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Intrinsic Frontolimbic Connectivity and Associated Patterns on Reported Mood Symptoms in Young Adult Cannabis Users

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INTRINSIC FRONTOLIMBIC CONNECTIVITY AND ASSOCIATED PATTERNS ON REPORTED MOOD SYMPTOMS IN YOUNG ADULT CANNABIS USERS

by

Skyler G. Shollenbarger

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ABSTRACT

INTRINSIC FRONTOLIMBIC CONNECTIVITY AND ASSOCIATED PATTERNS ON REPORTED MOOD SYMPTOMS IN YOUNG ADULT CANNABIS USERS

by
Skyler G. Shollenbarger

The University of Wisconsin-Milwaukee, 2017
Under the Supervision of Professor Krista M. Lisdahl, Ph.D.

Introduction: Recent legislation changes regarding cannabis in the United States highlights the importance of investigating the impact of regular cannabis use on populations, such as emerging adults, that will likely drive the market given their greater daily use (see Johnston et al., 2014). The endocannbinoid system plays a role in neurodevelopment (see Bossong & Niesink, 2010) and has been implicated in behavioral and emotional processing (see Moreira & Lutz, 2008; see Solinas et al., 2008; see Covey et al., 2014). The current study utilized a multisite functional magnetic resonance imaging (fMRI) dataset of intrinsic (a.k.a. no task/resting state) frontolimbic connectivity among healthy emerging adults. A secondary aim examined the relationship between cannabis group connectivity differences and self-reported mood and affect symptoms.

Methods: Participants included consortium data totaling 79 cannabis users (average of 58 past month joints) and 80 controls (0 past month joints & no history of regular use) emerging adults (ages of 18-30), balanced for gender, reading ability, and age. Exclusion criteria included history of medical/neurological illness or injury, independent DSM-IV-TR axis I disorders, and inability to maintain monitored abstinence. Structural and functional neuroimages were preprocessed and analyzed using CPAC software. Regions of interest included: anterior cingulate (rostral and caudal subdivisions), amygdala, insula, and ventral medial prefrontal cortex. Behavioral measurements included the Beck Depression Inventory-II, Beck Anxiety

Scale, and the State Trait Anxiety Inventory-Y1. Standard multiple regressions were used to predict if cannabis group status was associated with frontolimbic connectivity after controlling for site, past month alcohol and nicotine use, and days of abstinence from cannabis. Pearson r correlations were run to examine the relationship between group differences in connectivity and self-reported depression and anxiety total scores.

Results: On self-reported measures, cannabis users reported significantly more total depression (p=.02) and anxiety (p=.04) symptoms. After controlling for site, past month alcohol and nicotine use, and days of abstinence from cannabis, cannabis users demonstrated significantly greater connectivity between left rACC and the following: left amygdala (p=.03; corrected p=.47; f^2 = .17), left insula (p=.03; corrected p=.47; f^2 = .16), and right rACC (p=.001; corrected p=.05; f^2 =.55). Among cannabis users, greater bilateral rACC connectivity was associated with significantly greater total depressive scores (p=.02).

Discussion: Cannabis using young adults demonstrated greater connectivity within frontolimbic regions compared to controls with no recent or regular cannabis use. In cannabis users, greater bilateral rACC intrinsic connectivity was associated with higher levels of depression symptoms. Current findings suggest that regular cannabis use during neurodevelopmental periods may alter intrinsic brain characteristics involved in cognitive control and emotion regulation, and this finding should be considered when designing clinical interventions for this population. Future research may investigate the mechanisms underlying altered rACC connectivity, such as GABA and GLUT signaling, and the impact on mood in young cannabis users.

To

my beautiful, inspiring, and fiercely intelligent wife,

my supportive and hard-working parents,

my ‘family-friends’,

and those who have served our country

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1. INTRODUCTION

1.1 SIGNIFICANCE

Cannabis remains one of the most popular used substances worldwide (see Kuddos, Ginawi, & Al-Hazimi, 2013). Young adults in the United States represent the largest age group with recent and daily use, which has reached a new peak (SAMSHA 2014; Johnston et al., 2015; CBHSQ, 2015). Cannabis use during youth has been a recent focus in public health research, as it may influence one's risk for reporting symptoms of anxiety and depression (McGee, Williams, Poulton, & Moffitt, 2000; Degenhardt, Hall, & Lynskey, 2001; Brook, Brook, Zhang, Cohen, & Whiteman, 2002; Fergusson, Horwood, & Swain-Campbell, 2002; Patton et al., 2002; Rey, Sawyer, Raphael, Patton, & Lynskey, 2002; Georgiades & Boyle, 2007; Hayatbakhsh et al., 2007; Wittchen et al., 2007; Fleming, Mason, Massa, Abbott, & Catalano, 2008; de Graaf et al., 2010; Degenhardt et al., 2013). A potential mechanism underlying cannabis' influence on mood and affective symptoms may involve frontolimbic functioning (see Egerton et al., 2006; see Ellgren et al., 2008). Understanding differences in frontolimbic connectivity among young adults with frequent cannabis use may provide insight into the etiology of associated mood or affective risk.

1.2 ENDOCANABINOID SYSTEM & AFFECTIVE PROCESSING

Cannabinoids in cannabis, such as Δ9-tetrahydrocanabidiol (or THC) and cannabidiol (CBD), are chemicals that act on a particular receptor system known as the endocannabinoid (eCB) system with two receptor types, CB_1 and CB_2 (for review see Howlett et al., 2002; see Pacher, Bátkai, & Kunos, 2006; see Mechoulam, Peters, Murillo-Rodriguez, & Hanuš, 2007). THC is the main psychoactive molecule responsible

for psychopharmacological effects of cannabis use (Ashton, 2001; see Fišar, 2009; see Mechoulam & Parker, 2013); and works by mimicking the action of CB_1 ligands, such as anandamide (see Howlett, 2002; see Mechoulam & Parker 2013). CB_1 activity modulates the release of the neurotransmitters GABA and glutatmate (GLUT) (see Howlett, 2002), and has been associated with the generation of emotional and stress responses (see Moreira & Lutz, 2008; see Solinas et al., 2008; see Covey, Wenzel, & Cheer, 2014), as well as emotional states (see Witkin, Tzavara, & Nomikos, 2005).

Brain regions primarily involved in emotional interpretation, expression and regulation, also known as the affective system, include several interacting regions (e.g. amygdala, anterior cingulate gyrus or ACC, medial and inferior orbito-frontal, ventromedial or vmPFC, dorsomedial prefrontal cortex, and insula (see Patterson & Schmidt, 2003; see Frith & Frith, 2007; Lindquist, Wager, Kober, Bliss-Moreau, & Barrett, 2012). This system is highly innervated with CB_1 receptors (Glass, Dragunow, & Faull, 1997; see Mackie, 2005; see Svizenska, Dubovy, & Sulcova, 2008; Terry et al., 2009, 2010). Among daily cannabis users, Hirvonen and colleagues (2012) found relatively lower CB_1 receptor densities within frontolimbic regions (prefrontal cortex or PFC, ACC, and insula) compared to controls. Animal models demonstrate developmental changes in CB_1 expression within the mPFC, ACC and insula (Heng, Beverley, Steiner, & Tseng, 2011), suggesting the system demonstrates plasticity. Indeed, follow-up analysis among human samples revealed significant eCB density rebound in frontolimbic regions (PFC, anterior cingulate, amygdala, insula, and parahippocampus) following sustained abstinence (Hirvonen et al., 2012).

The eCB system has been implicated in mood and affect regulation (Martin,

Ledent, Parmentier, Maldonado, Valverde, 2002; Ashton, Moore, Gallagher, Young, 2005; Hill, Gorzalka, 2005; Witkin, Tzavara, Nomikos, 2005; Adamczyk, Golda, McCreary, Filip, Przegalinski, 2008; Hillard, Weinlander, Stuhr, 2012; see Marco & Laviola, 2012), integrating reward feedback (Hell et al., 2012), and threat related signals (Phan et al., 2008; Hariri et al., 2009; Cornelius, Aizenstein, & Hariri, 2010; Pietrzak et al., 2014). Activity within mPFC regions are influenced by eCB functioning, which are imperative for modulating limbic and ventral diencephalon activity purporting appropriate stress and anxiety reduction (see McLaughlin, Hill, & Gorzolka, 2014). Exposure to THC during development may impact naturally occurring changes in eCB functioning within mesocorticolimbic regions (see Ellgren et al., 2008), influencing emotional identification (Ballard, Bedi, & de Wit, 2012; Bossong et al., 2013; Hindocha et al., 2015), amygdala reactivity (Phan et al., 2008), and alter mediotemporal-prefrontal connectivity (Fusar-Poli et al., 2009; 2010; Bhattacharyya et al., 2015) and signaling (Bhattacharyya et al., 2010; Bossong et al., 2013). The type of risk associated with continued cannabis use may have unforeseeable long lasting effects on frontolimbic functioning due to continued development (see Egerton et al., 2006; see Ellgren et al., 2008).

1.3 FRONTOLIMBIC DEVELOPMENT & CLINICAL IMPLICATIONS

Connectivity changes between frontolimbic regions continue during late adolescence and emerging adulthood. Prefrontal maturation purports enhanced emotion regulation and behavior inhibition capabilities (Casey et al., 1997; Joseph, 1999; Monk et al., 2003; Casey, Tottenham, Liston, & Durston, 2005; Casey, Galvan, & Hare, 2005; Liston et al., 2006; Choudhury, Blakemore, & Charman, 2006; see Yurgelun-Todd, 2007;

Casey et al., 2008), giving rise to a functional coupling between frontal and limbic regions (i.e. the frontolimbic network). Collectively, the developmental changes in frontolimbic connectivity are thought to enhance socioemotional regulation (see Blakemore, 2008; see Braun, 2011; Hariri, Bookheimer, & Mazziotta, 2000), specifically via functioning within the amygdala, medial PFC, ACC, insula, and inferior frontal gyrus (see Frith & Frith, 2007).

Connectivity changes continue to occur during adolescence and young adulthood. Vink and colleagues (2014) found that young adulthood was associated with a decline in amygdala activation concomitant with increased ventral PFC activity during emotionally stimulating stimuli, as well as enhanced connectivity between the regions (Vink et al., 2014). The ventral medial PFC or vmPFC displays functional coupling among young adults with the cingulate cortex regions (Fair et al., 2008). Older age is associated with greater utilization of the vmPFC , which is related to enhanced performance in target detection (Durston et al., 2006). A particular region within the PFC, the ACC, also undergoes significant age-related changes in intrinsic functional connectivity, particularly in rostral ACC (rACC) subregions involved in social cognition and emotion regulation (Kelly et al., 2008). This aligns with intrinsic connectivity studies demonstrating enhanced long-range connectivity among young adults in regions that share functional similarities (see Johnson, 2001; Stevens, Pearlson, & Calhoun, 2009), particularly within paralimbic and limbic regions (Kelly et al., 2008; Supekar, Musen, & Menon, 2009). Thus, frequent cannabis use during connectivity development may have adverse affects on modulatory regions with high eCB signaling.

