were instructed to: 1) light the cigarette (30 sec), 2) prepare (5 sec), 3) inhale (5 sec), 4) hold the smoke in their lungs (10 sec), and 5) exhale. They smoked one puff every minute with a 40-s interval between each puff, until they had smoked 50% of the cigarette.

Safety and follow-up procedures. Participants had to agree not to drive to and from sessions and were provided with public transportation fare. Before each session, participants were administered biological tests, field sobriety tests (FST) and clinical questionnaires. No participant was found to be intoxicated before any session, and all participants equaled or surpassed their baseline FST performance after each session. Psychiatric staff were readily available during all CHR sessions, and CHR participants were required to pass a brief psychiatric exam before leaving. Study debriefing was conducted following the final session. Clinical follow-up sessions were scheduled for 1 week (for the CHR group), and 30, 90 and 180 days (for all participants) after the study, and included clinical interview and measures of substance use and psychopathology. CHR participants also received motivational interviewing (Miller and Rollnick, 2002) for marijuana use at the 1 week session, and were monitored by clinical staff (who were blind to all of participants' study data) for the duration of their enrollment in the study and COPE.

Statistical analyses. Demographic, substance use and clinical data were compared between groups with independent sample t-tests for continuous variables and chi-square/Fisher's exact tests for categorical variables.

For acute marijuana effects, missing data were imputed for specific session time points that were missed by individual participants (0.02% of all acute data). Data were not imputed for variables where entire sessions or measurements of a particular variable were missed. Data were imputed by replicating that participant's adjacent (preceding or following) time point that was most conservative (i.e., whichever was least likely to lead to a significant effect of time or drug condition). Adjusted group sample sizes are noted where data were not imputed.

Acute drug effect data were first examined separately for each group (e.g., D'Souza et al., 2005) due to the relatively small group sample size for a mixed design. Two-tailed repeated measures Analysis of Variance (ANOVA) were used to examine the effect of drug condition (5.5% vs. placebo) and the interaction between drug condition and time (across session time points) on subjective effects, heart rate and neurocognitive performance (e.g., Hart et al., 2001; Vadhan et al., 2007). Huynh-Feldt corrections for violations of sphericity were employed where necessary. ANVOA was not performed for datasets where all values across time were 0. Significant drug condition × time interactions were probed with dependent samples t-tests comparing drug conditions at each time point.

Alpha was set at 0.05 for all statistical tests. All data analyses were performed using SuperANOVA (Gagnon et al., 1990) and SPSS version 22.

Study completion and follow-up. Ten of the fourteen study enrollees completed all three study sessions. One participant from each group left the study for personal reasons, and one participant from each group experienced an aversive reaction to the active marijuana (e.g., dizziness, nausea) and was discharged from the study after appropriate monitoring. Of these noncompleters, the two CHR participants completed the minimum number and type of sessions (active and placebo) prior to discharge, so their data were retained for analysis. The control noncompleters' data were not retained since they did not complete the minimum number of sessions. No participant exhibited residual (i.e., between-session) worsening of psychiatric

symptoms, nor did they report a residual negative effect of study participation at debriefing or any follow up session. According to standard criteria (McGlashan et al., 2001) on the SIPS/SOPS (administered by COPE research clinicians, who were blind to the marijuana administration data), two of the CHR participants converted to a psychotic disorder (33% conversion rate) at approximately 4 and 48 months after participation, respectively.

