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Integrating Brain and Behavior: Evaluating Adolescents' Response to a Cannabis Intervention

Sarah W. Feldstein Ewing,

University Honors Program, University of New Mexico

Amber D. McEachern,

Mind Research Network, Albuquerque, New Mexico

Uma Yezhuvath

Advance MRI, Frisco, Texas

Angela D. Bryan, Kent E. Hutchison

Department of Psychology and Neuroscience, University of Colorado at Boulder

Francesca M. Filbey

Center for BrainHealth, School of Behavioral and Brain Sciences, University of Texas at Dallas

Abstract

Client language (change talk [CT] and counterchange talk [CCT]) is gaining increasing support as an active ingredient of psychosocial interventions. Preliminary work with adults suggests that there may be a neural basis for this. With a diverse sample of adolescent cannabis users, we evaluated the influence of CT and CCT on blood oxygen level dependent (BOLD) response during an fMRI cannabis cue-exposure paradigm. We also investigated how BOLD activation related to treatment outcomes. Adolescent cannabis users ($N = 43$; 83.7% male; 53.5% Hispanic; M age = 16 years) were presented with CT and CCT derived from their prescan intervention session during the fMRI paradigm. Additionally, BOLD activation during CT (vs. CCT) was tested as a predictor of 1-month follow-up cannabis use behavior (frequency of cannabis use, cannabis problems, cannabis dependence). We observed a significant interaction, with greater activation during CT (vs. CCT) during the cannabis (but not control) cues in several areas key to self-referential processes (uncorrected $p < 0.001$; medial frontal gyrus, insula). Furthermore, BOLD activation during CT (vs. CCT) during cannabis (but not control) cues in areas that underlie introspection (posterior cingulate, precuneus) was significantly related to youths' 1-month follow-up cannabis use behavior (frequency of cannabis use, cannabis problems, cannabis dependence; uncorrected $p < 0.001$). These data indicate a unique interaction pattern, whereby CT (vs. CCT) during the cannabis (but not control) cues was associated with significantly greater activation in brain areas involved in introspection. Further, this activation was related to significantly better treatment outcomes for youth.

Keywords

cannabis; adolescents; motivational interviewing; fMRI; client language

Cannabis is the most widely abused illicit substance among adolescents (e.g., G. Martin & Copeland, 2008). By the start of high school, 23% of American youth have used cannabis, a proportion that increases to 46% by the end of the twelfth grade (Centers for Disease Control and Prevention, 2010). Justice-involved adolescents have even greater rates of use. Cannabis is the most abused substance among justice-involved youth (e.g., Feldstein & Ginsburg, 2006), with approximately half (45%) meeting criteria for cannabis use disorders (CUDs; Aarons, Brown, Hough, Garland, & Wood, 2001). This is concerning, as adolescent cannabis use is strongly correlated with a number of pediatric health risk behaviors (e.g., Chabrol, Chauchard, & Girabet, 2008; Feldstein & Miller, 2006; French & Dishion, 2003), protracted use into adulthood (Perkonig et al., 2008; Swift, Coffey, Carlin, Degenhardt, & Patton, 2008), and poorer life outcomes (e.g., lower educational attainment, lower life satisfaction; Fergusson & Boden, 2008).

Studies have indicated the impact and efficacy of brief interventions in reducing substance abuse (Miller & Wilbourne, 2002). One brief intervention, motivational interviewing (MI; Miller & Rollnick, 2002), has gained support for its robust effects in reducing substance use behaviors among adults (Hettema, Steele, & Miller, 2005). Although not developed for youth, this brief, empathic, and strength-based intervention approach offers a particularly good way to reach non-treatment-seeking youth (D'Amico, Miles, Stern, & Meredith, 2008; McCambridge, Slym, & Strang, 2008; Peterson, Baer, Wells, Ginzler, & Garrett, 2006). And, qualitatively, youth report that the approach of MI resonates with them (D'Amico, Osilla, & Hunter, 2010; Stern, Meredith, Gholson, Gore, & D'Amico, 2007). Despite its promise, MI has had equivocal outcomes with cannabis-using youth (G. Martin & Copeland, 2008; Walker, Roffman, Stephens, Wakana, & Berghuis, 2006; Walker et al., 2011). This may be because we do not fully understand how MI works (Feldstein Ewing, Filbey, Hendershot, McEachern, & Hutchison, 2011; Miller & Rose, 2009), particularly with younger samples (Feldstein Ewing et al., in press). Thus, to improve its efficacy with youth, innovative approaches are needed to elucidate how MI operates.

One promising avenue is through deconstructing in-session client language. Across developmental periods and substances of abuse, client language has been found to predict treatment outcomes in MI interventions (Amrhein, Miller, & Yahne, 2003; Apodaca & Longabaugh, 2009; Baer et al., 2008; Bertholet, Faouzi, Gmel, Gerhard, & Daeppen, 2010; Daeppen, Bertholet, & Gaume, 2010; Gaume, Gmel, & Daeppen, 2008; T. Martin et al., in press; Moyers et al., 2007; Moyers, Martin, Houck, Christopher, & Tonigan, 2009; Strang & McCambridge, 2004; Vader, Walters, Prabhu, Houck, & Field, 2010; Walker et al., 2011). Specifically, client speech in favor of change, or change talk (CT; e.g., “*I need to back off my marijuana use—its causing problems with my family*”), has been positively associated with reductions in substance use up to 15 months postintervention. In contrast, client speech supporting the status quo, or counter change talk (CCT; e.g., “*Marijuana isn't a problem for me*”), has been associated with sustained use. Therefore, CT appears to be a promising route

toward improving understanding of the underlying mechanisms of MI (Miller & Rose, 2009).

One hypothesis is that CT represents a neurocognitive shift, or change, that takes place during the course of an MI session. It is proposed that this shift is responsible for catalyzing and sustaining behavior change following addictions treatment. In one investigation of this hypothesis with a sample of adults with alcohol dependence, Feldstein Ewing, Filbey, Sabbineni, Chandler, and Hutchison (2011) found significant activation of striatal (reward) areas during CCT, but not CT during an alcohol cue paradigm. The authors concluded that CT effectively dampened the profile of risk (increased reward activation) frequently observed among adults with substance dependence (Filbey et al., 2008; Filbey, Schacht, Myers, Chavez, & Hutchinson, 2009). By potentially reducing the reward and craving response, the authors surmised that this dampened activation might serve a protective function for adults in high-risk situations where alcohol cues are present.

To build upon prior work (Feldstein Ewing, Filbey, Hendershot, et al., 2011; Feldstein Ewing, Filbey, Sabbineni, et al., 2011), we sought to evaluate how CT might influence brain response during a salient neurodevelopmental period (adolescence), with a highly desired substance of abuse (cannabis), and how this activation might relate to follow-up treatment outcomes (frequency of cannabis use, cannabis problems, and cannabis dependence symptoms at a 1 month follow-up). To directly test the extent to which CT reduces activation of these neural substrates, we adapted an empirically validated fMRI-based cannabis cue-exposure paradigm (Filbey et al., 2009). Based upon prior research in this area (Feldstein Ewing, Filbey, Sabbineni, et al., 2011; Filbey et al., 2008, 2009), we posited that CT would operate by reducing the ability of cannabis cues to access reward structures and initiate craving. Thus, we hypothesized that relative to CCT, CT would be associated with less activation in cortical regions associated with reward (e.g., OFC, nucleus accumbens, caudate, putamen). We also hypothesized that greater levels of BOLD activation in these reward-related areas during CT would correspond with poorer treatment outcomes (greater levels of cannabis use behaviors at the 1 month follow-up).