1.4 AFFECTIVE PROCESSING AND MOOD IN YOUNG CANNABIS USERS

Only a few studies have examined affective processing in chronic cannabis using youth. Thus far, studies have found slower response times in users when identifying emotional faces and more liberal criterion for selecting sadness (Platt, Kamboj, Morgan, & Curran, 2010), poorer facial recognition and emotion matching (Huijbregts, Griffith-Lendering, Vollebergh, & Swaab, 2014), and emotion identification and discrimination impairments (Bayrakci et al., 2015) compared to non users; though accuracy in emotion identification may not display a dose-dependent relationship (Hindocha et al., 2014). fMRI studies have found aberrant amygdala and ACC activity in young cannabis users during affective processing tasks, including blunted ACC and amygdala activation during sub-conscious facial viewing (Gruber, Rogowska, & Yurgelun-Todd, 2009), blunted amygdala response among youth with comorbid cannabis dependence and depression (Cornelius, Aizenstein, & Hariri, 2010), and greater amygdala reactivity to angry faces in young adolescents (Spechler et al., 2015). Thus, cannabis may negatively influence regions involved with affective processing.

With regard to mood and anxiety, a handful of studies have reported increased depressive and/or anxiety symptoms in chronic cannabis using youth. In a sample devoid of mood or anxiety diagnoses, greater self-reported trait anxiety and depressive symptoms were associated with higher levels of past year cannabis use (Medina & Shear, 2007). Further, greater mood and/or anxiety symptoms in young cannabis users with no comorbid Axis I diagnoses were significantly associated with reduced prefrontal white matter (Medina, Nagel, Park, McQueeny, & Tapert, 2007) and larger amygdala volumes in females (McQueeny et al., 2011). A recent longitudinal study found that heavy cannabis using youth had more negative emotionality in comparison to controls despite

no differences earlier in adolescence (Heitzeg, Cope, Martz, Hardee, & Zucker, 2015). The same study found blunted right insula, PFC, and amygdala activity during a negative word viewing fMRI task. Thus, affective processing and frontolimbic structural and functional abnormalities have been linked with increased mood symptoms in young cannabis users.

1.5 ifcMRI STUDIES IN ADOLESCENT/EMERGING ADULT CANNABIS USERS

To date very few studies have examined intrinsic functional connectivity (ifcMRI) in adolescents and emerging adults (Houck, Bryan, & Ewing, 2013; Orr et al., 2013; Behan et al., 2014; Cheng et al., 2014; Pujol et al., 2014). Orr and colleagues (2013) examined constraint-free assessment of functional whole-brain and interhemispheric connectivity in adolescents with cannabis dependence (mean age 16.5, range 15-18). Results indicated increased frontolimbic and cerebellar resting fluctuations in comparison to controls; specifically, in the right superior frontal, right inferior frontal gyrus, right inferior temporal gyrus, and right inferior semilunar lobe in the cerebellum (Orr et al., 2013). Further, regression data indicated that cannabis dependence symptoms predicted neural activity as opposed to demographic or premorbid individual differences. Connectivity increases among cannabis users showed the most robust activity correlations between right inferior frontal gyrus and right inferior temporal, as well as the right superior frontal and right superior parietal gyrus. Cannabis users also demonstrated reduced homotopic connectivity between matching hemispheric standardized voxel coordinates in the superior frontal hemispheres. Nonetheless, the sample consisted of 94% male cannabis users and did not control for gender effects, which may not generalize (Medina et al., 2009; McQueeny et al., 2011; Schepis et al., 2011; Lisdahl &

Price, 2012). Further, the study did not control for the effects of alcohol (given no group differences) or exclude for lifetime diagnosis Axis I disorders aside from ADHD. Thus, psychiatric effects may have contributed to connectivity patterns, and no brain-behavior relationships were examined making interpretation difficult.

A separate study controlling for alcohol use found greater cannabis use was associated with increased middle frontal gyrus resting activity and reduced middle temporal activity, in a relatively small sample of high-risk youth (Houck et al., 2013). Though behavioral data were collected, the authors did not examine behavioral relationships with resting connectivity. In a slightly older cannabis using cohort, reduced blood flow in bilateral medial PFC and left insula was found, and abstinence periods were associated with blood flow in this region such that group differences dissipated following four weeks of cannabis abstinence (Jacobus et al., 2012). Behan and colleagues (2014) examined connectivity differences among a predominantly male sample of adolescent cannabis users and controls during a behavioral inhibition paradigm and while at rest. Cannabis use was associated with greater lateral frontal-parietal-cerebellar connectivity during an inhibitory control task, with the same network demonstrating greater connectivity while at rest compared to controls. Intrinsic connectivity also increased with greater past week and month cannabis use in the sample, suggesting that intrinsic connectivity is altered to a greater extent depending upon use characteristics. The authors proposed that heightened coupling of lateral fronto-parietal and cerebellar co-activation may be the result of less efficient prefrontal modulation (Behan et al., 2014). In a separate study among men (ages 18-30), cannabis use status was associated with increased intrinsic connectivity within the anterior insula coupled with decreased

connectivity to the anterior cingulate and midbrain compared to controls, which persisted following one month of abstinence (Pujol et al., 2014). Relative to controls, cannabis users reported significantly greater state/trait anxiety; however, cannabis users demonstrated greater negative correlations between insula connectivity and state anxiety, suggesting enhanced insula activity. The insula is associated with visceral awareness (Critchley, Wiens, Rotshtein, Ohman, & Dolan, 2004; Caseras et al., 2011). Nonetheless, group differences existed in years of education and the effects of alcohol were not evaluated (Pujol et al., 2014). After controlling for the effects of recent alcohol use, we previously reported a reduction in frontolimbic white matter integrity, which was associated with mood symptoms in emerging adults (Shollenbarger, Price, Wieser, & Lisdahl, 2015a). Lastly, using a multi-voxel pattern analysis approach, Cheng and colleagues (2014) found greater resting connectivity in cannabis users compared to controls within the middle frontal gyrus and cingulate gyrus, among other regions identified. The same study also reported an accuracy of detecting cannabis group status ranging from 84-88% based on connectivity pattern, suggesting that group differences in brain activation appear to be localized. Ultimately, the previous studies among young cannabis users highlight general increases in intrinsic functional activation within frontolimbic regions.

1.6 PURPOSE OF CURRENT STUDY

The purpose of the current study was to explore whether heavy cannabis use among youth was associated with aberrant ifcMRI frontolimbic connectivity during non-task engagement. We employed a priori region of interest analysis focusing on regions with reported cortical differences between young cannabis users and non/light

using controls, including: vmPFC (Shollenbarger, Price, Wieser, & Lisdahl, 2015; Price et al., 2015b), ACC (Spechler et al., 2015; Lisdahl et al., 2016), insula (Lopez-Larson et al., 2011), and amygdala (Gilman et al., 2014; McQueeny et al., 2011; Schacht, Hutchinson, & Filbey, 2012). Given the success in demonstrating replicable intrinsic/resting-state networks among independently collected data sets (Biswal et al., 2010), this project utilized ifcMRI data from three collection sites (The University of Wisconsin-Milwaukee or UWM; McLean Hospital/Harvard University or McLean; The University of Texas – Dallas or UTD). Prior research with multisite neuroimaging collection has indicated no significant scanner by Alzheimer's disease interaction between 6 different scanners that received upgrades (Stonnington et al., 2008). Additionally, results within the default mode network remain relatively similar across resting conditions (i.e., eyes open, fixated, closed) (Fox et al., 2005; Fransson, 2005; Yan et al., 2009; Patriat et al., 2013), suggesting reliable connectivity data can be obtained for differing sites regardless of instruction.

Lastly, in order to interpret the findings, a secondary aim examined if group differences in connectivity were associated with cannabis users' self-reported anxiety and depressive symptoms.

1.7 HYPOTHESIS

Primary Aim: To examine whether cannabis users significantly differ in frontolimbic ifcMRI connectivity compared to non-using controls. Hypothesis 1a: It was hypothesized that cannabis users would demonstrate increased intrinsic connectivity patterns consistent with the intrinsic connectivity of the amygdala (Roy et al., 2009; see Kim et al., 2011b) in regions subserving emotional expression: amygdala with the insula

and caudal ACC (cACC). Hypothesis 1b: We also hypothesized that cannabis users would demonstrate decreased intrinsic connectivity in emotion regulation regions consistent with the intrinsic connectivity of amygdala (Quirk, Likhtik, Pelletier, & Paré, 2003; Roy et al., 2009; see Kim et al., 2011b): amygdala with the vmPFC and rACC. Additionally, it was hypothesized that cannabis users would demonstrate reduced insula with rACC connectivity given prior findings of reduced ACC with insula connectivity (Pujol et al., 2014).

Secondary Aim: To examine the relationship between group differences in frontolimbic ifcMRI and anxiety and depressive symptoms among cannabis users. Hypothesis 2: It is hypothesized that among cannabis users, elevated anxiety and depressive symptom scores would be significantly associated with increased connectivity between: amygdala with the insula and cACC; low anxiety and depressive scores would be significantly associated with increased connectivity between: amygdala with vmPFC and rACC.

2. MATERIALS AND METHODS

2.1 PARTICIPANTS

Participants included 79 cannabis users (42 men and 37 women) and 80 (45 men and 35 women) controls aged 18-30 year old young adults devoid of major medical, psychiatric or neurologic comorbidities. This age restriction is to reduce potential differences in developmental stage since emerging adults may have greater inferior PFC development and top-down socioemotional and inhibitory control compared to younger participants (Casey et al., 1997; Joseph, 1999; Monk et al., 2003; Gogtay et al., 2004; Casey, Tottenham, Liston, & Durston, 2005; Casey, Galvan, & Hare, 2005; Casey et al.,

2008), and the available age range of the MNI registration template (18-44 years of age) (Fonov et al., 2009). Study participants were selected from the IDEAA (Imaging Data in Emerging Adults with Addiction) consortium subject pool (PIs: Krista Lisdahl, Ph. D. – The University of Wisconsin-Milwaukee (UWM), Staci Gruber, Ph. D. –McLean Hospital/Havard (McLean), Susan Tapert, Ph.D. –University of California-San Diego (UCSD), and Francesca Filbey Ph.D. –University of Texas at Dallas (UT-Dallas). Data from Dr. Tapert's lab (UCSD) did not include intrinsic fMRI collection and therefore was not used in the current study.

