Summary Page

Title: Effects of Marijuana on Symptoms of Obsessive-Compulsive Disorder

Protocol #: NCT03274440

Document Date: 5/10/2018

Documents Included:

1. Study Protocol
2. Consent Form
3. Data Analytic Plan

Protocol Title:
Effects of Marijuana on Symptoms of Obsessive-Compulsive Disorder

Version Date:
05/10/2018

Protocol Number:
7405

First Approval:
06/08/2017

Clinic:
Anxiety Disorders Clinic

Expiration Date:
05/14/2019

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Faculty Sponsor:
Helen Simpson, MD

Cover Sheet

Choose ONE option from the following that is applicable to your study
If you are creating a new protocol, select "I am submitting a new protocol." As 5 Year Renewals are no longer required, this option remains for historical purposes.
I am submitting an annual continuation with modifications

Division & Personnel

Division

What Division/Department does the PI belong to?
Clinical Therapeutics
Within the division/department, what Center or group are you affiliated with, if any?
Anxiety Disorders Clinic

Unaffiliated Personnel

List investigators, if any, who will be participating in this protocol but are not affiliated with New York State Psychiatric Institute or Columbia University. Provide: Full Name, Degrees and Affiliation.

N/A

Amendment

Describe the change(s) being made
1. Added studies that participants may be recruited from.
2. Removed inclusion criteria #7
3. We will not be providing breakfast to participants.
4. We will pay participants after each session they complete instead of at study end.
5. This study is not covered by a certificate of confidentiality.
Provide the rationale for the change(s)

1. To include all current studies in our clinic.
2. Since participants will be able to perform study criteria if they meet all other criteria, practice sessions are not necessary.
3. We will not be providing breakfast to participants since sessions may take place at any time of the day. Instead, they will be asked to maintain their regular meal times and will be given a snack halfway through the session.
4. To reduce burden on participants who are not able to complete all 3 sessions.
5. Due to changes in NIH policy.

Comment on the extent to which the proposed change(s) alter or affect risks/benefits to subjects
The proposed changes do not alter risks/benefits to participation.
Comment on if the proposed change(s) require a modification to the Consent Form (CF)
The changes require minor modifications to the CF, which have been made.

Application for Continuation of Research

Status

Current Status of Study:
Subject enrollment is ongoing.

Summary of Experiences to Date

Please provide a summary of scientific progress of the study and the experience of research participants, to date. This requirement is designed to allow for the investigator and the IRB to reassess the study's risks and benefits in terms of developments in the field, changing practice patterns, and new IRB policies and procedures.
Five subjects have enrolled the study of which one is currently enrolled and two have completed without complications. Two subjects decided to discontinue study involvement due to changes in employment that made them unable to commit the time necessary to complete the study.

Funding

Have there been any changes in funding status since the prior approval?
No
Have the principal investigator and other investigators made all required disclosures of financial interest in the study sponsor/product?
Yes

Summary

Have there been any study findings, recent literature, or untoward events occuring here or at other sites in the past year which might affect the analysis of the safety, risks or benefits of study participation?
No
Have there been any serious adverse events (serious and/or unanticipated problems involving risks to subjects or others at this site which occured in the past year)?
No
Have all study staff with a significant role in the design or implementation of the human subject components of this study received required training in human research subject protections?
Yes
Is the study covered by a certificate of confidentiality?
No

Overall Progress

Approved sample size
20
Total number of participants enrolled to date
5
Number of participants who have completed the study to date
2
Have there been any significant deviations from the anticipated study recruitment, retention or completion estimates?
No
Comments / additional information

Sample Demographics

Specify population
Adults with Obsessive-Compulsive Disorder
Total number of participants enrolled from this population to date
4
Gender, Racial and Ethnic Breakdown
2 Female, 3 Males. 4 White, 1 Other. 1 Hispanic, 4 Non-Hispanic.

Summary of Current Year's Enrollment and Drop-out

Number of participants who signed consent in the past year
5
Number of participants currently enrolled
1
Did the investigator withdraw participants from the study?
No
Did participants decide to discontinue study involvement?
Yes
Circumstances of discontinuation:
2 participants decided to discontinue study involvement due to changes in employment that made them unable to commit the time necessary to complete the study.