Materials and Methods

Participants

Eighty-six non-treatment-seeking youth were recruited from juvenile justice programs in the Southwest to participate in a translational study aimed at reducing adolescent health risk behavior. To recruit potential participants, trained research staff introduced the project at various juvenile justice programs (such as diversion programs), informing youth that study participation was voluntary and would not affect their treatment within the juvenile justice system. Written assent was directly obtained from participants. Similar to prior work with high-risk youth (e.g., Schmiede, Broaddus, Levin, & Bryan, 2009), parent/guardian informed consent was obtained via telephone following youth assent. All consent conversations were audio recorded and logged for proof of consent. Additionally, all study procedures were conducted with approval from the participating institutional review board, the Office for Human Research Protections (OHRP), and with a federal Certificate of Confidentiality.

To participate, youth had to be between the ages of 14 and 17, English-speaking, currently involved with a juvenile justice program (e.g., diversion), currently using cannabis (e.g., using cannabis 7 of the last 30 days), willing to abstain from cannabis for 24 hours prior to the scan, have parent/guardian consent, and provide their own informed assent. Exclusion criteria included currently taking antipsychotics or anticonvulsants; being pregnant, as indicated by a urine pregnancy test obtained by research staff prior to scan session; having nonremovable metallic implants or braces; having welded without required protection; having a tattoo in the past month; and having a history of injury to the brain and/or brain-related medical problems. Eligible participants were invited to participate in the study, which took place over the course of three sessions. Participants received \$30 for completing the first session, \$30 for the second session, and \$45 for completing the 1-month follow-up (earning a possible total of \$105).

Of the 86 eligible youth, several youth did not complete a scanning session for the following reasons: youth were unreachable or disinterested after the assent/consent ($n = 4$), youth were intoxicated upon arrival for the scan session ($n = 2$), and technical difficulties with the scanner ($n = 1$). Of the 79 participants with scan data, 43 had motion within the selected threshold (<3 mm translational and <3 degrees rotation in any direction) with at least one run of CT and CCT. To evaluate potential group differences, youth who were excluded due to movement (> 3 mm) were compared against retained youth. No group differences were found across any of the behavioral cannabis use measures (frequency of cannabis use, cannabis problems, cannabis dependence) at baseline or follow-up. This indicates that there were no behavioral differences in baseline behavior and, more importantly, no differences in response to treatment.

Thus, data from 43 youth were postprocessed and included in the second-level analyses. Reflective of the demographic representation at the broader justice center, this sample was predominantly male (83.7%), approximately age 16.09 ($SD = 1.09$), and self-reported their race/ethnicity as Hispanic (53.5%), Caucasian (20.9%), bi- or multiracial (14%), African American (7%), and American Indian/Alaska Native (4.7%). In addition to being current cannabis users, 65% of the sample also reported using alcohol (> 1 day) during the past month, with another 65% having used tobacco (> 1 day) during the past month. Because many of these youth were participating in justice programs with a low level of justice monitoring (e.g., diversion), most youth were not enrolled in programs that included urine drug testing at baseline ($n = 1$) or follow-up ($n = 3$). Additional sample characteristics are presented in Tables 1 and Table 2.

Procedures

In this study, youth completed a psychosocial assessment, two MI sessions focused on reducing cannabis use (vs. reducing alcohol, tobacco, and/or other drug use), an fMRI-based cue-exposure paradigm to assess the strength of CT and CCT in a high-risk setting, and a behavioral follow-up at 1 month. All youth completed the baseline behavioral assessment and the first MI session during their first appointment. One week later, youth completed the fMRI scan, immediately followed by their second MI session. One month after the scan session, youth completed their final behavioral follow-up.

Baseline Assessment Session

Participants completed several questionnaires, including an assessment of demographic factors; a 58-item measure evaluating past-month cannabis-related problems (e.g., “Have you had a persistent chest infection or cough?”, “Have you driven while stoned?”; Cannabis Problems Questionnaire-Adolescents (CPQ-A); G. Martin, Copeland, Gilmour, Gates, & Swift, 2006); a 10-item dichotomous measure assessing the *Diagnostic and Statistical Manual of Mental Disorders* (4th ed., text rev.; *DSM-IV-TR*; American Psychiatric Association, 2000) criteria for past-month cannabis dependence (e.g., “The need to smoke more marijuana to achieve the same high,” “A failure to cut back or reduce your marijuana smoking habits”; Stephens, Roffman, & Curtin, 2000); and a four-item measure evaluating youths’ current intentions to change their cannabis use (e.g., “How likely is it that you will reduce your marijuana use in the next month?”, “I intend to reduce my marijuana use in the next month”; adapted from Bryan, Aiken, & West, 1996). To evaluate past-month frequency of cannabis use (cannabis use days) and use of other substances (alcohol and tobacco use days), research staff administered the Timeline Followback interview (TLFB; Sobell & Sobell, 1992). Following other adolescent MI studies (e.g., McCambridge & Strang, 2004), we included each of these measures because they tap into unique constructs around cannabis use, and further, because adolescents can evidence postintervention change on one indicator (e.g., reducing number of cannabis use days) while still retaining high scores on another indicator (e.g., high problem scores due to a cannabis-related arrest that occurred 6 months ago). Notably, all items were distinct across these measures. Research staff also administered a brief measure to assess current performance on a standardized measure of vocabulary and abstract reasoning (Wechsler Abbreviated Scale of Intelligence [WASI]; Wechsler, 1999). All participants completed their first intervention session (60 minutes of MI) immediately after completion of the baseline assessment.

Intervention Sessions

Similar to other MI interventions with non-treatment-seeking adolescent cannabis abusers (Walker et al., 2011), the intervention condition followed a manualized approach (Feldstein Ewing, 2010) focusing explicitly on reducing cannabis use, without addressing potential comorbid alcohol, tobacco, and other drug use. All interventions were administered by eight doctoral-level students/PhD-level therapists over the course of the project. The first author (S. W. Feldstein Ewing), who is an experienced MI therapist, actively oversaw all project therapists. Intervention integrity and fidelity was monitored and maintained by the first author, who reviewed random audio-recorded sessions during weekly therapist supervision. The MI condition included two 60-minute sessions scheduled 1 week apart. Across both sessions, therapists relied on MI-consistent approaches (see Moyers et al., 2007), including reliance on reflections, open-ended questions, affirmations, and summary statements, with the goal of demonstrating accurate empathy, helping youth develop discrepancy between their ideal and current cannabis use, supporting self-efficacy, and reducing resistance (Miller & Rollnick, 2002). With participant permission, all sessions were audio recorded for the purposes of gathering the requisite statements for the neuroimaging paradigm and maintaining therapist fidelity.

The therapists opened the first MI session by eliciting the youth's story about their cannabis use. Following this open-ended exploration, therapists guided youth through a values clarification task (Miller, C'de Baca, Matthews, & Wilbourne, 2001). Following prior work (Feldstein Ewing, Filbey, Sabbineni, et al., 2011), this session also included the MI-based "talking into and out of change exercise" to obtain five unique statements for changing their cannabis use (CT) and five unique statements for sustaining their cannabis use (CCT) for the fMRI session. Consistent with prior studies (Feldstein Ewing, Filbey, Sabbineni, et al., 2011), a minimum of five CT and five CCT statements were consistently generated during this exercise for each participant within this study. Therapists closed this session with a summary of the session and a broad and nonjudgmental query of where the participants were in terms of their substance use (e.g., "Tell me how you would like your marijuana use to look in the next week.").