Inclusion criteria included: right-handedness; had usable intrinsic ifcMRI data; fluency in English; and fit one of two groups: cannabis users (at least weekly cannabis use within the past month or year) and controls (never had a history of regular use; and no recent past month use). Exclusion criteria included history of neurological illness or loss of consciousness > 2 minutes; MRI contraindications (pregnancy, claustrophobia, weight over 250 lbs., ferromagnetic implants of any kind, pacemakers or other devices in body); current use of psychoactive medication; current DSM-IV-TR (APA, 2000) independent Axis I disorders (aside from substance use disorders); and inability to remain abstinent from all drugs and alcohol for at least 12 hours (ranged from 12 hours-21 days monitored abstinence across sites) (See Table 1 for abstinence percentages).

Insert Table 1 Here

2.2 PROCEDURES

The Institutional Review Board for each site approved all aspects of data collection and each institution has approved ongoing analysis. Participants underwent site-specific IRB-approved consenting procedures, and completed screening sessions to ensure inclusion/exclusion criteria. Following study inclusion, the participants completed psychological questionnaires, underwent substance toxicology screening, and received an MRI at the individual collection sites. The ifcMRI data was collected before any cognitive tasks for each site.

2.3 SCREENING INVENTORIES & QUESTIONNAIRES

Substance Use. Drug use prior to study participation was recorded by interview using temporal memory cues from a modified version of the Time-Line Follow-Back at each site (Sobell, Maisto, Sobell, & Cooper, 1979). Drug categories included quantity-standardized collection of: nicotine cigarettes (total number), alcohol (total standardized drinks), and cannabis (total number of joints or days spent using). Due to variability across sites in cannabis use measurement, grams were converted to joints for McLean and UT-Dallas sites (1 gram = 1.5 joints). The standardized units, included: number of nicotine cigarettes; total alcohol drinks with one equivalent represented as 1.25 oz. of hard liquor, 12 oz. of beer, or 5 oz. of wine; number of joints, grams, or days of cannabis use (See Table 1 for site collection method). Substance use data was collected on quantity and frequency, which ranged from 2 weeks (McLean) to past 30 days (UWM, UTD). Thus, total past month substance use was averaged for each participant collected from McLean, though the users reported consistent patterns during this time allowing average past month to accurately reflect typical use for the past month.

Psychological Tests. Anxiety Symptoms: The State-Trait Anxiety Inventory-Form Y (STAI-State) (collected from UWM & McLean) measured current self-reported symptoms of anxiety with a range of 20-80 total points and a test-retest reliability ranging .16-.62 (Spielberger, Gorsuch, Lushene, Vagg, & Jacobs, 1983). This measure has demonstrated reliable internal consistency in a variety of populations (Barnes, Harp, & Jung, 2002). The Beck Anxiety Inventory (BAI) (collected by UTD) measured self-reported symptoms of past two-week anxiety symptoms with a possible range of 0-63 total scores (Beck & Steer, 1993), reflecting a measure of state anxiety as opposed to trait (Creamer, Foran, & Bell, 1995). This measure has also demonstrated reliable internal consistency and test-retest reliability (Fydrich, Dowdall, & Chambless, 1992). Total anxiety scores for the STAI-Y1 and BAI were used in all analyses.

Depression Symptoms: The Beck Depression Inventory – second edition (BDI-II) (collected from all sites) measured self-reported symptoms of past two-week depressive symptoms with a possible range of 0-63 total scores (Beck, Steer, & Brown, 1996). This measure has demonstrated reliable internal consistency and validity in college samples (Storch, Roberti, & Roth, 2004). Total depression scores were used in the current study. For interpretation, low anxiety scores are represented by ≤ 29 on STAI-State or ≤ 15 on BAI, whereas elevated scores occur from ≥ 30 on STAI-S or ≥ 16 on BAI (Spielberger et al., 1983; Beck & Steer, 1990). Low scores on the BDI-II are interpreted as ≤ 16 and elevated ≥17.

2.4 PREMORBID INTELLIGENCE

The Wechsler Abbreviated Scale of Intelligence (WASI) – Vocabulary subtest (Wechsler, 1999) (collected from McLean, & UTD) and the Wide Range Achievement

Test – 4th edition (WRAT-IV) Reading subtest (Wilkinson, 2006) (collected from UWM) measured verbal intelligence and quality of education, since years of education may not adequately reflect education experience across cultures (see Manly, Jacobs, & Touradji, 2002). Standardized (age-corrected) T-scores for each participant were used in the analyses. Reading ability is an established method of estimating premorbid intellectual functioning (Willshire, Kinsella, & Prior, 1991).

2.5 DATA ANALYSIS

Covariates. Covariates included variables that significantly differed between cannabis users and controls, including past month alcohol and nicotine use, duration of abstinence, and behavioral/MRI collection site.

Image Preprocessing. Image processing followed the most up to date recommendations for fMRI processing (Power, Schlaggar, & Petersen, 2015; Shirer, Jiang, Price, Ng, & Greicius, 2015). ifcMRI scans were combined from three research sites. De-identified raw DICOM files were uploaded to the McLean Hospital server. Following this upload, The UWM team preprocessed all structural and resting state images. The current analysis consisted of each subject's anatomical volume and resting-state fMRI scan for each participant (time of scan age 18 - 30).

MRI Parameters. Each site utilized standard imaging protocols using 3T scanners listed below by site. UWM: Structural MRI (sMRI) scans were collected using a 3T GE MR750 scanner and SPGR sequence with the following parameters: TR/TE/TI = 8.2/3.4/450 ms, flip angle = 12°, FOV = 240, matrix size: 256x256 mm, slice thickness = 1 mm (along left-right direction), voxel size =1x1x1 mm, 150 slices, total scan time = 8 min. ifcMRI scans were collected using a gradient echo, echoplanar sequence with ramp

sampling correction using the intercomissural line (AC-PC) as a reference (TR: 2000 ms, TE: 25ms, FOV: 240, flip angle = 77°, matrix size: 64 x64, 40 slices, reps: 240, thickness 3.7mm). McLean: sMRI scans were collected using a 3T Siemens Magnetom TrioTim sngo MR B17 and MPRAGE sequence with the following parameters: TR/TE/TI = 2000/2.15/1100 ms, flip angle = 12°, FOV = 256x256 mm, slice thickness = 1.33mm (along left-right direction), voxel size =1.5x1.0x1.3 mm, total scan time = 9 min. ifcMRI scans were collected using a gradient echo, echo-planar sequence (TR: 2500ms, TE: 30ms, flip angle: 82° degrees, matrix size: mm, 41 slices, voxel size: 3.5x3.5x2.5 mm3). UT Dallas: sMRI images were collected using a 3T Philips whole body scanner equipped with Quasar gradient subsystem (40 mT/m amplitude, a slew rate of 220 mT/m/ms). A 32-channel receive head phased array coil combined with body coil transmission to achieve greater sensitivity in cortical areas. sMRI scans utylized an MPRAGE sequence with the following parameters: TR/TE/TI = 2100/3.70/1100 ms, flip angle = 12°, FOV = 256x256 mm, slab thickness = 160 mm (along left-right direction), voxel size =1x1x1 mm, total scan time = 3 min 57 sec. fMRI scans were collected using a gradient echo, echo-planar sequence with the intercomissural line (AC-PC) as a reference (TR: 2.0 s, TE: 29ms, flip angle: 75 degrees, matrix size: 64 x 64, 39 slices, voxel size: 3.44x3.44x3.5 mm3).

Preprocessing Details. All images were preprocessed utilizing an identical pipeline, computing system, and software versions (no updates were conducted during data analysis) at UWM. Anatomical preprocessing utilized the CPAC analysis software for large multisite datasets (see: http://fcp-indi.github.io), which utilized pre-existing imaging software, including AFNI (Cox, 1996), FSL (Smith et al., 2004), and ANTS

(http://stnava.github.io/ANTs/). First, data were deobliqued to align with X, Y and Z coordinates. Next, the data was resampled to FSL friendly RPI anatomical convention, and skull stripped. Anatomical segmentation and binarized threshold masks were created utilizing FSL's FAST. Next, functional images were linearly registered to anatomical native space using FSL's FLIRT, followed by nonlinear transformation of preprocessed anatomical images to MNI152 (voxel size =$2mm^3$) standard brain template using ANTS.

fMRI was also preprocessed using the CPAC software. Preprocessing included: removal of the initial 5 time points to allow T1 stabilization; deoblique; resampling to RPI space; skull stripping; data was then "scrubbed" using Framewise Displacement (Power, Barnes, Snyder, Schlaggar, & Petersen, 2012) with a maximum TR displacement set to 4 mm; image intensity normalization; linear and quadratic detrending to remove residual drift due to scanner heating and/or slower head movement; nuisance regression (white matter and cerebrospinal fluid) using 6 displacement and motion correction parameters using CompCor (applied prior to smoothing); spatial smoothing (Gaussian Kernal =4mm FWHM; Sigma =2.54); and temporal filtering (Band Pass filter = 0.1 - 0.01 Hz).

Frontolimbic ROI's. Cortical and subcortical ROI's were created using FreeSurfer's (Dale, Fischl, & Sereno, 1999) cortical parcellation atlas (DKT40 atlas; Klein & Tourville, 2012) and subcortical segmentation (Fischl et al., 2002). ROI's included the rostral anterior cingulate (rACC), caudal anterior cingulate (cACC), ventral medial PFC (vmPFC), insula, and amygdala (see Figure 1 for a video of all ROI's).

Insert Figure 1 Here

2.6 GROUP ANALYSIS

Primary Aim 1. For each subject, the average time series was extracted for all ROI's using the CPAC software. Next, the correlation coefficients for the time series were created using MATLAB (Version 8.0.0.783 64-bit maci64, 2012). Lastly, a series of standard multiple regressions were run to predict correlation coefficients between ROIs; the primary predictor variable (cannabis group status), and covariates (past month nicotine use, past month alcohol use, behavioral/MRI collection site, and duration of abstinence from cannabis prior to scan) were entered utilizing standard least squares multiple regression in SPSS (version 24). Specifically, the first block included all covariates (past month nicotine use, past month alcohol use, behavioral/MRI collection site, and duration of abstinence) and the second block included cannabis group status. False Discovery Rate correction (FDR; Benjamini & Hochberg, 1995) was implemented to correct for multiple comparisons. All correlation coefficients were visually inspected for normality in distribution. Skewed distributions were transformed using a $\log_{10}$ transformation and used in the regression in place of the skewed correlation coefficients. There was no evidence of multicollinearity or homoscedasticity following inspection of the standardized residual for the variables of interest. Interpretations of statistical significance were made if $p<.05$. For ease of interpretation, regions with connectivity differences after correction for multiple comparisons were also displayed on an average template brain provided by BrainNet Viewer software (Xia, Wang, & He, 2013).

Secondary Aim. Pearson r correlations were run between group differences in connectivity coefficients and total anxiety and depression scores among cannabis users. A total of two cannabis users were identified as outliers following visual inspection of scatter plots. These individuals were removed from the correlation analyses.