Procedures

To create the protocol summary form, first indicate if this research will include any of the following procedures

- ✓ Psychiatric Assessment
- ✓ Medication Trial
- ✓ Use of Placebo or Sham Treatment
- ✓ Administration of Substance of Abuse
- ✓ Use of Investigational Drug or Device

Population

Indicate which of the following populations will be included in this research

- ✓ Adults
- ✓ Adults over 50
- ✓ Substance Users

Research Support/Funding

Will an existing internal account be used to support the project?
Yes
Describe internal account
This study will be supported by Dr. Blair Simpson's gift account (through Columbia).
Is the project externally funded or is external funding planned?
No

Study Location

Indicate if the research is/will be conducted at any of the following
✓ NYSPI
This protocol describes research conducted by the PI at other facilities/locations
No

Lay Summary of Proposed Research

Lay Summary of Proposed Research
Previous research has suggested that certain areas of the brain are receptive to chemicals like those found in the marijuana plant (cannabinoids), and that these systems may be involved in anxiety disorders and Obsessive Compulsive Disorder (OCD). More recent data shows that synthetic drugs that target these systems may be helpful in conditions like anxiety disorders and Tourette's syndrome, and that they could also be useful for the treatment of OCD symptoms. However, to date there has been little research regarding the role of these compounds in OCD. The purpose of this study is to examine the effects of different cannabinoids on OCD symptoms in humans. In order to accomplish this in a laboratory setting, patients with OCD who are also occasional marijuana smokers will receive different combinations of two of the most well-studied cannabinoids, tetrahydrocannabinol (THC, the active ingredient in marijuana) and cannabidiol (CBD, another component of the marijuana plant). We will then measure whether or not they respond to these agents (i.e. experience a significant reduction in their OCD symptoms) in the acute setting.

Background, Significance and Rationale

Background, Significance and Rationale

Previous research has suggested that the endocannabinoid system may serve a regulatory function in frontal-striatal brain circuits which have been implicated in anxiety disorders and Obsessive Compulsive Disorder (OCD) (Lutz et al. 2015, Gremel et al. 2016). In addition, there is an emerging body of evidence which demonstrates a potential role for drugs that target cannabinoid receptors in the treatment of anxiety disorders and Tourette's syndrome (Curtis et al. 2009, Müller-Vahl et al. 2013, Blessing et al. 2015). Data from animal studies (Deiana et al. 2011, Nardo et al. 2013, Breuer et al. 2016) suggest a potential benefit to these compounds in OCD as well. However, to date studies in humans are limited to case reports (Schindler et al. 2008). The purpose of this double-blind, placebo-controlled, within-subject study is to examine the effects of different cannabinoids, delivered in a laboratory setting, on adults with primary OCD. In order to accomplish this, adults with OCD who are also occasional marijuana smokers will be recruited for 3 outpatient laboratory sessions over the course of 2-3 weeks. In the laboratory, patients will receive different combinations of the cannabinoids tetrahydrocannabinol (THC, the active ingredient in the marijuana plant) and cannabidiol (CBD, a cannabinoid constituent of marijuana which has demonstrated therapeutic potential across a variety of psychiatric disorders including depression, anxiety, and psychosis [Campos et al. 2012]) or placebo. We will then measure whether or not patients respond to these agents (i.e. experience a significant reduction in their OCD symptoms) in the acute setting.

The need to understand the impact of smoked THC and CBD in clinical populations is supported by 3 prior studies by Valerie Curran's group at University College London. In a 2008 study, hair samples collected from a population of 140 users of a variety of illicit substances were screened for THC and CBD. Subjects who screened positive for THC alone showed higher levels of positive schizophrenia-like symptoms compared to both those who screened negative for cannabinoids and those who screened positive for THC and CBD, suggesting that smoked CBD may have antipsychotic properties. A second study in 2010 in which subjects were assessed after using their chosen strain of cannabis indicated that smokers of high CBD:THC strains showed a decreased attentional bias towards drug and food stimuli and less self-reported liking of cannabis stimuli. These data suggest that CBD may mitigate the effects of THC and may have utility as a treatment for cannabis dependence. Finally, in a 2014 study of 48 cannabis-using subjects who received inhaled THC, CBD, THC+CBD, and placebo, subjects showed improved recognition of facial affect without any effect on feelings of being "stoned" after receiving CBD alone. In contrast, THC produced a reduction in facial affect recognition, while THC+CBD and placebo showed no effect. Both THC alone and THC+CBD in combination increased feelings of being "stoned" relative to placebo. The results of this laboratory study provide early evidence that agents that target the endocannabinoid system may produce contrasting neurocognitive effects. In total, the findings from these studies suggest that further study of the impact of THC and CBD in psychiatrically ill populations (including OCD) is warranted.