Timepoint (min)		Active marijuana						Placebo marijuana						ANOVA results					
		B	15	85	150	195	245	B	15	85	150	195	245	N	Main effect of drug condition			Drug condition × time interaction		
S3A) CLINICAL HIGH-RISK																			
Subjective VAS (mm)															Test value	p	η_p^2	Test value	p	η_p^2
"I feel *Paranoid"*	M	**5**	**27.3**	**24.2**	**20.0**	**20.8**	**10.3**	**9**	**0**	**3.8**	**0.3**	**2.5**	**0.3**	6	**F(5,1) = 9.3**	**0.03**	**0.65**	F(5,5) = 1.8	0.19	0.27
	SEM	**3.2**	**9.8**	**10.3**	**7.9**	**11.2**	**4.3**	**8.2**	**0.0**	**3.6**	**0.3**	**2.5**	**0.2**							
"I feel *Anxious"*	M	**25.2**	**48.2****	**43.3****	**44.2***	**44.8****	**20.3**	**22.0**	**16.7**	**16.3**	**12.8**	**13.0**	**14.5**	6	F(5,1) = 2.9	0.15	0.36	**F(5,5) = 2.9**	**0.03**	**0.37**
	SEM	**6.6**	**11.0**	**9.5**	**8.7**	**10.5**	**2.9**	**8.1**	**8.5**	**9.4**	**10.0**	**10.0**	**9.7**							
"I feel *Time is Moving Slower than Usual"*	M	**0.3**	**33.2****	**7.7**	**16.0**	**6.2**	**0.7**	**0.7**	**6.3**	**4.3**	**5.0**	**3.8**	**8.7**	6	F(5,1) = 1.3	0.30	0.21	**F(5,5) = 3.1**	**0.03**	**0.38**
	SEM	**0.3**	**13.3**	**4.7**	**8.4**	**4.4**	**0.4**	**0.5**	**4.4**	**4.3**	**4.4**	**3.6**	**8.7**							
"Things look *Strange, Different or Distorted*"	M	**0.8**	**18.4**	**14.4**	**0.2**	**13.2**	**0.4**	**0.0**	**0.4**	**0.0**	**0.2**	**0.0**	**0.2**	5	**F(4,1) = 11.7**	**0.03**	**0.75**	F(4,5) = 1.1	0.38	0.22
	SEM	**0.8**	**8.3**	**9.9**	**0.2**	**13.2**	**0.3**	**0.0**	**0.3**	**0.0**	**0.2**	**0.0**	**0.2**							
"I feel *Something Strange is Happening to Me"*	M	**1.8**	**27.8**	**8.6**	**0.2**	**13.0**	**3.0**	**9.2**	**0.0**	**0.0**	**0.0**	**0.0**	**0.4**	5	**F(4,1) = 11.9**	**0.03**	**0.75**	F(4,5) = 2.0	0.20	0.34
	SEM	**1.2**	**11.5**	**4.3**	**0.2**	**12.8**	**2.1**	**8.2**	**0.0**	**0.0**	**0.0**	**0.0**	**0.4**							
"I am *Having Difficulty Concentrating"*	M	**33.8**	**39.7**	**37.7**	**32.0**	**34.0**	**20.5**	**28.7**	**19.8**	**17.5**	**16.8**	**13.7**	**21.7**	6	**F(5,1) = 11.3**	**0.02**	**0.69**	F(5,5) = 1.4	0.28	0.21
	SEM	**16.7**	**16.2**	**14.2**	**16.4**	**15.6**	**16.2**	**14.8**	**14.5**	**13.3**	**13.0**	**13.3**	**12.6**							
"I feel *High*"	M	**0.7**	**67.3****	**56.5****	**41.2****	**34.8****	**16.3***	**0.5**	**9.3**	**3.7**	**1.2**	**1.2**	**1.5**	6	**F(5,1) = 19.6**	**0.007**	**0.80**	**F(5,5) = 12.2**	**0.0001**	**0.71**
	SEM	**0.5**	**12.6**	**12.0**	**11.6**	**11.1**	**5.9**	**0.5**	**4.5**	**1.8**	**0.1**	**0.8**	**1.5**							
"I feel *Stimulated*"	M	**38.7**	**41.7**	**51.8**	**47.7**	**33.8**	**38.0**	**25.8**	**13.3**	**19.0**	**19.3**	**18.3**	**11.5**	6	**F(5,1) = 18.6**	**0.008**	**0.80**	F(5,5) = 1.5	0.23	0.77
	SEM	**15.7**	**9.8**	**10.7**	**12.4**	**7.8**	**8.3**	**15.8**	**5.6**	**7.7**	**9.4**	**7.9**	**5.4**							
Heart rate (BPM)	M	**69.3**	**108.3****	**87.7****	**79.7****	**73.7**	**80.1***	**66.8**	**66.3**	**61.5**	**60.2**	**64.0**	**66.7**	6	**F(5,1) = 16.6**	**0.01**	**0.77**	**F(5,5) = 5.9**	**0.008**	**0.54**
	SEM	**4.5**	**12.1**	**12.7**	**11.0**	**7.2**	**8.2**	**2.2**	**4.2**	**4.1**	**5.7**	**4.2**	**4.4**							