The second MI session took place 1 week later, immediately after the scan session. To address youths' experiences in the scanner, therapists began the second MI session with an open-ended query of participants' experience during the scan session, including a qualitative evaluation of their level of craving following the cue-exposure task, and an evaluation of youths' resources, in the event that their level of craving increased. Relying upon MI-consistent strategies, therapists then evaluated where youth were with their cannabis use during the intervening week, provided youth with personalized feedback (PF) of their cannabis use as derived from their baseline assessment, actively and collaboratively engaged participants in the development of discrepancy (exploring how cannabis use fit with immediate and long-term goals), identification of high-risk situations and triggers for cannabis use, and an exploration of strategies to manage those risks and triggers. Similar to the first MI session, therapists closed the second session with a summary of the session and a broad and nonjudgmental query of where the participants were in terms of their substance use (e.g., "Tell me how you would like your marijuana use to look in the next month.").

Scan Session

All participants were scheduled for an fMRI session 1 week after their first MI session. As verified by self-report, all participants abstained from cannabis for 24 hours, and from caffeine and cigarettes for the hour preceding the fMRI scan.

Imaging parameters.—fMRI images were collected using a 3T Siemens Trio whole-body scanner equipped with Sonata gradient subsystem (40 mT/m amplitude, 200 μ s rise time, 100% duty cycle). A 12-channel receive head phased array coil combined with body coil transmission to achieve greater sensitivity in cortical areas was employed. fMRI scans were collected using a gradient echo, echoplanar sequence, with ramp sampling correction using the intercomissural line anterior commissure-posterior commissure (AC-PC) as a reference (repetition time; TR; TR: 2.0 s; echo times; TE; TE: 27 ms [39 ms for 1.5T]; α : 70°; matrix size: 64 $\times$ 64; 32 slices; voxel size: 3 $\times$ 3 $\times$ 4 mm). Because the orbitofrontal cortex (OFC) is involved during craving and reward and can suffer from severe signal dropout caused by susceptibility effects, a tilting acquisition was applied. The high resolution anatomical MRI scan was collected with a T1-weighted multiecho Magnetization Prepared Rapid Gradient Echo (MPRAGE) Multi-Echo Multi-Planar (MEMPR) sequence with the following

parameters: TR/TE/inversion time (TI) = 2300/2.74/900 ms; flip angle = 8° field of view; (FOV) = 256 × 256 mm; slab thickness = 176 mm; matrix = 256 × 256 × 176; voxel size = 1 × 1 × 1 mm; number of echos = 4; pixel bandwidth = 650 Hz. With four echoes, the TR, TI, and time to encode partitions for the MEMPR are similar to that of a conventional MPRAGE, resulting in similar gray matter; GM/white matter; WM/cerebrospinal fluid (CSF) contrast. Total scan time for the anatomical and functional scans was 56 min.

Cue exposure with client language.—Prior to the fMRI task, a volume set-up was conducted to establish ideal audio settings above the scanner noise. The fMRI task was designed to assess the effects of salient client language (see Figure 1). CT and CCT statements were taken from each participant's MI session (CT statements regarding their motivation to change, e.g., “*I need to back off my marijuana use—its causing problems with my family*” and CCT statements regarding their reasons for cannabis use, e.g., “*Marijuana is not a problem for me*”). Specifically, through the counterbalanced “talking into and out of change exercise” obtained during the first MI session, where participants were prompted to provide five reasons for changing and five reasons for staying the same, five different CT statements (maximum length = 16 s) and five different CCT statements (maximum length = 16 s) were taken for each participant. Following the design developed in prior work (Feldstein Ewing, Filbey, Sabbineni, et al., 2011), participants were simultaneously presented with their own CT and CCT statements in the scanner by sight (seeing the written words of their statements) and sound (hearing their own audio-recorded voice from their session).

The presentation of CT and CCT was immediately followed by the presentation of a tactile cannabis and/or control cue from a cue-exposure task (Filbey et al., 2009; Filbey, Schacht, Myers, Chavez, & Hutchinson, 2010). In terms of the cannabis cue-exposure task, we selected a paradigm that employed tactile cues rather than other potential cue approaches (visual or olfactory cues), based upon promising preliminary studies, who found differential activation following exposure to tactile cannabis cues (e.g., Haughey, Marshall, Schacht, Louis, & Hutchison, 2008; Schacht, Selling, & Hutchison, 2009). In terms of the cue design, following prior research (Filbey et al., 2009) and our own clinical work with justice-involved youth, we selected a cannabis pipe. As predicted, this was the most common form of cannabis administration for this sample as well (preferred route of administration: pipe = 65.2%, cannabis cigarette = 25.6%, other = 9.3%).

To assess the effects of CT and CCT on cue-elicited craving, paralleling the design developed in Feldstein Ewing, Filbey, Sabbineni, et al. (2011), participants were pseudorandomly presented with a single run of each of the four statement/cue combinations: (1) CT/cannabis, (2) CCT/cannabis, (3) CT/control, and (4) CCT/control. Each of the four runs consisted of 10 × 65 s trials (TR 2s/volume; 1 run = 10 trials × 65 s/30 TRs per trial = 325 TRs/10 min). Each of the five statements was presented to the participants two times, yielding 10 CT and 10 CCT statements per participant. During the presentation of the CT and CCT statements, participants were instructed to silently read their visually presented words and listen to their audio-recorded voice. For a single run, each trial started with a 16-s audio clip (recorded from participant's first MI session), simultaneously presented with a visual presentation (seeing the written words) of a CT or CCT statement, followed by the

cue-exposure period (see Figure 1). The cue-exposure period followed methods described in Filbey et al. (2009). Specifically, each trial consisted of a 20-s cue-exposure period, followed by a single 5-s urge question, and ended with a 20-s washout period to allow the hemodynamic response to return to baseline before the next trial. The task was presented using a front projection to a mirror system mounted on the head coil. Responses were recorded using a fiber-optic pad. Stimulus presentations were delivered by using E-Prime (Psychology Software Tools, Inc.) The timing of the stimulus presentation was synchronized with trigger pulses from the scanner to ensure precise temporal integration of stimulus presentation and fMRI data acquisition.

One Month Behavioral Follow-Up

Using the contact information collected at baseline, all participants were scheduled for a behavioral follow-up 1 month after their scan session. Similar to other high-risk adolescent studies (e.g., Schmieg et al., 2009; Strang & McCambridge, 2004), follow-ups were completed in person at a confidential location of the participants' choice (i.e., justice center, research center). Similar to the baseline assessment, participants completed measures of past-month cannabis use and related symptoms (frequency of cannabis use, cannabis problems, cannabis-dependence symptoms). To evaluate potential confounding factors, past-month frequency of alcohol and tobacco use were also queried. At the end of the follow-up, all participants were given a resource sheet that contained local adolescent-friendly substance use intervention resources, in case youth decided to pursue further treatment.