3. RESULTS

Demographic Variables. ANOVAs and χ^2's tests examined whether cannabis users and controls differed in demographic variables (see Table 2). Cannabis users and controls did not differ in age [$F(1,157)=1.1, p=.3$], ethnicity group [64.6% Caucasian for cannabis users and 52.5% for controls, χ^2 (1)2.4, $p=.12$], gender [46.8% female for cannabis users and 43.8% for controls, χ^2 (1).15, $p=.7$], and premorbid intelligence [$F(1,156)=.46$, $p=.5$].

Insert Table 2 Here

Mood Inventories. ANOVAs examined whether cannabis users and controls differed in mood scores. Cannabis users reported significantly greater total BDI-II [$F(1,124)=5.7$, $p=.02$] and total BAI scores [$F(1,54)=4.6$, $p=0.04$] compared to controls. Cannabis users marginally differed from controls total STAI-State [$F(1,68)=2.9$, $p=0.09$].

Substance Use. As expected, cannabis users differed from controls in past month total joints [$F(1,157)=91.1$, $p<.01$], past month total days of cannabis use [$F(1,85)=9{,}208.4$, $p<.01$], past month total standard alcohol drinks [$F(1,157)=20$, $p<.01$], and past month total cigarettes [$F(1,157)=7.3$, $p=.01$].

ROI intrinsic connectivity. After controlling for behavioral/MRI collection site, past month alcohol and nicotine use, and days abstinent from cannabis, cannabis users demonstrated significantly increased connectivity between left rACC and the following: left amygdala [t(80)=2.2, *beta*=.45, *p*=.03; FDR corrected *p*=.47; Cohen's f^2 = .17], left insula [t(80)=2.2, *beta*=.45, *p*=.03; FDR corrected *p*=.47; Cohen's f^2 = .16], and right rACC [t(80)=3.3, *beta*=.59, *p*=.001; FDR corrected *p*=.05; Cohen's f^2 =.55]. There were no group differences where cannabis users demonstrated significant decreases in connectivity compared to controls (see Figure 2 for an image of the rACC; see Figure 3 for raw connectivity matrices; see Figure 4 for group connectivity differences).

Insert Figures 2, 3, & 4 Here

Behavioral Measures. Among cannabis users, greater bilateral rACC connectivity was significantly associated with greater total depressive symptoms [*r*=.29, *n*=66, *p*=.02] (see Figure 5 for a scatterplot).

Insert Figures 5 Here

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4. DISCUSSION

The current study examined whether cannabis use predicted frontolimbic intrinsic connectivity using a cross-sectional design in a sample devoid of independent Axis I anxiety or mood disorders. Contrary to the hypotheses, after controlling for behavioral/MRI collection site, recent alcohol and nicotine use, and abstinence period

from cannabis use, cannabis users demonstrated increased intrinsic connectivity between the left rACC and the following: left insula, left amygdala, and right rACC in comparison to controls, though only group differences between bilateral rACC survived after correcting for multiple comparisons. Further, we found that increased bilateral rACC connectivity was associated with greater mood related symptoms in cannabis users.

Current findings parallel previous intrinsic functional studies indicating frequent cannabis use among youth is associated with greater connectivity between frontal and temporal regions (Orr et al., 2013), and increased ACC connectivity in an all male emerging adult sample (Cheng et al., 2014). Resting increases in comparison to controls was also reported within the medial frontal gyrus among a high-risk mostly male adolescent group (Houck et al., 2013). The present study adds to existing literature by including more women, controlling for other substance use and cannabis abstinence period, and relating the observed connectivity differences to mood-related symptoms. Task-based studies also report altered medial PFC activity associated with cannabis use among emerging adults (Eldreth, Matockhik, Cadet, & Bolla, 2004; Schweinsburg et al., 2005; Chang, Yakupov, Cloak, & Ernst, 2006; Tapert et al., 2007; Gruber et al., 2009; Hester, Nestor, & Garavan, 2009; Schweinsburg et al., 2010; Wesley, Hanlon, & Porrino, 2011; Sneider, Gruber, Rogowska, Silveri, & Yurgelun-Todd, 2013), suggesting chronic cannabis use is associated with region-specific changes in brain activity and connectivity among regions implicated in emotion regulation, identification, and modulation. Emerging adulthood represents a unique life stage in which continued PFC development (Giedd et al., 1996b; see Steinberg, 2005; Galvan et al., 2006; Yurgelun-Todd, 2007; see Casey, Getz, & Galvan, 2008; see Ernst & Fudge, 2009; Casey et al., 2010; Bava &

Tapert, 2010; Crone & Dahl, 2012; Carlisi, Pavletic, & Ernst, 2013) facilitates greater influence on underlying limbic structures intended to direct behavior and emotional responding (for e.g. Vink et al., 2014).

The ACC, which undergoes significant developmental shifts in functional connectivity during young adulthood (Kelly et al., 2008), has been implicated in ones' ability to detect and monitor self-produced errors (Nieuwenhuis et al., 2001; Klein et al., 2007), whether one is conscious/aware of the error or not (Hester et al., 2005; O'Connell et al., 2007). The ACC may be less engaged in cannabis users compared to controls during tasks requiring inhibitory control and error monitoring (Hester et al., 2009). The rostral subdivision of the ACC is functionally connected with the amygdala (Beckmann, Johansen-Berg, & Rushworth, 2009), forming a network for processing affective facets of behavior (Devinsky, Morrell, & Vogt, 1995; Bush, Luu, & Posner, 2000). In concert with the insula, the ACC also serves to incorporate perceptual information with autonomic and emotional information (Seeley et al., 2007). More specifically, the rACC has been posited to have top-down control influence, serving as a gatekeeper, between regions processing negative affective information and those integrating environmental stimuli (Cooney, Joormann, Atlas, Eugène, & Gotlib, 2007; see Etkin, Enger, & Kalisch, 2011), and demonstrates protracted development during young adulthood (Kelly et al., 2008). Indeed, lesions in the rACC are posited to impair ones' sensitivity to adjustments in personal performance during a cognitive control task (Di Pellegrino, Ciaramelli, & Làdavas, 2007). Thus, abnormalities in rACC function may impact various behavioral aspects, including cognitive control and appropriate environmental responses.

Our team previously found that greater cannabis use was related to reduced left

rACC volume among young cannabis users, and smaller rACC volumes were also significantly associated with lower performance in an emotional discrimination task (Maple et al., In Prep). Further, we also found reduced right ACC cortical thickness in a sample of young cannabis users, including a subset of cannabis users with a history of childhood attention deficits, compared to non-using controls (Lisdahl et al., 2016). Given the anatomical connections, regions within the medial PFC integrate internal visceral changes with external environmental information allowing for appropriate behavioral responding (Price, 2005). Indeed, Dorard and colleagues (2008) found that young frequent cannabis users report greater difficulty identifying internal emotional states. The current study suggests that chronic cannabis may increase intrinsic connectivity between emotion regulation regions, which was opposite of our original hypothesis. A potential interpretation may include the inefficiency of prefrontal top-down regulation, as hypothesized by Behan and colleagues (2014), suggesting reduced intrinsic amygdala responsiveness. Further, Pujol and colleagues (2014) found reduced ACC and insula connectivity; however, the study did not examine subcomponents of the ACC and used seed-based rather than region of interest approaches. Thus, disruptions in rACC function may lead to challenges in modulating ones' mood, consistent with the current study findings, or adjusting to emotionally salient internal and external information.

The current study also found that increased depressive symptoms among cannabis users were associated with greater connectivity between the bilateral rACC. Alterations in rACC functioning have been previously linked with depressive and affective symptoms. Historically, the subgenual cingulate, a subregion within the rACC, has been a region of focus for mood related dysfunction and stress response (see Drevets, Savit, &

Trimble, 2009), demonstrates altered connectivity associated with mood symptoms in youth (Strikwerda-Brown et al., 2015), and may be smaller in volume among those with mood disorders (Botteron, Raichle, Drevets, Heath, & Todd, 2002; Hajek, Kozeny, Kopecek, Alda, & Höschl, 2008). Greicius and colleagues (2007) found that subegnual ACC with thalamic resting connectivity was significantly greater in those diagnosed with depression compared to controls, and the length of depressive episode was associated with increased subgenual connectivity. In a sample of patients with treatment-resistant depression, stimulation of the subgenual cingulate was linked with sustained remission of symptoms (Mayberg et al., 2005) and greater rACC activity has been associated with better response to antidepressant medication (Pizzagalli et al., 2001). Aberrant rACC affective processing may also occur in those with anxiety-related disorders (Etkin & Wager, 2007). Though the current sample did not meet criteria for an Axis I mood or anxiety disorder, cannabis use may impact regions implicated in symptom manifestation. For example, medial and ventral portions of the PFC, including the ACC, show functional alterations in adolescents experiencing a mood, anxiety or affective regulation disorder (Hare et al., 2008; Cullen et al., 2010a; Cullen et al., 2010b; Roy et al., 2013; Ho et al., 2015; Strikwerda-Brown et al., 2015), and also demonstrate altered connectivity patterns (Kim, Gee, Loucks, Davis, & Whalen, 2011a). Indeed, cross-sectional (Rey et al., 2002; Wittchen et al., 2007; Fleming et al., 2008; de Graaf et al., 2010) and longitudinal (Brook et al., 2002; Ferguson et al., 2002; Georgiades & Boyle, 2007; Moore et al., 2007) studies among cannabis-using youth have found increased risk of mood and affective symptoms. Thus, abnormalities within the rACC may result in mood specific dysregulation.

Proposed theories accounting for functional and behavioral differences may have multiple underlying etiologies. Youth may be at high risk for the negative effects of cannabis (see Schneider, 2008) due to the profound neurodevelopmental changes occurring in affective processing during this stage in life. PET studies note changes in ACC CB_1 receptor density (Hirvonen et al., 2012); thus, frequent cannabis use may influence continued white matter myelination and grey matter pruning within this region, impacting structural integrity (Spechler et al., 2015; Shollenbarger et al., 2015a, 2015b; Lisdahl et al., 2016). Further, altering CB_1 availability and eCB signaling may impact GABA and GLUT signaling, which is observed in the ACC of adolescents with chronic cannabis use (Prescot, Locatelli, Renshaw, & Yurgelun-Todd, 2011; Prescot, Renshaw, & Yurgelun-Todd, 2013), suggesting continued cannabis use may impact healthy ACC functioning. Indeed rACC glutamate levels have been associated with interactions between task-positive (supragenual ACC) and task-negative (perigenual ACC) subregions (Duncan, Enzi, Wiebking, & Northoff, 2011), suggesting excitatory activity at rest may alter one's ability to engage networks involved in environmental interaction. Indeed, glutamatergic pathways connecting the rACC and amygdala modulate animal behavior (Bissière et al., 2008). On balance, intrinsic GABA concentration is associated with predicting ACC BOLD signaling during affective processing, as opposed to glutamine (Northoff et al., 2007). Thus, altered inhibitory eCB activity may account for changes in intrinsic ACC connectivity among users. Further, disruption in dopaminergic tone within the subgenual ACC may explain symptoms such as anhedonia and apathy among those with depression (see Drevets, 1999), which are symptoms commonly associated with frequent cannabis use (Bovasso, 2001; Janiri et al., 2005). Reductions in

mesolimbic dopamine, which project to the rACC, may negatively impact sensitivity to reward processing resulting in anhedonic symptoms reported by chronic cannabis users (Bloomfield, Morgan, Kapur, Curran, & Howes, 2014), and reduced dopamine may increase activation (i.e. reduce suppression) within mPFC and cingulate cortices during task-based processing (Nagano-Saito et al., 2008). The relationship between depression and cannabis use may also be influenced by genetic status (Lynskey et al., 2004). In sum, chronic cannabis use may impact ACC functioning and increase or prolong the risk for functional brain changes within networks sensitive to eCB modulation.