Timepoint (min)		Active marijuana						Placebo marijuana						ANOVA results					
		B	15	85	150	195	245	B	15	85	150	195	245	N	Main effect of drug condition			Drug condition × time interaction		
S3B) CONTROLS																			
Subjective VAS (mm)															Test value	p	η_p^2	Test value	p	η_p^2
"I feel *Paranoid"*	M	0.2	2.7	0.0	4.0	2.2	3.0	0.0	0.0	0.0	0.0	0.0	0.0	6	F(5,1) = 1.1	0.35	0.18	F(5,5) = 1.0	0.37	0.16
	SEM	0.4	6.1	0.0	9.8	5.3	7.4	0.0	0.0	0.0	0.0	0.0	0.0							
"I feel *Anxious"*	M	0.2	1.8	3.5	7.2	5.0	4.7	1.8	0.7	0.0	0.0	0.0	0.0	6	F(5,1) = 0.9	0.39	0.15	F(5,5) = 1.2	0.32	0.20
	SEM	0.2	1.6	3.5	7.2	5.0	4.7	1.2	0.7	0.0	0.0	0.0	0.0							
"I feel *Time is Moving Slower than Usual"*	M	0.0	12.0	17.7	4.2	2.0	2.0	0.0	0.0	5.3	0.0	0.0	0.0	6	F(5,1) = 1.4	0.29	0.22	F(5,5) = 1.3	0.32	0.20
	SEM	0.0	29.4	31.0	10.2	4.9	4.9	0.0	0.0	4.8	0.0	0.0	0.0							
"Things look *Strange, Different or Distorted*"	M	0.0	0.0	2.5	3.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	4	F(3,1) = 1.0	0.39	0.25	F(3,5) = 1.0	0.39	0.25
	SEM	0.0	0.0	2.5	3.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0							
"I feel *Something Strange is Happening to Me"*	M	0.3	0.3	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	4	F(3,1) = 1.0	0.39	0.24	F(3,5) = 1.0	0.39	0.25
	SEM	0.3	0.3	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0							
"I am *Having Difficulty Concentrating"*	M	3.0	14.5	12.3	8.7	8.0	7.8	0.0	0.0	7.0	0.0	0.0	0.0	6	F(5,1) = 1.2	0.32	0.19	F(5,5) = 1.2	0.33	0.20
	SEM	2.8	9.2	8.3	8.7	8.0	7.6	0.0	0.0	4.8	0.0	0.0	0.0							
"I feel *High*"	M	**0.2**	**57.2****	**28.3****	**14.2***	**8.8**	**6.8**	**0.0**	**4.8**	**2.0**	**0.0**	**0.0**	**0.0**	6	**F(5,1) = 10.6**	**0.02**	**0.68**	**F(5,5) = 8.2**	**0.0007**	**0.62**
	SEM	**0.2**	**12.3**	**11.1**	**7.9**	**5.8**	**6.1**	**0.0**	**3.1**	**1.4**	**0.0**	**0.0**	**0.0**							
"I feel *Stimulated*"	M	**33.7**	**45.5****	**35.3****	**19.2**	**23.8**	**14.2**	**11.7**	**21.3**	**13.7**	**16.0**	**17.0**	**14.5**	6	F(5,1) = 4.3	0.09	0.46	**F(5,5) = 2.5**	**0.05**	**0.34**
	SEM	**11.2**	**11.4**	**12.1**	**11.7**	**10.7**	**11.0**	**7.4**	**10.3**	**8.8**	**11.1**	**11.0**	**9.0**							
Heart rate (BPM)	M	**67.7**	**90.0****	**70.7**	**65.5**	**69.0***	**75.5**	**73.0**	**71.5**	**68.8**	**66.8**	**77.3**	**72.3**	6	F(5,1) = 2.9	0.16	0.36	**F(5,5) = 9.6**	**0.002**	**0.66**
	SEM	**4.6**	**5.7**	**4.1**	**3.7**	**4.4**	**4.4**	**5.6**	**5.8**	**4.6**	**4.4**	**4.1**	**4.4**							

Table S3. Subjective and cardiovascular effects of marijuana in the Clinical High-Risk (A) and control (B) groups. B = baseline; VAS = Visual Analogue Scale; M = mean; SEM = standard error or measurement; BPM = beats per minute. **Bold** indicates a significant main effect of drug condition or drug condition × time interaction ($p<0.05$). For every significant interaction, a difference between active and placebo marijuana at specific timepoints is indicated by: **$p<0.01$; *$p<0.05$.