Imaging Analyses

BOLD data pre- and postprocessing.—The functional imaging time series was processed offline using SPM8 (Wellcome Department of Imaging Neuroscience, London, United Kingdom). Before starting statistical analysis, the first six volumes of each Echo Planar Imaging (EPI) run were discarded to allow the MR signal to reach steady state. Preprocessing of these volumes started with motion correction using SPM's realignment module (Friston et al., 1995). Subjects with motion parameters >3 mm (translation) or 3 degrees (rotation) were excluded from the analysis. This was followed by slice timing correction, which corrected for temporal differences in acquisition time of the BOLD signal across slices within each volume. The functional data were then normalized (Ashburner & Friston, 1999) into the Montreal Neurological Institute (MNI) standard space using the template provided in SPM. The resultant time series was then smoothed using a 10 mm Full Width Half Maximum (FWHM) Gaussian kernel.

The postprocessing module was implemented next. fMRI signal intensity was scaled by its grand mean (the averaged signal intensity over all intracerebral voxels, across all volumes acquired within a run) and the data were high-pass filtered (filter frequency 1/128.0 Hz) to reduce low-frequency noise in the MRI signal. Serial correlations in the data were modeled using the autocorrelation correction with order 1 (AR[1]; Purdon & Weisskoff, 1998). Neural activation after the initial delivery of tactile cues (pencil/pipe), until the removal of the cues, was modeled in the analysis (for details, see Filbey et al., 2008). Explanatory variables (e.g., exposure periods for tactile cues during CT or CCT condition) were created by convolving the stimulus timing files with the canonical hemodynamic response function,

characterized by two gamma functions, one modeling the peak and the other modeling the undershoot of a typical BOLD impulse response, provided within SPM. The rating period was modeled as a condition of no interest to remove the effect of BOLD signal evoked by the rating task. The remaining conditions were not modeled and formed the implicit baseline for the design matrix. Standard voxel-by-voxel GLM analysis (Friston et al., 2007) of the preprocessed functional time series was performed against the resultant design matrix, generating beta maps corresponding to each modeled condition. The beta maps for tactile cues (pipe/pencil) following CT and CCT conditions were then contrasted to generate the following contrast images: (a) a CT condition with cannabis pipe versus pencil; (b) a CCT condition with cannabis pipe versus pencil; (c) a CCT versus CT condition, with cannabis pipe versus pencil; and (d) a CT versus CCT condition, with cannabis pipe versus pencil.

Statistical tests performed at the group level included one-sample *t*-tests to check for main effects for the four contrasts. For further voxel-by-voxel analysis, we conducted a correlation analysis of contrast images c and d against behavioral scores at baseline: (a) baseline frequency of cannabis use (number of cannabis use days), (b) baseline cannabis problems, and (c) baseline cannabis-dependence symptoms. Additional covariates that modeled follow-up behavior (namely, follow-up number of cannabis use days, follow-up cannabis problems, follow-up cannabis-dependence symptoms) were also correlated with the contrast images. To control for the potential influence of the baseline behavior on follow-up outcomes, we also looked at the correlation of the BOLD contrast images to follow-up scores, while controlling for baseline behavior scores. In addition, to explore observed interactions, we looked at the average percent BOLD signal change (expressed as a percentage of global mean) in clusters of activation for the six conditions, namely, CT(Pipe), CT(Pencil), CCT(Pipe), CCT(Pencil), Pipe(CT-CCT), and Pencil(CT-CCT). The activation masks were created using MARSBAR (Brett et al., 2002). We plotted the average percent BOLD signal change to determine the direction of activation across different conditions.

All statistical tests were thresholded at a false discovery rate (FDR)-corrected *p* level of 0.05 (cluster threshold = 20), which corrects for multiple comparisons. For tests that did not reveal activations at this corrected *p* level, we also looked at the activation maps using a less stringent *p* level (uncorrected *p* = 0.001; extent threshold = 20). The anatomical localization for the regions of activation was found using the Talairach Daemon software (Lancaster et al., 2000). For visualization and display of significant activation, the *z* maps were overlaid on the T1 canonical MNI template provided within SPM. Multislice overlay of activation maps was also obtained using the visualization toolbox, xjview version 8.

Results

Baseline Cannabis Use

This sample reported heavy cannabis use and related symptoms, as indicated by their frequency of cannabis use ($M = 18.33$ cannabis use days in the past month, $SD = 9.93$), the prevalence of weekday cannabis use (97.7%), their average cannabis related problems score ($M = 16.53$, $SD = 9.17$; note: average score among a sample of youth recent cannabis users = 8.5; G. Martin et al., 2006), and their mean cannabis-dependence symptoms score ($M =$

3.26, $SD = 2.01$; note: total score >3 is indicative of cannabis dependence; Stephens et al., 2000).

Intervention Outcomes

All but one youth was retained at the 1-month follow-up ($N = 42$; 97.67%). Consistent with the challenges in retaining high-risk youth, the missing youth was unreachable despite repeated staff efforts. Youth evidenced significant reductions in cannabis use at the 1-month follow-up (see Table 2). Specifically, adolescents significantly reduced their frequency of cannabis use (number of cannabis use days), level of cannabis related problems, and cannabis-dependence symptoms (73.8%, 81%, 73.8% evidenced positive behavior change, respectively). Outcome scores for the three 1-month cannabis measures were significantly intercorrelated (frequency of cannabis use and cannabis problems $r[42] = .36$, $p < .05$; frequency of cannabis use and cannabisdependence symptoms $r[42] = .59$, $p < .01$; cannabis problems and cannabisdependence symptoms $r[42] = .72$, $p < .01$). Consistent with the target of the intervention (cannabis use), youth did not significantly change their alcohol or tobacco use following the intervention.

Main Effects of In-Session Client Language on Response to Cannabis (vs. Control) Cues

CT.—During the CT condition, there was widespread activation for participants' response to the cannabis (vs. control) cues after seeing and hearing their statements in favor of changing their cannabis use behavior (e.g., “*I need to back off my marijuana use—its causing problems with my family*”). Specifically, we found significant BOLD activation across 12 clusters (FDR-corrected $p < .05$, extent threshold 20 voxels; peaks listed in Table 3). Consistent with prior work (Feldstein Ewing, Filbey, Sabbineni, et al., 2011), activation had peaks in the pre- and postcentral gyri and superior parietal lobe. Activation was also found in the inferior frontal gyrus, superior frontal gyrus, anterior cingulate, insula, thalamus, caudate, parahippocampal gyrus, occipital lobe, and cerebellum. A multislice overlay of these activations has been provided in Figure 2A.

CCT.—During the CCT condition, we found a significant pattern of positive activation for participants' response to the cannabis (vs. control) cues after seeing and hearing their statements in support of sustaining their cannabis use behavior (e.g., “*Marijuana isn't a problem for me*”). Specifically, we found significant BOLD activation across eight clusters (FDR-corrected $p < .05$, extent threshold 20 voxels). The most significant activation was in the postcentral gyrus, inferior parietal lobe, and bilateral visual centers. Frontal networks (primarily superior frontal gyrus) were also recruited, along with activation in the thalamus, parahippocampal gyrus, and cerebellum (see Table 4 and Figure 2B).

Comparison of CT and CCT on Response to Cannabis (vs. Control) Cues

CT > CCT.—We found significant activation when comparing CT (vs. CCT) on response to cannabis (vs. control) cues following CT. Specifically, adolescents evidenced significantly greater response for CT than CCT for cannabis cues but not for control cues. In this Talk x Cue interaction, we found significant activation across parietotemporal regions, with peaks in the superior temporal gyrus, postcentral gyrus and claustrum (uncorrected $p < 0.001$, extent threshold 20 voxels). Additional clusters of activation were observed in the frontal

cortex (medial frontal gyrus), parietal lobe (postcentral gyrus), and sub-lobar regions (insula). Activation in the insula has been overlaid onto orthogonal sections in Figure 2C (see Table 5 for peaks).