Lastly, though we controlled for various potential confounds (collection site and number of days abstinent from cannabis), the current results should be interpreted in light of potential withdrawal symptoms among users. For example, common withdraw symptoms reported among young cannabis users include depressive or anxiety symptoms, including decreased appetite, irritability, nervousness/anxiety, restlessness, shakiness, sleep difficulty, stomach pains, or sweating (Budney, Mooe, Vandrey, Hughes, 2003). With regard to the current sample, the most commonly reported symptoms included the following, depressive symptoms: changes in sleep, agitation, past failure, loss of interest, self-criticalness, and changes in appetite, and anxiety symptoms: feeling hot, inability to relax, nervousness, heart pounding or racing, and abdominal/indigestion discomfort. Nonetheless, both groups were within the minimal range of depressive or anxious affect intensity and no participant met DSM-IV-TR criteria for an independent mood disorder (APA, 2000).

4.1 LIMITATIONS

Findings from the current study should be considered in light of potential limitations. In the current sample, young cannabis users reported significantly greater depressive and anxiety symptoms compared to controls despite failing to meet full criteria for a mood or anxiety disorder. Thus, the present study may not generalize to populations that meet criteria for a major mood or affective disorder. Given the cross-sectional nature of the current study, potential differences in frontolimbic connectivity may exist *prior to* the onset of frequent cannabis use and serve as a risk factor for regular cannabis use during adolescence. In a self-report study among youth, cannabis users reporting using cannabis in order to "stop worrying" were significantly younger than cannabis users reporting other reasons for use (Boys et al., 2001), indicating that negative mood or affective states may occur at an earlier age and relate to other environmental influences compared to recreational users. For example, McCarty and colleagues (2012) found recent psychosocial stress significantly increased substance use initiation in youth. Environmental heterogeneity exists among heavy using cannabis youth (Miller & Plant, 2002) and psychosocial stress is known to alter frontal connectivity and functioning (Liston, McEwen, & Casey, 2009). The relationships between such factors and substance use patterns among youth have previously been investigated (Lopez et al., 2009; Prado et al., 2009; Connell, Gilreath, Aklin, & Brex, 2010; Kiesner, Poulin, & Dishion, 2010; Branstetter, Low, & Furman, 2011; see Karriker-Jaffe, 2011; Van Ryzin, Fosco, & Dishion, 2012; Eisenberg, 2014; Sitnick, Shaw, & Hyde, 2014; Unger, 2014; Bacio et al., 2015). Therefore, longitudinal studies are necessary to determine causality.

Lastly, the design of the current study relied upon temporal correlations in BOLD response between two regions and readers cannot assume causality. This method relates regions of the brain in terms of how they relate over time, as opposed to effective connectivity analysis, which examines the influence of particular region(s) on the response pattern(s) in other regions using data driven structural equation modeling, independent component analysis, or graph theoretical approaches (see Friston, 2011 for more details). Future studies may consider these alternative approaches to connectivity analyses.

Future Directions. Altered activation of the subgenual ACC has been linked with clinical depression (for review see Drevets, Savitz, & Trimble, 2008). Indeed, decreases in subgenual activity have been linked with antidepressant effects following treatment (Wu et al., 1999; Mayberg et al., 2000; Drevets et al., 2002; Mayberg et al., 2005; Mayberg et al., 2009; Kito et al., 2008; Kito et al., 2011; Nahas et al., 2007). Targeting a cortical area more easily accessible by transcranial magnetic stimulation (TMS; see Dayan, Censor, Buch, Sandrini, & Cohen, 2013), Fox and colleagues (2012) identified ideal stimulation sites in the dorsolateral PFC (dlPFC) that were associated with reduced subgenual ACC activity. Thus, hyper connectivity of rACC, as observed in the current study, may be associated with symptoms of depression, given the risk associated with early-onset cannabis and protracted depressive spells (de Graaf et al., 2010). Replication of the current study is needed to confirm hyperconnectivity of the rACC among young chronic cannabis users.

In light of the current study, future studies may consider examining interactions between subregions of the ACC (for seed-based coordinates see Kelly et al., 2008) in

young cannabis users, given the influence of ACC task-negative regions on ACC task-positive interactions (Duncan et al., 2011); such studies may uncover the negative influence associated with chronic cannabis use on cognitive performance (for review see Lisdahl, Wright, Medina-Kirchner, Maple, Shollenbarger, 2014). Additionally, examining the influence of GABA and GLUT signaling on ACC connectivity may elucidate neural connectivity associated with frequent cannabis use.

In terms of youth treatment, there are potential interventions that appear to involve ACC functioning. For example, activation within the ACC was associated with positive treatment outcomes following change talk among a diverse group of cannabis-using youth (Feldstein Ewing et al., 2013). Mindfulness-based mediation and a combination of mindfulness with aerobic exercise have also been associated with ACC specific changes (see Paulus, Stewart, & Haase, 2013). Additional intervention studies may consider examining ACC functional changes among young adult populations, who reflect an age group with continued ACC functional development (Kelly et al., 2008). Such research may elucidate the relationship between localized brain changes and behavioral outcomes.

5 CONCLUSIONS

In conclusion, the present multisite imaging study found that among otherwise healthy young adults devoid of independent mood or affective disorders, cannabis group status predicted greater intrinsic connectivity between left and right rACC. The current study also found that greater intrinsic bilateral rACC connectivity was associated with more depressive symptoms among cannabis users. Results coincide and expand upon

prior intrinsic and task-based imaging projects among young adults with chronic cannabis use, suggesting altered connectivity between regions with high cannabinoid receptor density that are imperative for emotional inhibition, recognition, and regulation. As THC content continues to rise (Burgdorf et al., 2011; ElSohly et al., 2000; Mehmedic et al., 2010), today's users may be at increased risk for changes in mood or anxiety (Gage et al., 2015; Kedzior & Laeber, 2014) and emotional health (see Chadwick et al., 2013). The current cross-sectional young adult sample was likely undergoing continued changes in frontolimbic connectivity, and collectivity used cannabis on a daily basis. Thus, current findings may not generalize to lighter users or young adults with comorbid Axis I mood or anxiety disorders. Considering ongoing research and growing changes in cannabis availability, it is recommended that youth delay regular use of cannabis until after peaks in brain maturation are achieved (see Lisdahl, Gilbart, Wright, & Shollenbarger, 2013), particularly frontal-limbic regions (Kelly et al., 2008). In light of the current paper, cannabis interventions for youth may target improving anterior cingulate functioning, including aerobic exercise and mindfulness-based approaches (see Paulus, Stewart, & Haase, 2013).

Table 1. Abstinence Period for Cannabis Users

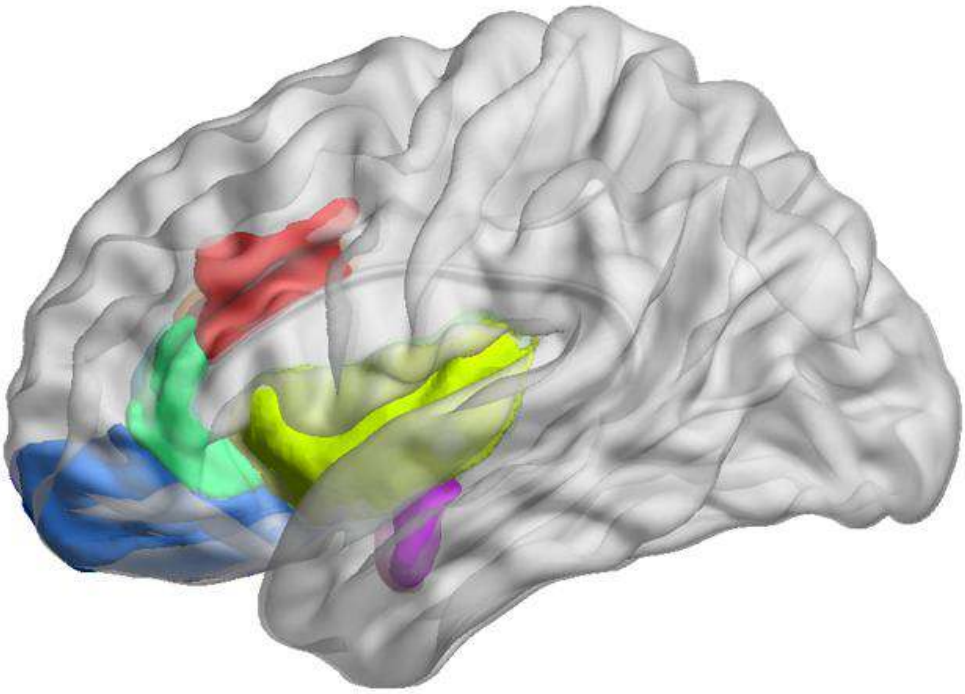
Abstinence Period	Percent within category	Total subjects in category
12 hours – 24 hours	27.8%	22
2 days – 3 days	39.2%	31
4 days – 7 days	5.1%	4
8 days – 14 days	-	0
15 or greater days	27.8%	22

Table 2. Demographics by Group Status.

	Cannabis Users (n=79)	Controls (n=80)
Age	23.4 (3.4) [18-30]	22.9 (2.6) [18-29]
Premorbid Intelligence Reading Standardized Score	53.1 (9.7) [31-74] n=79	54.1 (8.9) [30-72] n=79
Gender (% female)	46.8%	43.8%
% Caucasian	64.6%	52.5%
Beck Depression Inventory (BDI-II) Total-2	7.1 (9.3) * [0-53] n=68	3.9 (4.4) * [0-19] n=58
State -Trait Anxiety Inventory –State (STAI-Y1) Total Score	27.2 (6.9) [20-46] n=38	24.7 (4.6) [20-38] n=32
Beck Anxiety Inventory (BAI) Total	10.2 (10.4) * [0-39] n=30	5.3 (5.5) * [0-23] n=26
Past Month Cannabis Use Total Joints	57.9 (54.3) ** [0-217.5] n=79	0 (0) ** [0] n=80
Past Month Cannabis Use Total Days (UT-Dallas only)	29.8 (.67) ** [26-30] n=41	0 (.00) ** [0-0] n=46
Past Month Alcohol Use Total Standard Drinks	22.3 (28.4) ** [0-137] n=79	7.1 (10.9) ** [0-62.5] n=80
Past Month Total Cigarettes Total Number	6.9 (22.1) ** [0-121] n=79	.24 (1.4) ** [0-12] n=80

Notes: * p<.05; ** p<.01. Due to the variability of data collection assessment across sites, the total number of subjects used to calculate each value listed above is included.