Timepoint		Active marijuana		Placebo marijuana		ANOVA results						
		Baseline	Post-MJ	Baseline	Post-MJ	N	Main effect of drug condition			Drug condition × time interaction		
S4A) CLINICAL HIGH-RISK							Test value	p	η_p^2	Test value	p	η_p^2
A not B Correct "Simple" RT (msec)	M	**2162.8**	**2845.0***	**2262.0**	**2171.5**	5	F(4,1) = 1.3	0.32	0.24	**F(4,1) = 13.3**	**0.02**	**0.77**
	SEM	**425.0**	**491.0**	**301.9**	**589.5**							
A not B Correct Negations RT (msec)	M	**3197.8**	**4034.8#**	**3616.3**	**3201.1**	5	F(4,1) = 0.4	0.55	0.09	**F(4,1) = 7.9**	**0.048**	**0.66**
	SEM	**686.4**	**635.6**	**957.5**	**504.0**							
Stroop Color-Word Reaction T (msec)	M	**627.9***	**611.1****	**593.0**	**537.5**	5	F(4,1) = 5.2	0.09	0.56	**F(4,1) = 11.6**	**0.03**	**0.74**
	SEM	**39.1**	**23.7**	**42.0**	**32.6**							
Continuous Performance Task (d')	M	1.7	1.8	1.9	2.5	5	F(4,1) = 1.8	0.25	0.31	F(4,1) = 0.3	0.66	0.05
	SEM	0.3	0.6	0.2	0.3							
Choice RT (msec)	M	432.4	427.0	400.6	391.3	5	F(4,1) = 2.1	0.22	0.34	F(4,1) = 0.02	0.90	0.00
	SEM	21.9	29.3	17.7	11.1							
S4B) CONTROLS												
A not B Correct "Simple" RT (msec)	M	2235.6	2584.3	2418.3	2175.3	6	F(5,1) = 0.2	0.68	0.04	F(5,1) = 4.0	0.10	0.45
	SEM	678.4	658.5	491.4	313.9							
A not B Correct Negations RT (msec)	M	3197.8	4034.8	3616.3	3201.1	6	F(5,1) = 0.003	0.96	0.00	F(5,1) = 0.7	0.43	0.13
	SEM	686.4	635.6	957.5	504.0							
Stroop Color-Word RT (msec)	M	673.2	577.1	572.7	566.1	6	F(5,1) = 1.2	0.33	0.19	F(5,1) = 0.6	0.48	0.11
	SEM	126.5	25.3	42.0	45.2							
Continuous Performance Task (d')	M	2.7	3.1	2.3	2.3	6	F(5,1) = 2.1	0.21	0.00	F(5,1) = 2.7	0.16	0.05
	SEM	0.3	0.2	0.4	0.4							

Choice RT (msec)	M	401.4	399.0	502.0	514.5	6	F(5,1) = 1.1	0.34	0.18	F(5,1) = 0.7	0.45	0.12
	SEM	32.8	31.8	120.9	118.2							

Table S4. Neurocognitive effects of marijuana. MJ = marijuana; M = mean; SEM = standard error of measurement; RT = reaction time. **Bold** indicates a significant main effect of drug condition or drug condition × time interaction ($p<0.05$). For every significant interaction, a difference between active placebo marijuana at specific timepoints is indicated by: **$p<0.01$; *$p<0.05$; $^{\#}p<0.10$.

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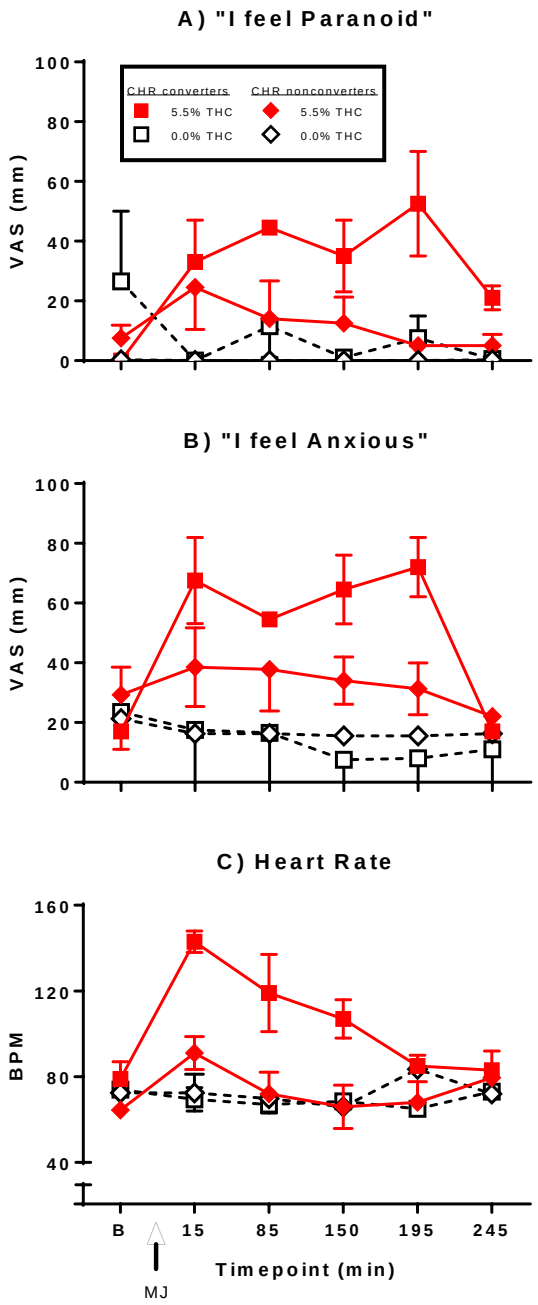
Figure S1



Paranoia (A), anxiety (B) and heart rate (C) before and after active (5.5% THC) and placebo marijuana (0.0% THC) administration for the Clinical High-Risk [CHR] group by psychotic disorder conversion status; "CHR converters" developed a psychotic disorder during follow-up. VAS = Visual Analogue Scale; BPM = beats per minute. B = baseline; MJ = marijuana administration. Error bars reflect SEM.