CCT > CT.—We found no significant activation when comparing CCT (vs. CT) on response to cannabis (vs. control) cues. This indicates that there were no areas where adolescents' response to CCT was greater than their response to CT.

Correlations Between Treatment Outcome Measures and BOLD Activation During CT > CCT and Response to Cannabis (vs. Control) Cues

Follow-up frequency of cannabis use.—To evaluate how BOLD response during CT (vs. CCT) was associated with post-treatment cannabis use behavior, we evaluated the relationship between follow-up frequency of cannabis use (past-month cannabis use days) and the BOLD activation during CT > CCT on response to cannabis (vs. control) cues comparison while controlling for the baseline frequency of cannabis use. We found that BOLD activation in the medial globus pallidus and cerebellum were positively correlated with follow-up frequency of cannabis use when controlling for baseline cannabis use (uncorrected $p < .001$, extent threshold 20 voxels; Table 6A). This suggests that during CT > CCT, the greater response in the globus pallidus, a striatal area within the reward network, the greater the change in frequency of cannabis use at follow-up.

Follow-up cannabis problems.—We also examined the relationship between follow-up cannabis problems and BOLD activation during CT > CCT on response to cannabis (vs. control) cues while controlling for baseline levels of cannabis problems. The results showed a significantly negative relationship in several key areas, including the inferior temporal gyrus and precuneus when controlling for baseline cannabis use (uncorrected $p < .001$, extent threshold 20 voxels; Figure 4A, Table 6B), indicating that youth with greater activation during CT > CCT had a significantly greater reduction (change) in cannabis problems at follow-up.

Follow-up cannabis-dependence symptoms.—Finally, we investigated the relationship between follow-up cannabis-dependence symptoms and BOLD activation during CT > CCT on response to cannabis (vs. control) cues while controlling for baseline cannabis-dependence scores. There was a significant negative pattern of response across the posterior cingulate and superior temporal gyrus when controlling for baseline cannabis use (uncorrected $p < .001$, extent threshold 20 voxels; Figure 4B; Table 6C). This highlights that youth with greater activation during CT > CCT had a significantly greater reduction (change) in cannabis-dependence symptoms at the follow-up.

Post Hoc Examination: Potential Correlates and Influential Factors

To evaluate the degree to which the observed results may have been influenced by potential confounding factors, the effects of CT and CCT were examined in the context of various additional variables. Neither age nor gender resulted in significant activation during CT > CCT on response to cannabis (vs. control) cues. Similarly, vocabulary and abstract reasoning (as measured by the WASI) were not significantly correlated with BOLD activation during

CT > CCT on response to cannabis (vs. control) cues. Finally, based on the interactive effects observed between cannabis and alcohol use among adolescent substance users (e.g., Mahmood, Jacobus, Bava, Scarlett, & Tapert, 2010; Schweinsburg, Schweinsburg, Nagel, Eyster, & Tapert, 2011), we examined past-month frequency of alcohol use (past-month number of alcohol use days). No significant association emerged between frequency of alcohol use and BOLD activation during CT > CCT on response to cannabis (vs. control) cues. Thus, these variables (age, gender, vocabulary, abstract reasoning, frequency of alcohol use) were not associated with the patterns of BOLD activation examined in the data.

Associations Between Subjective Craving Ratings for Cannabis and BOLD Response to Cues

As the focus of this study was to characterize the neural mechanisms that influence behavior change following CT, we sought to evaluate how this pattern of activation might relate to subjective behavior. Specifically, we investigated the correlation between BOLD response and each participant's "real-time" evaluation of their craving experience within the scanner. Notably, because prior reports utilizing the same tactile cue (Filbey et al., 2009) and client language paradigm (Feldstein Ewing, Filbey, Sabbineni, et al., 2011) have not found a correlation between real-time craving ratings and BOLD response during CT, we did not expect BOLD response during CT and subjective craving ratings to be associated within this sample. In this analysis, despite explicit instructions to complete the in-scanner craving ratings, some youth did not enter their real-time craving scores during the scan session. Similar to prior cannabis craving studies (Filbey et al., 2009), within the CT condition, following exposure to the cannabis cue, 33 participants reported an average urge of 4.27 ($SD = 1.74$). In contrast, following the control cue, 37 participants reported an average urge of 2.68 ($SD = 1.26$, Cohen's d for cannabis vs. control cues = 1.05). Thus, despite the slightly higher urge ratings reported for the cannabis cue condition, we found no significant correlation between the in-scanner subjective urge ratings and BOLD response following CT in either the cannabis or control condition.

Discussion

Using sight (having participants view the written words of their statements) and sound (replaying their own voice), adolescent cannabis users were represented with their in-session CT and CCT statements during an fMRI-based cue-exposure paradigm. In contrast with predictions, following presentation of their CT statements (statements made in favor of changing their cannabis use; "*I need to back off my marijuana use*"), we found a pattern of significant positive activation in areas important for introspection/memory processes (insula, parahippocampal gyrus [PHG]), reward-directed behavior (caudate), conflict monitoring (anterior cingulate), and response inhibition (inferior frontal gyrus). This pattern of greater activation (CT relative to CCT during cannabis but not control cues) was significantly related to treatment outcome.

This follows the literature, as many of these areas have been implicated in treatment response. Specifically, the insula has been found to be important in the processing of emotional experiences (Phan, Wager, Taylor, & Liberzon, 2002), interoception (Critchley,

Wiens, Rothstein, Ohman, & Dolan, 2004), substance-related cues (e.g., Paulus, Tapert, & Schuckit, 2005; Schneider et al., 2001), and substance-related decision making (Naqvi & Bechara, 2010). Additionally, recent volumetric studies with adolescent cannabis users have found reduced cortical thickness in the insula (Lopez-Larson et al., 2011), suggesting that an intact and functional insula may be protective against and/or reflective of lower levels of cannabis use. In terms of the PHG, whereas greater parahippocampal activity may be a liability for effective learning among adult cannabis users (e.g., Nestor, Roberts, Garavan, & Hester, 2008), this region has also demonstrated differential activation following different psychosocial interventions across a number of problem behaviors (e.g., Straube, Glauer, Dilger, Mentzel, & Miltner, 2006; Vocks et al., 2010), indicating its potential involvement in successful treatment response. Similarly, the anterior cingulate gyrus and inferior frontal gyrus have been found to be important in inhibitory control in substance abusers (Filbey, Claus, Morgan, Forester, & Hutchison, in press), indicating that successful recruitment and functioning of these areas during CT may facilitate treatment response.

Potentially even more important than the main effects in this study was the observed interaction, whereby BOLD activation in response to CT was significantly greater than it was during CCT for cannabis (vs. control) cues. In fact, thinking about changing, relative to thinking about staying the same, resulted in greater activation in the insula, medial frontal gyrus, postcentral gyrus, and superior temporal gyrus when the participants were exposed to the pipe relative to the pencil.