Figure 1. Regions of Interest Video



Note: Right click on image and select ‘Play’

Figure 2. Region Displaying Group Differences: Bilateral Rostral Anterior Cingulate

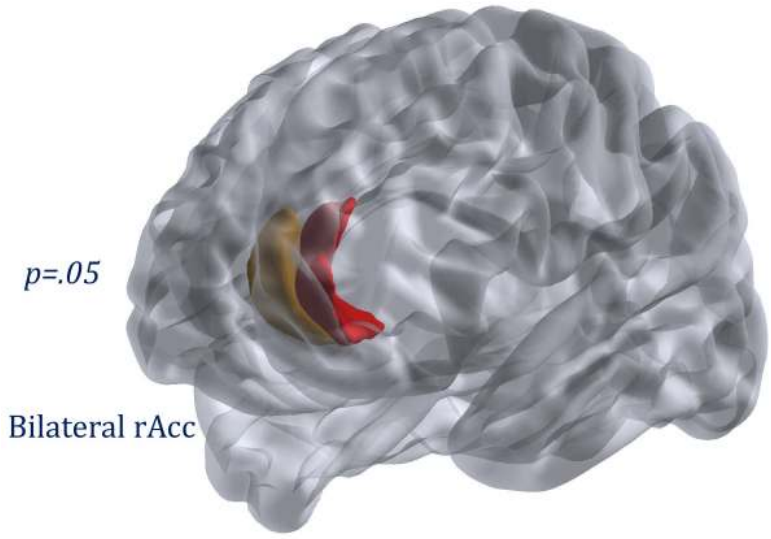


Figure 3. Connectivity Matrices for Cannabis Users and Controls

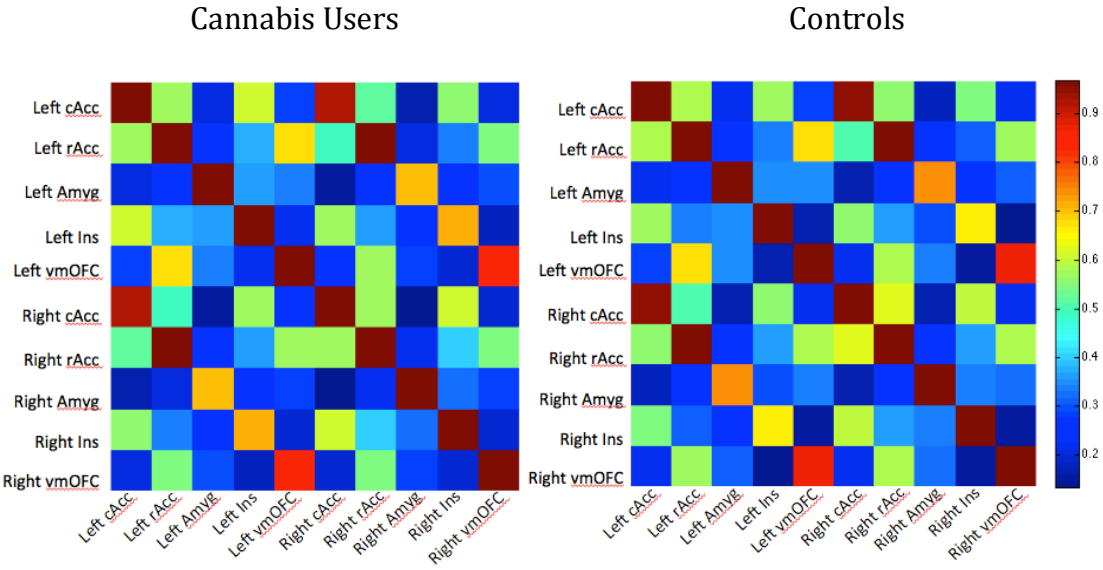
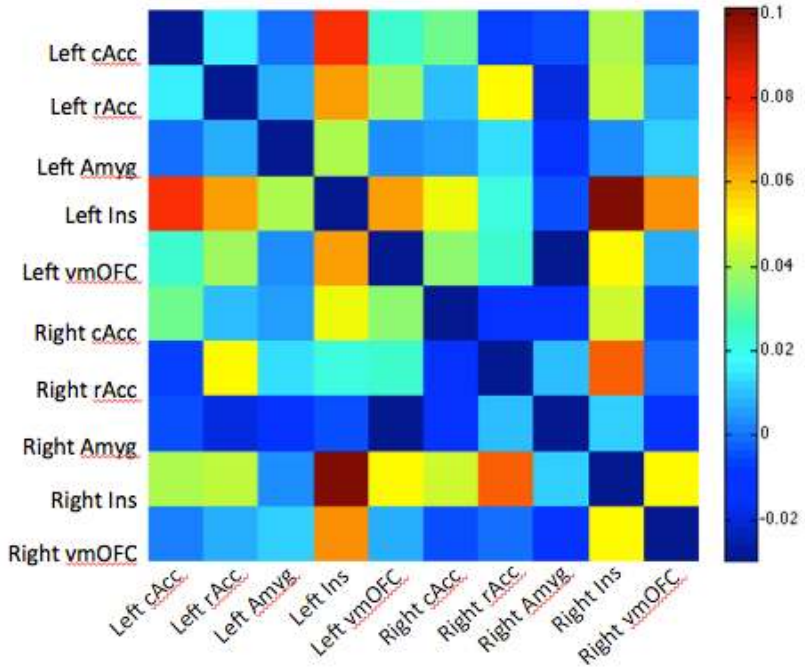


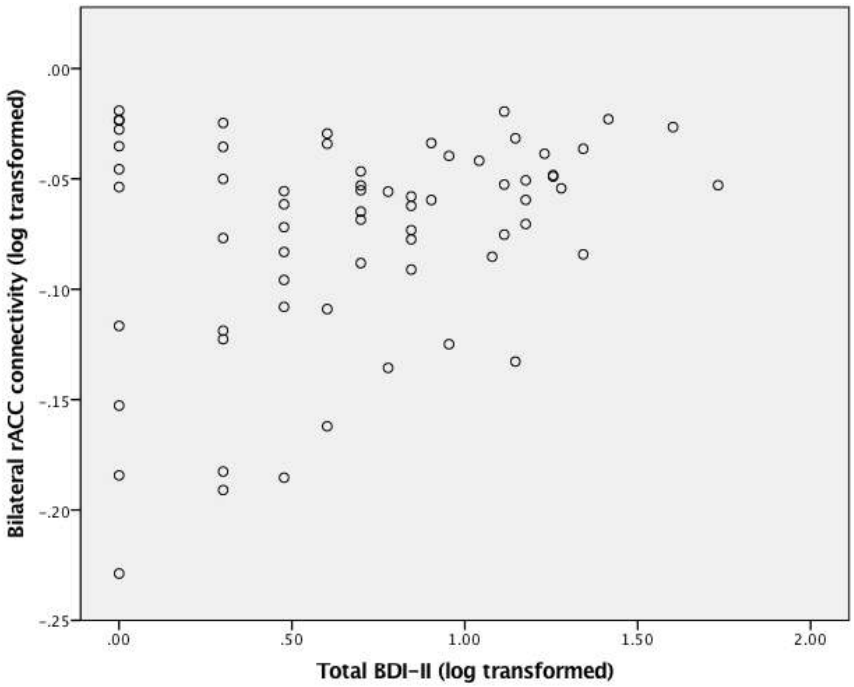
Figure 2 Abbreviations: Caudal Anterior Cingulate = cAcc; Rostral Anterior Cingulate = rAcc; Amygdala = Amyg; Insula = Ins; Ventral Medial Orbital Frontal = vmOFC.
Note: not controlling for covariates.

Figure 4. Group Differences in Connectivity Matrix



Note: Cannabis mean raw connectivity matrix minus control mean connectivity matrix (not controlling for covariates).

Figure 5. Scatterplot for Cannabis Users: Depression Total By Bilateral rAcc Connectivity.



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Xia, M., Wang, J., He, Y. (2013). BraiNet viewer: a network visualization tool for human brain connectomics. PLOSone. http://dx.doi.org/10.1371/journal.pone.0068910.

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Skyler G. Shollenbarger, M.S.

CURRICULUM VITAE

EDUCATION

2016-present	Internship	(Anticipated) Clinical Psychology, Neuropsychology (Adult), Clement J. Zablocki VA Medical Hospital, Milwaukee, WI.
2014-present	Ph. D.	(Anticipated) Clinical Psychology, University of Wisconsin-Milwaukee, WI
		Dissertation Title (oral defense passed 10/2016): INTRINSIC FRONTOLIMBIC CONNECTIVITY AND ASSOCIATED PATTERNS ON REPORTED ANXIETY AND DEPRESSION SYMPTOMS IN EMERGING ADULT CANNABIS USERS.
		Advisors: Krista M. Lisdahl, Ph.D., Chair; Christine Larson, Ph.D., Co-Chair; Han Joo Lee, Ph.D.; Deborah Hannula, Ph.D.; Raymond Fleming, Ph.D.
2011-2014	M.S.	Clinical Psychology, University of Wisconsin-Milwaukee, WI.
		Thesis Title: IMPACT OF *FAAH* GENOTYPE AND MARIJUANA USE ON BRAIN STRUCTURE AND NEUROPSYCHOLOGICAL PERFORMANCE IN EMERGING ADULTS.
2004-2008	B.A.	Psychology, University of Cincinnati, Cincinnati, OH.

AWARDS & HONORS

2016	UWM Student Organization Association Travel Award
2014	UWM Advanced Opportunity Program Travel Award
2014-2016	UWM Advanced Opportunity Program Fellowship for minority students
2014	UWM Graduate Student Travel Award
2013	APA Student Poster Award – Division 40 Society for Clinical Neuropsychology
2013	UWM Graduate Student Travel Award
2004-2008	The University of Cincinnati Dean's List

CLINICAL EXPERIENCE

2016-Present **Clinical Psychology Intern** (APA accredited since 1978)
Clement J. Zablocki VA Medical Hospital
Director: James D. Hart, Ph.D.
Rotation Supervisors: Eric R. Larson, Ph.D., ABPP-CN, Kathleen Patterson, Ph.D., ABPP-CN, Angela Gleason, Ph.D., ABPP-CN, Patrick Martin, Ph.D., Melissa Lancaster, Ph.D., & Peter Graskamp, Ph.D.
Participating in scientist-practitioner model of professional training in clinical psychology. Rotations include: Neuropsychology (50% full year),

Polytrauma, Post-Deployment/PTSD (12.5% full year); (anticipated rotations): Geropsychology & Spinal Cord Injury. Neuropsychology rotation: Co-facilitated and independent clinical interviewing/consultation, administering cognitive batteries, scoring, report writing, participating in providing feedback, attending weekly case conference, and didactics, including Grand Rounds at MCW. Polytrauma rotation: Participating in interdisciplinary clinical TBI interviewing and diagnostic formulation, attending team meetings, and report writing. PTSD rotation: Interventions include Prolonged Exposure, Interpersonal, and Cognitive Processing. Attend weekly supervision and write progress notes. Internship responsibilities: Attending weekly intern seminar didactic series. Participate in weekly group and individual supervision. Attend diversity committee meetings.