To further deconstruct this compelling interaction, we examined the percent signal change in the key areas important to introspection (medial frontal gyrus, insula) during the client language and cue conditions *post hoc* (see Figure 3). We found a fascinating relationship. In contrast to the linear range of activation expected, with the greatest percent signal change in the CT-cannabis condition, followed by the CT-control, CCT-cannabis, and CCT-control conditions, for these two areas, the percent signal change was greatest for the CT-cannabis condition, immediately followed by the CCT-control condition. Although we were heartened to see that our control condition was indeed an “active” condition, the observed effects for CCT-control were unexpected. One possibility for the observed relationship might be the pseudorandom nature of presentation of the runs/cue-talk combinations, whereby a CT-cannabis run could be immediately followed by a CCT-control run. With a relatively brief inter-run delay (<1 min), lingering processes/activation generated during the CT-cannabis could contaminate the CCT-control processes/activation. Clinically, this makes sense, as thinking about changing behavior, and the neural substrates that underlie this process are unlikely to cease once that language and cue is removed. Rather, a person may continue to reflect on the highly salient cues (CT, cannabis) even when being presented a non-cannabis-related cue (pencil) or client language in favor of staying the same (CCT).

Another important aspect of this interaction are the key roles of the insula and the medial prefrontal gyrus/anterior cingulate areas. Specifically, in addition to the protective role that the insula may play, these data suggest the relevance of the anterior cingulate in response to client change language. These data are in line with recent theoretical papers (Feldstein Ewing, Filbey, Hendershot, et al., 2011) which suggest that the ability to estimate the salience and potential rewarding effects of a substance may influence not only a person's

expression of CT but also their thoughts about their substance use (e.g., introspection/contemplation about CT). Consistent with our findings, the areas posited to be important in the processing of CT (e.g., Feldstein Ewing, Filbey, Hendershot, et al., 2011) include the anterior cingulate, which has been integral to processing high-valence emotional experiences and reward (e.g., Nakao et al., 2005; Paulus et al., 2005; Filbey et al., 2009), along with the striatum and the insula.

Furthermore, this key interaction (greater activation during CT relative to CCT during cannabis but not control cues) was related to treatment outcome for this sample of adolescents. Youth showed significant behavioral changes from pre- to posttreatment across all three cannabis use indicators (frequency of use, cannabis problems, cannabis dependence). Furthermore, BOLD activation during CT (vs. CCT) during cannabis (but not control) cues was strongly associated with a change in each of these follow-up use indicators (frequency of use, cannabis problems, cannabis dependence) across the several areas, including striatal (globus pallidus) and posterior cingulate/precuneus area, even when controlling for baseline use. Ultimately, these data indicate that the extent to which adolescents can recruit these areas during CT may be predictive of their level of behavior change in response to treatment.

These empirical findings are firmly in line with recent translational models connecting in-session client language to posttreatment behavior change (Feldstein Ewing, Filbey, Hendershot, et al., 2011), along with recent empirical evaluations of postintervention behavior change (Falk, Berkman, Whalen, & Lieberman, 2011). In terms of treatment outcome, similar to the areas observed within these data, Falk and colleagues (2011) found that activation in the medial prefrontal cortex, precuneus, and posterior cingulate explained an additional 20% in the variability in behavior following a behavioral smoking cessation intervention, doubling the variance explained by self-reported measures, such as self-efficacy and intentions to change (Falk et al., 2011). The posterior cingulate and precuneus may be particularly important in successful addictions treatment response, due to their structural and functional connection to other key areas (e.g., Dosenbach et al., 2010; Hagmann et al., 2008; Tomasi & Volkow, 2010), their role in human awareness (Gusnard, Akbudak, Shulman, & Raichle, 2001), emotional and episodic memory, self-reference in memory retrieval, self-reflection, and consciousness (e.g., Legrand & Ruby, 2009; Northoff & Bermpohl, 2004), and their relationship to substance use severity (e.g., Claus, Feldstein Ewing, Filbey, Sabbini, & Hutchison, 2011).

Following CCT (statements made in favor of sustaining their cannabis use; “*Marijuana isn’t a problem for me*”), we found significant positive activation across the postcentral gyrus, inferior parietal lobe, superior frontal gyrus, thalamus, PHG, and cerebellum. There were no areas in which BOLD activation during CCT was greater than during CT. Yet, at the most fundamental level, the data from the CCT condition suggest that the task worked effectively, as there was a basic level of overlap with the response observed among older, more severe alcohol- and cannabisdependent adults (e.g., activation within the precentral gyrus, postcentral gyrus, superior temporal gyrus, inferior parietal lobe, thalamus; Feldstein Ewing, Filbey, Sabbini, et al., 2011; Filbey et al., 2009). At the same time, we did not observe the

expected level of reward (striatal) activation previously found among adults within this adolescent sample.

Thus, although the observed findings build upon emerging evaluations of adolescents' response to cannabis cues (Gray, LaRowe, & Upadhyaya, 2008; Gray, LaRowe, Watson, & Carpenter, 2011; Nickerson et al., 2011), the broader pattern of findings from this adolescent sample contrast with the pattern observed among adults (Feldstein Ewing, Filbey, Sabbineni, et al., 2011). More specifically, although both age groups displayed a key interaction (with response to one type of change statement greater than the other), the nature of the relationship was almost opposite. For example, during exposure to the alcohol cue condition, the adults evidenced greater activation during CCT (vs. CT), and predominantly within reward (striatal) areas. However, this sample of youth displayed greater activation during the CT (vs. CCT) condition and in several regions involved in introspection (e.g., insula, medial frontal gyrus). Although these areas are important for many processes, we interpret these data to suggest that the neural mechanism of behavioral change among adolescents may be introspection/contemplation, whereas among adults, it may be the successful suppression of the craving-reward systems (e.g., Feldstein Ewing, Filbey, Sabbineni, et al., 2011; Filbey et al., 2007, 2009).

The divergence from the adult data is interesting but not altogether surprising. Although seemingly modest, the levels of cannabis craving observed for youth within this study were comparable to those observed among adults with CUDs (Filbey et al., 2009). At the same time, youth in this sample may simply not have the levels of brain-based reward activation that we would expect to find among adults. To that end, extended substance use exposure is likely to shape the development of (often problematic) neuro-adaptations in the reward learning circuitry (e.g., Hutchison, 2010; Kalivas, 2004). Thus, with their relatively shorter substance use histories (~4 years vs. >7 years; e.g., Feldstein Ewing, Filbey, Sabbineni, et al., 2011; Filbey, et al., 2008, 2009), these youth might not have the substance use volume and/or sustained use pattern to sufficiently alter these neural pathways (or to enable observable changes in reward activation). It is subsequently possible that the recruitment of introspection/contemplation areas may be occurring independently of (or may even be potentially co-occurring with) suppression of the reward areas, but this activation may not yet be evident. Ultimately, these data suggest that MI is likely to exert its influence through a number of pathways, including, but not limited to, those involved in introspection/memory (emotional learning/memory) and craving (incentive reward; Feldstein Ewing, Filbey, Hendershot, et al., 2011).

A second important consideration is that, although some studies have suggested otherwise (e.g., Delisi et al., 2006), most neurodevelopmental groups contend that adolescence is a distinct (e.g., Luna, Padmanbhan, & O'Hearn, 2010; Paus, Keshavan, & Giedd, 2008; Sturman & Moghaddam, 2011) and highly vulnerable period of neurodevelopment, which may be particularly sensitive to cannabis exposure (e.g., Ashtari, Cervellione, Cottone, Ardekani, & Kumra, 2009; Jager & Ramsey, 2008; Schweinsburg, Brown, & Tapert, 2008). We believe that these data highlight the existence of a unique pattern of brain activation associated with this salient neurodevelopmental period. And, as demonstrated by the relatively lower level of efficacy of MI among adolescents, compared with adults (ES for MI

among adults = .25 vs. ES for MI among adolescents = .16; Burke, Arkowitz, & Menchola, 2003; Jensen et al., 2011), this specialized response may, in fact, subserve different treatment mechanisms for this age group.