2015-2016 **Clinical Psychology Practicum Student**
Clement J. Zablocki VA Medical Hospital; Post-Deployment/PTSD Clinical Team
Supervisor: M. Christina Hove, Ph.D.
Provided group and individual therapy to Veterans with co-occurring Substance Use Disorders and PTSD symptoms. Interventions utilized included Seeking-Safety, Acceptance and Commitment Therapy, Interpersonal, and Motivational Interviewing. Participated in trauma-related didactics and individual supervision. Administered psychodiagnostic assessment interviews and completed psychodiagnostic reports.

2014-2015 **Clinical Neuropsychology Practicum Student**
The Medical College of Wisconsin & Froedert Hospital
Supervisors: Sara Swanson, Ph.D., ABPP-CN, Laura Umfleet, Psy.D., Julie Bobholtz, Ph.D., ABPP-CN, David Sabsevitz, Ph.D., ABPP-CN, Michael McCrea, Ph.D., ABPP-CN
Administered neuropsychological batteries serving populations including those with: epilepsy, traumatic brain injury, movement disorders, neuro-oncology, and memory disorders. Other duties involved scoring, interpreting, report writing, observing neuropsychological interviews and feedback sessions. Attended weekly didactics involving clinically relevant material presented in clinical case conference, journal club, and neurology grand rounds.

2013-2014 **Psychotherapy Practicum**
UWM Psychology Clinic
Supervisors: Shawn Cahill, Ph.D. & Robyn Ridley, Ph.D.
Provided psychotherapy for students and community members for two clinical teams focusing in adults with anxiety, mood, and adjustment disorders. Treatment methods including Exposure and Response Prevention for OCD and Cognitive Behavioral Therapy for Social Anxiety and mood disorders. Responsibilities involved attending weekly case conference team meetings, reviewing treatment plans with clients, session progress notes, and intervention termination summaries. Received clinical feedback and supervision.

2012-2013 **Psychological Intake Assessment Student**
UWM -NIMH Program of Excellence Training in Scientifically Validated Interventions Traumatic Stress & Anxiety Disorders Specialty Team
Supervisor: Shawn Cahill, Ph.D.

Received specialized training and supervision in providing empirically supported assessment for anxiety disorders including PTSD and OCD. Provided comprehensive clinical interviews (SCID I & II, PSS-I, Y-BOCS) and intake reports for adults seeking treatment for anxiety related disorders; preparing integrated assessment reports, and attending weekly case conference team meetings. Received report writing feedback.

2012-2013 **Assessment Practicum**
UWM Psychology Clinic
Supervisors: Bonita Klein-Tasman, Ph.D. & Han Joo Lee, Ph.D.
Performed comprehensive clinical interviews, psychodiagnostic testing, scoring, interpretation of results, and client feedback for students and community members in the greater Milwaukee area. Received supervised feedback from faculty members and advanced graduate students in the doctoral program.

2011-2012 **First Year Practicum**
UWM Psychology Clinic
Supervisors: Gwynne Kohl, Ph.D. & Douglas Woods, Ph.D.
Observed psychotherapy sessions conducted by doctoral students on two clinical teams. Populations served included students and community members with symptoms of anxiety, eating, depression, tic/hair pulling, Tourette's. Participated in weekly clinic team meetings, didactics on interviewing and test administration, and case conceptualization with a team approach.

2009-2011 **Study Coordinator & Lab Manager -Funding Source NIAAA**
The University of Cincinnati - Anxiety and Alcohol Lab
Supervisor and PI: Giao Q. Tran, Ph.D.
Received basic Cognitive Behavioral Therapy (CBT) and MI training under supervision of PI along with study therapists. Edited and collaborated on study therapist intervention manual. Attended Motivational Interviewing (MI) 2-day intensive training. Assisted training of study therapists for study conditions and participated in clinical interventions training. Participated in weekly didactics relating to Substance Use Disorders, physiological and psychological effects of substances, anxiety, and CBT, MI, and personalized substance use feedback treatment approaches.

RESEARCH EXPERIENCE

2011-2016 **Graduate Research Assistant -Funding Source NIDA**
UWM - Brain Imaging & Neuropsychology (BraIN) Lab
Supervisor: Krista M. Lisdahl, Ph.D.
Research: Effects of Physical Activity & Marijuana Use on Frontolimbic Functioning During Adolescence: An fMRI Study (1 R01 DA030354-01). National Institute of Health (NIH)/National Institute on Drug Abuse (NIDA). Direct costs $1,625,000. The objective of this proposal is to examine whether physical activity or cardiorespiratory fitness ameliorate the negative consequences of marijuana use during adolescenceutilizing functional and structural MRI.
Lab Duties: Conducting semi-structured psychodiagnostic interviews (MINI, CDDR, FHH) drug use interviews (TLFB), biological samples

collection (DNA saliva samples, sweat and urine toxicology, hair toxicology), administering comprehensive neuropsychological batteries (e.g. measures in: executive functioning, attention, memory, decision-making, distress tolerance); database creation and coding; administering Vo2 maximum testing; running MRI sessions; structural and functional brain imaging pre-processing, quality assessment and manual editing for Dr. Lisdahl's R01 and IDEAA (Neuroimaging Consortium) grants; training and evaluation of research assistants; assisting with lab grants and manuscripts.

2009-2011 **Study Coordinator & Lab Manager -Funding Source NIAAA**
The University of Cincinnati - Anxiety and Alcohol Lab
Supervisor and PI: Giao Q. Tran, Ph.D.
Research: Created flow chart for online clinical assessment data collection. Supervise
undergraduate research assistants. Performed literature search on psychometric properties of study assessments. Created recruitment materials. Participant recruitment. Prepare or assist in preparation of protocols, informed consents, amendments and other necessary documents for review by the Institutional Review Board and NIH. IRB communication for protocol submissions, modifications, and study renewals. Assisted PI with annual NIH progress reports.
Teaching: Performed year round teaching assistant responsibilities for PI: guest lecture, graded final exams, assisted students with research idea formulation, and uploaded grades to registrar. Presented in lab didactics training.

2010-2011 **Research Assistant**
The University of Cincinnati - Brain Imaging & Neuropsychology (BraIN) Lab
Supervisor: Krista M. Lisdahl, Ph.D.
Determined eligibility of participants examining the effects of MDMA (Ecstasy) and Marijuana on the brain via semi-structured clinical phone interview according to DSM-IV-TR criteria for major mood and psychiatric disorders.
Acquired basic AFNI skills: talariaching and skull stripping anatomical images.
Acquired basic Unix Skills. Participant recruitment. Data entry. Various lab projects.

2008-2010 R**esearch Assistant**
The University of Cincinnati - Human Factors and Human Performance Lab
Supervisor: Gerald Matthews, Ph.D.
Operated driving simulator and administered assessments for investigating two studies including: effects of hands free cell phone use on driver performance and subjective state following active versus passive fatigue manipulations, and whether personality factors have an impact on the decision to use automated vehicle control in high workload simulated conditions. Data collection and storage.

2006-2007 **Research Assistant**
The University of Cincinnati - Chemical Senses Lab
Supervisors: Lloyd Hastings, Ph.D. and Robert Frank, Ph.D.

Conducted olfactory battery tests for investigating the importance of verbal labeling on odor memory. Contributed to ongoing lab projects investigating the clinical signs (loss of olfaction) of neurodegenerative disorders. Acquired basic Excel skills. Data collection, presentation and storage.

PEER-REVIEWED PUBLICATIONS

Avallone, K., **Shollenbarger, S**., Howe, S., (2011). Safe Zone Training: One approach in creating a positive LGBT climate at US universities. The Community Psychologist (44) No. 1 (newsletter of APA Division 27).

Lisdahl, K., Gilbart, E.R., Wright, N.E., **Shollenbarger, S.G.** (2013). Dare to Delay?: The Impacts of adolescent alcohol and marijuana use onset on cognition, brain structure, and function. *Front Psychiatry*, 53(4).

Lisdahl, K., Write, N.E., Medina-Kirchner, C., Maple, K.E., **Shollenbarger, S.G.** (2014). Considering Cannabis: The effects of regular cannabis use on neurocognition in adolescents and young adults. *Current Addiction Reports.,* 1 (2); 144-156.

Price, J., McQueeny, T. **Shollenbarger, S.G.**, Browning, E., Wieser, J., Lisdahl, K.M.(2015). Effects of marijuana use on prefrontal and parietal volumes and cognition in emerging adults. *Psychopharmacology, 232*(16). doi: 10.1007/s00213-015-3931-0.

Shollenbarger, S.G., Price, J., Wieser, J., Lisdahl, K.M. (2015). Poorer frontolimbic white matter integrity is associated with chronic cannabis use, *FAAH* genotype, and increased depressive and apathy symptoms in adolescents and young adults. *Clinical-Neuroimage,* (8), 117-125*.* doi:10.1016/j.nicl.2015.03.024.

Shollenbarger, S.G., Price, J., Wieser, J., Lisdahl, K.M. (2015). Impact of cannabis use on prefrontal cortex gyrification in adolescents and emerging adults. *Developmental Cognitive Neuroscience, 16*, 46-53. doi:10.1016/j.dcn.2015.07.004.

Wright, T., Strong, J., Gilbart, E., **Shollenbarger, S.G.**, Lisdahl, K.M. (2015). *5-HTTLPR* Genotype moderates the effects of ecstasy on verbal memory performance in adolescent and emerging adults. *PLOS One*. doi:10.1371/journal.pone.0134706.

Miskovich, T.A., Walker, S.P., Belleau, E.L., **Shollenbarger, S.G**., Lisdahl, K.M., Larson, C.L. (In Press). Cortical Gyrification patterns associated with trait anxiety. *PLoS ONE.*

Maple, K., McDaniel, K.A., **Shollenbarger, S.G.**, Lisdahl, K.M. (In Press). Dose-Dependent Cannabis Use and FAAH Genotype Predict Sleep Quality in Emerging Adults: A Pilot Study. *The American Journal of Drug and Alcohol Abuse.*

Lisdahl, K.M., **Shollenbarger, S.**, Sagar, & Gruber, S (In press). *Chapter 2: The Neurocognitive Impact of Alcohol and Marijuana Use on the Developing Adolescent and Young Adult Brain*. In Monti, Colby & Tevyaw (Eds) *Adolescents, Alcohol, and Substance Abuse: Reaching Teens through Brief Interventions (2nd Ed.).* New York: Guilford Press.