Together, the positive behavioral change observed for adolescents receiving this intervention suggests that MI continues to be a promising psychosocial treatment for adolescent cannabis users and that engagement of introspective/contemplative areas is involved in facilitating successful treatment response. Furthermore, these findings underscore the importance of explicitly evaluating potential treatment mechanisms (brain-based and behavioral) within this neurodevelopmental period to determine their fit and applicability.

Limitations and Future Directions

This study is an important first step toward understanding the basic biological substrates underlying effective psychosocial interventions for cannabis-using adolescents. And, we recommend that the observed findings be interpreted in light of the following limitations. First, this sample only included high-risk, justice-involved youth; subsequently, evaluating this paradigm with mainstream youth would be useful (e.g., Schweinsburg et al., 2011; Walker et al., 2006). Second, reflective of our recruitment setting, youth in this study were predominantly male; reexamination of this paradigm with females would be beneficial. Third, future studies would benefit from the inclusion of a control group, such as a sample of alcohol users (e.g., Mahmood et al., 2010; Schweinsburg et al., 2011), youth with a broader range of substance use exposure, and a comparison treatment condition (e.g., Walker et al., 2011). This would help determine whether the observed pattern of activation may be attributable to the substance, the length of substance use exposure, and/or the robustness of CT and CCT across intervention types. Fourth, this sample evidenced quite a bit of movement. Notably, there were no group differences on baseline behavior, or more importantly, in treatment outcomes, indicating that the two groups were behaviorally comparable despite the levels of movement. However, as a preventive measure, steps have already been taken to ensure less movement among participants in subsequent studies (e.g., use of a fMRI-compatible tempurpedic pillow that helps youth limit head movement). Fifth, although in line with current studies with cannabis-abusing adults (Filbey et al., 2009), the levels of cannabis craving were relatively modest; future studies may examine ways to strengthen the cue-exposure paradigm to strengthen craving effects. Sixth, not all youth completed the within-scanner subjective craving ratings; future studies would benefit from encouraging youth to complete this aspect of this paradigm, as well as further evaluating the relationship between subjective ratings and BOLD activation. Seventh, to maximize available data, our analyses included subjects with one to two runs of CT/CCT and used the mean for datasets with two runs; replication would clearly strengthen results. Finally, although the insula and medial frontal gyrus are involved in several processes throughout the brain, we interpret the observed pattern of data in CT as reflective of their role in introspection. However, based on both the complex interactions observed, and the involvement of these areas across many additional processes, the possibility remains that introspection might not be the driving force. Continued evaluation of this paradigm would strengthen the proposed relationships.

Together, these integrative data ultimately suggest the salience of CT during adolescent cannabis interventions. These data also highlight an important avenue for future research; understanding how to sustain the protective profile (increased activation in introspection/contemplation areas) observed during this investigation will be key to improving intervention outcomes for cannabis-abusing youth. Following pioneering work in the field of adolescent neurodevelopment (e.g., Schumann et al., 2010), these data provide a foundation for, and highlight the importance of, crafting and empirically evaluating a developmentally targeted translational model of adolescents' response to psychosocial interventions.

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Figure 1.

Schematic of a single trial of the fMRI paradigm. In each of the runs, participants were presented with *either* change talk (CT) or counter change talk (CCT one type of talk during each run), with either exposure to the tactile cannabis cue (pipe) or the control (pencil). Runs were counterbalanced in order of presentation (e.g., CT/cannabis, CT/control, CCT/cannabis, CCT/control). CT and CCT were presented via audio (replay of their in-session statements) and visual (written text of their statements) inputs. Participants were handed the cue 2 s before the cue exposure, and the cue was removed 2 s after the cue exposure. Please note that the 16-s presentation of the scripts (CT and CCT) also included a buffer during which no audio was presented.

Figure 2.

Activation maps obtained for one-sample t -test on cannabis (vs. control) with (A) change talk (CT) and (B) counter change talk (CCT; $n = 43$). Maps were thresholded at false discovery rate (FDR)-corrected p of 0.05 (extent threshold = 20 voxels). Activations have been overlaid onto contiguous slices of the canonical T1 template spaced 5 mm apart. (C) Difference between activation maps, showing greater activation during CT (A) compared with CCT (B). The difference map was thresholded at uncorrected p of 0.001 (extent threshold = 20 voxels) and activations have been overlaid onto orthogonal slices of the canonical T1 template. Bilateral activation in the insula is seen, which also extends along the left postcentral gyrus. The color bar indicates t values, with warmer colors denoting more significant activation. Left (L) and right (R) sides are marked in the bottom of the figure.

Figure 3.

Percent signal change per condition. The BOLD signal intensity within functional ROIs created using MARSBAR (Brett et. al, 2002) was applied on the group-averaged contrast maps ($n = 43$) for CT/pipe, CT/pencil, CCT/pipe, CCT/pencil. In terms of simple effects, the average percentage BOLD signal change within the activated voxels in the medial frontal gyrus was $M(SD) = 0.501 \pm 0.148$, $M(SD) = 0.299 \pm 0.133$, $M(SD) = 0.270 \pm 0.131$ and $M(SD) = 0.479 \pm 0.132$ for the conditions (CT/pipe, CT/pencil, CCT/pipe, CCT/pencil, respectively), $M(SD) = 0.231 \pm 0.110$ for Pipe (CT-CCT), and $M(SD) = -0.180 \pm 0.118$ Pencil (CT-CCT). Within the insula, the averaged BOLD signal change was $M(SD) = 0.311 \pm 0.069$, $M(SD) = 0.157 \pm 0.068$, $M(SD) = 0.174 \pm 0.071$ and $M(SD) = 0.277 \pm 0.060$ for CT/pipe, CT/pencil, CCT/pipe, and CCT/pencil, respectively. The percent BOLD signal change was $M(SD) = 0.138 \pm 0.058$ for pipe (CT-CCT) and $M(SD) = -0.121 \pm 0.067$ for pencil (CT-CCT).

Figure 4.

Regions of significant negative correlation between BOLD response during CT (vs. CCT) in cannabis (vs. control) and (A) follow-up cannabis problems while controlling for baseline cannabis problems ($n = 42$), and (B) follow-up cannabis dependence symptoms while controlling for baseline cannabis dependence symptoms ($n = 42$). An uncorrected p value of 0.001 (extent threshold = 20 voxels) was used. The color bar indicates t values. Right side (R) represents right hemisphere.