MANUSCRIPTS UNDER REVIEW OR IN PROGRESS

Miskovich, T.A., Baskin-Sommers, A.R., Newman, J.P., Hanson, J.P., Stout, D.M., Koenigs, M., Kiehl, K. A., **Shollenbarger, S.G.,** Lisdahl, K.M., Larson, C.L. (Under Review). Abnormal anterior midcingulate cortex gyrification in males with psychopathy.

Lisdahl, K., Price, J.S., **Shollenbarger, S.G.** & Padula, C. (Under Review). High body mass index predicts poorer inhibitory processing and verbal learning in adolescents and emerging adults. *Archives of Clinical Neuropsychology*.

PEER-REVIEWED ORAL PRESENTATIONS

Shollenbarger, S.G., Wright, N.E., Lisdahl, K. (2013, June). *FAAH* Genotype and MJ Use Interact to Predict Executive Functioning in Adolescent and Emerging Adults. Oral communication presented at The College on Problems of Drug Dependence, San Diego, California.

Lisdahl, K., **Shollenbarger, S.G**., Maple, K. (2014, February). *Symposium: Potential moderators of marijuana effects: Age of onset, gender, body mass, and genetics.* Presented at The International Neuropsychological Society, Seattle, WA.

Shollenbarger, S.G., Price, J., Wieser, J., Lisdahl, K. (2014, June). Impact of *FAAH* Genotype and Marijuana Use on Brain Structure and Neuropsychological Performance in Emerging Adults. Oral communication presented at The College on Problems of Drug Dependence, San Juan, Puerto Rico.

Lisdahl, K., Price, J., **Shollenbarger, S.G**. (2015, June). *Symposium: Endocannabinoid genetics moderate the impact of regular cannabis use on cognition and brain structure in adolescents and emerging adults.* Paper presented in a symposium entitled: *Cannabis Use in Youth: Neurocognitive Effects, Genetic Moderators, and Epigenetic Findings (Chair: Lisdahl)* at The College on Problems of Drug Dependence, Phoenix, AZ.

Lisdahl, K.M., Price, J.P., **Shollenbarger, S.G.**, & Maple, K. (2015, August). *Neurocognitive Effects of Cannabis use on Youth: Genetic Moderators.* Paper presented in a symposium *Marijuana on the Adolescent Brain? Exploring Neurodevelopment and Behavior* at the annual APA convention, Toronto, Canada.

Lisdahl, K. **Shollenbarger, S.G.,** McDaniel, K., & Thomas, A. (2016, June). *Past year binge drinking and gender interact to predict abnormal prefrontal gyrification in adolescents and young adults.* Roundtable discussion presented at The Research Society on Alcoholism, New Orleans, LA.

Lisdahl, K., **Shollenbarger, S.G.**, Maple, K., & Thomas, A. (to be presented 2016, Dec). *Cannabis Use is Associated with Frontoparietal Structural and Functional Abnormalities and Executive Dysfunction in Young Adults With and Without ADHD.* Oral presentation to be presented at The American College on Neuropsychopharmacology. Hollywood, Florida.

POSTERS

Baillie, J., Rybalsky, K., Hastings, L., Knauf, B., **Shollenbarger, S.**, Mannea, E. Gesteland, R., and Frank, R. (2007, April). Odor Memory: The Importance of verbal labeling. Poster presented at The Association for Chemoreception Sciences, Sarasota, FL.

Capehart, K., Tran, G., **Shollenbarger, S.**, Stein, A., (2010, November). Effects of intimate partner violence and alcohol on anger in victim. Poster presented at The Ohio Psychological Association, Columbus, OH.

Shollenbarger, S., McQueeny, T., Patel, S., Lisdahl, K.M., (2010, November). Nicotine effects on PFC morphometry and executive dysfunction. Poster presented at The Ohio Psychological Association, Columbus, OH.

Tran, G.Q., Haaga, D.A.F., Heffner, J.L., **Shollenbarger, S.G.**, Eiler, B.N. (2012, June). Comparison of alcohol-focused and integrated brief psychosocial interventions for anxious and depressed college hazardous drinkers. Poster presented at Research Society on Alcoholism Conference, San Francisco, California.

Boyd, J.T., Zaturenskaya, M., **Shollenbarger. S.**, Tran, G.Q. (2012, June). Drinking motives of college hazardous and nonhazardous drinkers. Poster presented at the University of Cincinnati Undergraduate Conference, Cincinnati, OH.

Wright, N.E., **Shollenbarger, S.G.**, Lisdahl, K.M. (2013, June). *5-HTTLPR* Genotype, Gender and ecstasy use interact to predict verbal memory in adolescent and emerging adults. Poster presented at In Women's Conference, San Diego, CA.

Shollenbarger, S.G., Wright, N.E., Browning, E., Lisdahl, K. (2013, August). Executive functioning in adolescent and emerging adult poly-substance users. Poster Presented at The American Psychological Association Conference, Honolulu, HI. *Division 40 Award*

Browning, E.L., **Shollenbarger, S.G**., Wieser, J., Strong, J., Lisdahl, K. (2013, November). The Effects of BMI and *BDNF* genotype on prefrontal cortex morphology. Poster Presented at The Society for Neuroscience Conference, San Diego, CA.

Price, J.S., McQueeny, T., **Shollenbarger, S.G**., Browning, E.L., Wieser, J., & Lisdahl, K.M. (June, 2014). Prefrontal and parietal volumes and cognition in emerging adult marijuana users. Poster presented at The College on Problems of Drug Dependence Conference, San Juan, Puerto Rico.

Shollenbarger, S.G., Maple, K., Lisdahl, K. (2015, February). Impact of sleep on prefrontal gyrification in cannabis using emerging adults. Poster to be presented at The International Neuropsychological Society Conference, Denver, Colorado.

Maple, K., **Shollenbarger. S.G.**, Gilbart, E. R., Lisdahl, K. M. (2015, June). Sleep quality does not predict frontolimbic white matter integrity in young marijuana users. Poster to be presented at The College on Problems of Drug Dependence Conference, Phoenix, Arizona.

Shollenbarger, S.G., Maple, K., Lisdahl, K. (2015, June). The relationship between prefrontal gyrification and underlying white matter integrity in young cannabis users. Poster presented at The College on Problems of Drug Dependence Conference, Phoenix, Arizona.

TEACHING EXPERIENCE

Invited Lectures

2014	**Topic: Neuroanatomy and Temporal Lobe Epilepsy,** Neuropsychology, Fall Semester, University of Wisconsin-Milwaukee
2009	**Topic: Diversity Issues,** Diversity (graduate students), Spring Quarter, University of Cincinnati
2008	**Topic: Diversity Issues,** Diversity (graduate students), Spring Quarter, University of Cincinnati
2007	**Topic: Diversity Issues,** Abnormal Psychology, Spring Quarter, University of Cincinnati
2006	**Topic: Diversity Issues,** Human Sexuality, Fall Quarter, University of Cincinnati

Teaching Assistantships

2010	**Undergraduate Teaching Assistant**, Research Methods in Personality, Fall Quarter, University of Cincinnati
2010	**Undergraduate Teaching Assistant,** Introduction to Psychology 102,

Summer Quarter, University of Cincinnati

2010 **Undergraduate Teaching Assistant,** Clinical Interventions, Spring Quarter, University of Cincinnati

2010 **Undergraduate Teaching Assistant,** Introduction to Psychology 102, Winter Quarter, University of Cincinnati

2009 **Undergraduate Teaching Assistant**, Research Methods in Personality, Fall Quarter, University of Cincinnati

2007 **Undergraduate Teaching Assistant**, Abnormal Psychology**,** Spring Quarter**,** University of Cincinnati

SPECIALIZED TRAINING

2015-2016 **Neuroimaging Journal Club, The University of Wisconsin-Milwaukee.** Participated in bimonthly journal club covering topics related advancements in neuroimaging analysis, conducting/designing neuroimaging studies, and imaging data interpretation.

2015 **Kognito Support: Veterans on Campus Virtual Workshop, The University of Wisconsin-Milwaukee.** Completed interactive online training in the unique needs of student Veterans, military culture, Veteran resources and support available on campus.

2015 **Parallel Computing Workshop, The University of Wisconsin-Milwaukee.** Attended a 2-day workshop on basic Unix commands, programing scripts for research needs, transmitting and computing research processes on super computing clusters.

2015 **Neurocognitive Networking: Modern Neuroimaging Methods for Understanding Neurocognition -International Neuropsychology Society, Denver, CO.** Attended a 3-hour CE workshop on techniques for investigating neurocognitive networks, neuroimaging meta-analytic approaches, and introduction to current neuroimaging databases. Presenters Angela R. Laird, Ph.D. & Jennifer Robinson, Ph. D.

2012 **Campus Connect Training Course: Suicide Prevention, The University of Wisconsin-Milwaukee.** Attended 2.5-hour interactive workshop on crisis response, supportive conversations, and suicide prevention.

2011 **FreeSurfer Training Workshop: Anatomical software 3-Day Intensive**, Boston, MA. Attended a 3-day workshop on FreeSurfer software. FreeSurfer is a set of tools for analysis and visualization of structural and functional brain imaging data. FreeSurfer contains a fully automatic structural imaging stream for processing cross sectional and longitudinal data. Presented by Freesurfer staff and guest lecturers.

2010 **MI Training Today: Motivational Interviewing 2-Day Intensive,** Nashville, TN. Attended a 2-day workshop on Motivational Interviewing (MI). The training consisted of developing basic MI knowledge, such as concept and skill building, engaging clients, handling resistance and evoking change talk. Presented by Katie Slack, MSW.

TECHNICAL SKILLS

Basic Unix Computer Language Knowledge
Basic FreeSurfer skills: Preprocessing structural and functional MRI data, Quality Assessment and Manual Editing
Multisite Data integration
Basic AFNI skills: brain alignment (talariaching)
Biological samples collection:
Clinical assessment web-site designing experience
Proficient SPSS, Excel, Word, PowerPoint
CPR/AED certified (2011-Present)

COMMUNITY OUTREACH

Interview, Wisconsin High School *Effects of Cannabis on Developing Brain*
Volunteer for Human Rights Campaign (HRC)
Student Volunteer University of Cincinnati's Safe Zone Training
Volunteer for STOP AIDS

SERVICE & MEMBERSHIPS

2012-2016 **President - UWM Health Psychology Graduate Student Club**
Responsible for attending bi-yearly grant training workshop, organizing conference travel grants, and community visibility.