Table 1*Demographic Characteristics of Participating Sample (N = 43)*

	Mean (SD)	Range
Age	16.09 (1.09)	14.00 to 17.00
Gender		
Male	36 (83.7%)	
Female	7 (16.3%)	
Self-reported race/ethnicity		
Hispanic	23 (53.5%)	
Caucasian	9 (20.9%)	
Bi-racial/Multiracial	6 (14.0%)	
African American	3 (7.0%)	
Native American	2 (4.7%)	
Highest grade completed		
7th grade	1 (2.3%)	
8th grade	11 (25.6%)	
9th grade	10 (23.3%)	
10th grade	11 (25.6%)	
11th grade	8 (18.6%)	
12th grade	1 (2.3%)	
GED	1 (2.3%)	
Vocabulary T score	46.29 (11.33)	24.00 to 67.00
Matrix reasoning T score	47.76 (9.73)	20.00 to 64.00
Age at first cannabis use	12.30 (2.17)	5.00 to 16.00
Baseline weekday cannabis use (% yes)	97.7%	
Baseline other substance use (>1 day; % yes)		
Alcohol	65.1%	
Tobacco	65.1%	

Table 2
Cannabis Use Behaviors at the Baseline (N = 43) and at the 1-Month Follow-Up (N = 42)

	Baseline mean (SD)	Follow-up mean (SD)	Dependent samples <i>t</i> -test (baseline vs. follow-up)	% Reporting positive behavior change at follow-up (reductions in substance use behavior)
Past-month cannabis use days (TLFB)	18.33 (9.93)	11.05 (11.01)	$t(41) = 4.47, p < .001$	73.8%
Cannabis Problems Questionnaire-Adolescent	16.53 (9.17)	9.74 (8.01)	$t(41) = 5.58, p < .001$	81%
Marijuana Dependence Scale	3.26 (2.01)	1.90 (1.56)	$t(41) = 2.46, p < .05$	73.8%
Intentions to reduce cannabis use	13.00 (8.70)	16.81 (6.88) ^a	$t(41) = -3.54, p < .001$	21.4%
Past-month alcohol use days (TLFB)	1.74 (2.33)	1.76 (3.01)	$t(41) = 0.00, p = 1.00$	38.1%
Past-month tobacco use days (TLFB)	13.09 (13.29)	11.43 (13.13)	$t(41) = 0.88, p = .38$	26.2%

Note. TLFB = Timeline Followback interview.

^aThis measure was collected immediately following the second motivational interviewing session versus the 1-month follow-up.

Table 3

Maximum Loci of Activation of BOLD Response to CT With Cannabis (vs. Control) Cues (FDR-Corrected $p < .05$, Extent Threshold > 20 Voxels)

No. voxels	Localization	BA	x (mm)	y (mm)	z (mm)	t value
18884	R. postcentral gyrus	2	46	-28	56	7.07
	R. precentral gyrus	4	34	-28	60	6.64
	R. superior parietal lobule	7	34	-50	64	6.42
12095	R. middle occipital gyrus	19	54	-68	-10	6.58
	L. middle occipital gyrus	37	-48	-68	-6	6.34
	L. cerebellar tonsil	—	-34	-42	-32	5.91
2496	L. inferior parietal lobule	40	-46	-30	46	6.23
2068	L. medial frontal gyrus	10	-2	54	2	4.6
	L. anterior cingulate	32	-2	36	-8	3.66
	L. anterior cingulate	—	-2	28	4	3.38
473	L. inferior temporal gyrus	20	-32	-4	-40	4.29
	L. uncus	28	-26	2	-24	3.72
239	R. inferior frontal gyrus	46	54	44	12	4.19
48	L. superior temporal gyrus	38	-38	22	-22	3.22
	L. superior frontal gyrus	8	-18	50	42	2.89
75	L. superior frontal gyrus	8	-14	48	50	2.82
32	L. insula	13	-38	-6	14	2.86
	L. thalamus/lateral posterior nucleus	—	-14	-18	12	2.78
160	L. caudate body	—	-16	-16	20	2.77
	L. thalamus/pulvinar	—	-14	-26	10	2.75
40	R. pons	—	2	-26	-24	2.71
44	L. parahippocampal gyrus	28	-16	-26	-8	2.71

Note. Total number of clusters = 12. BA = Brodmann area; BOLD = blood oxygen level dependent; CT = change talk; FDR = false discovery rate; L. = left; R. = right.

Table 4

Maximum Loci of Activation for BOLD Response to CCT With Cannabis (vs. Control) Cues (FDR-Corrected $p < .05$, Extent Threshold > 20 Voxels)

No. voxels	Localization	BA	x (mm)	y (mm)	z (mm)	t value
2607	R. postcentral gyrus	2	44	-32	62	7.23
	L. postcentral gyrus	40	36	-48	72	5.76
449	L. inferior parietal lobule	40	-48	-38	62	5.95
	L. inferior parietal lobule	40	-48	-30	48	4.85
689	R. middle occipital gyrus	19	50	-72	-6	5.2
357	L. middle occipital gyrus	19	-48	-74	-6	4.9
279	L. cerebellar tonsil	—	-28	-34	-40	4.8
	L. culmen	—	-30	-46	-26	4.05
	L. cerebellum	—	-28	-40	-50	3.78
132	R. thalamus/ventral posterior lateral nucleus	—	18	-22	4	3.95
31	R. parahippocampal gyrus/amygdala	—	20	-8	-16	3.73
68	R. superior frontal gyrus	6	26	-6	70	3.68

Note. Total number of clusters = 8. BA = Brodmann area; BOLD = blood oxygen level dependent; CCT = counter change task; FDR = false discovery rate; L. = left; R. = right.

Table 5
Maximum Loci of Activation for BOLD Response to Comparison Across CT (vs. CCT) With Cannabis (vs. Control) Cues (Uncorrected $p < .001$, Extent Threshold > 20 Voxels)

No. voxels	Localization	BA	x (mm)	y (mm)	z (mm)	t value
1756	L. superior temporal gyrus	22	-60	4	-2	4.91
	L. postcentral gyrus	43	-60	-12	16	4.45
	L. claustrum	—	-26	-10	18	3.83
147	L. medial frontal gyrus	6	-8	-12	56	3.93
	R. medial frontal gyrus	6	6	-6	52	3.4
	L. postcentral gyrus	3	-30	-32	50	3.85
294	L. postcentral gyrus	3	-16	-38	66	3.71
	L. postcentral gyrus	3	-42	-22	58	3.44
24	L. medial frontal gyrus	11	-4	32	-18	3.76
21	R. insula	13	34	-16	16	3.46

Note. Total number of clusters = 5. BA = Brodmann area; BOLD = blood oxygen level dependent; CCT = counter change talk; CT = change talk; L. = left; R. = right.

Table 6
Maximum Loci of Activation for Correlations Between Follow-Up Behaviors to BOLD Response for CT (vs. CCT) With Cannabis (vs. Control) Cues When Controlling for Baseline Scores (Uncorrected $p < .001$, Extent Threshold > 20 Voxels)

No. voxels	Localization	BA	x (mm)	y (mm)	z (mm)	t value
A. Follow-up frequency of cannabis use (positive correlation; 3 clusters)						
339	R. cerebellar tonsil	—	8	-44	-36	4.43
	L. cerebellar tonsil	—	-6	-44	-36	3.53
47	L. hypothalamus	—	-2	-4	-8	3.98
	L. lentiform nucleus/ medial globus pallidus	—	-14	-6	-6	3.47
47	R. lentiform nucleus/ medial globus pallidus	—	16	-4	-6	3.80
B. Follow-up cannabis problems (negative correlation; 2 clusters)						
53	R. inferior temporal gyrus	20	62	-32	-22	5.08
26	L. precuneus	31	-12	-56	-32	3.53
C. Follow-up cannabis dependence symptoms (negative correlation; 2 clusters)						
548	L. cingulate gyrus	31	-2	-26	40	4.16
	L. posterior cingulate	23	-6	-42	26	4.01
	R. cingulate gyrus	31	4	-40	28	3.62
74	R. superior temporal gyrus	22	64	-34	6	3.64

Note. BA = Brodmann area; BOLD = blood oxygen level dependent; CCT = counter change talk; CT = change talk; L. = left; R. = right.