Specific Aims and Hypotheses

Specific Aims and Hypotheses
Specific Aims:
To compare the effects of High THC (5-10%)/Low CBD (<1%) marijuana, Low THC (<1%)/High CBD (>10%) marijuana, and placebo (0% THC and CBD) marijuana in adults with primary OCD who also occasionally smoke marijuana.

Specific Hypothesis:
In the acute setting, smoked marijuana in both high THC/low CBD and low THC/high CBD concentrations will lead to a reduction in symptoms in adults with primary OCD who are also occasional marijuana smokers as compared to placebo.

Description of Subject Population

Sample #1

Specify subject population
Adults who meet DSM 5 criteria for OCD who are also occasional marijuana smokers
Number of completers required to accomplish study aims
15
Projected number of subjects who will be enrolled to obtain required number of completers
20

Age range of subject population
21 - 55

Gender, Racial and Ethnic Breakdown
Based on the community from which we will be drawing patients and proportions to those encountered during previous clinical trials at this site, we expect the sample to be approximately 5 percent Hispanic and 95 percent Non-Hispanic. Racially, we expect there will be 89 percent White, 9 percent Black, 2 percent Asian. Based upon the prevalence of OCD, it is expected that the sample will be approximately 1 to 1 = male to female.
Description of subject population
The sample will consist of a maximum of 15 female and male adults with a diagnosis of OCD and clinically significant symptoms (i.e., a Y-BOCS score of at least 16) who are also occasional marijuana smokers. Subjects may or may not be seeking treatment for their OCD but will not be seeking treatment for their marijuana use. ~~Minorities and females will be well represented in this study.~~

Recruitment Procedures

Describe settings where recruitment will occur

Recruitment will draw from the broadest possible population with respect to gender and ethnic origin. IRB-approved radio/internet/newspaper advertisements and flyers will be used to recruit subjects (materials to be submitted).

We will also use various internet sites (e.g., Twitter, Google advertising, Craigslist, Facebook, Linkedln, Research Match, Bangitout.com, Clinicaltrials.gov, twitter, Psychology Today, Craigslist, and other similar sites) as additional recruitment tools.

We will also use RecruitMe for recruitment. RecruitMe is a recruitment website launched by the Clinical Trials Office at Columbia University Medical Center and is meant to connect those that want to participate in research studies to the investigators that conduct them. To begin using RecruitMe, the volunteer will search for a medical condition or research field of the user's interest and answer a few eligibility questions. If the volunteer pre-qualifies for a study, he or she may either reach out directly to the research team or if he/she leaves their contact information a member of that research team will reach out to them. RecruitMe also allows users to join a research registry which will notify users via email whenever a study or clinical trial of interest enters the database. Investigators that join RecruitMe will have the ability to create a profile and submit their study for review. Upon approval from members of the Clinical Trials Office, their study will be visible to users that visit RecruitMe.

How and by whom will subjects be approached and/or recruited?
Potential participants who respond to our advertisements will be screened under IRB protocol #6112R (Anxiety Disorders Clinic and Hispanic Treatment Program Screening and Evaluation Process). Once deemed eligible, they will be enrolled through the Anxiety Disorders Clinic, located on the third floor of the New York State Psychiatric Institute.
How will the study be advertised/publicized?

IRB-approved radio/internet/newspaper advertisements and flyers will be used to recruit subjects (materials to be submitted)
Do you have ads/recruitment material requiring review at this time?
Yes
Does this study involve a clinical trial?
Yes
Please provide the NCT Registration Number
NCT03274440

Concurrent Research Studies

Will subjects in this study participate in or be recruited from other studies?
Yes
Describe concurrent research involvement

This study does not provide evidence-based treatment for OCD. Participants will be allowed to participate in other studies at our center at the same time if these studies do not involve treatment (e.g. IRB#7127, Toward Precision Medicine for OCD). Before and after finishing the study, participants will be allowed to participate in other treatment and nontreatment studies at our center if they meet the eligibility criteria for those studies (including time off medication prior to entry).

Subjects may be receiving either psychotherapy or medication management in the community while they participate in this study; however, they will not be eligible for participation in this study if they a) are taking a selective SRI or clomipramine and have altered their dose in the 6 weeks prior to study enrollment or are planning to make changes to their medications during the period of the study (approximately 3 weeks), b) are taking psychotropic medications other than selective SRIs or clomipramine, or c) have begun cognitive-behavioral therapy within 8 weeks prior to enrollment or plan to commence cognitive-behavioral therapy during the period of the study (approximately 3 weeks). For subjects who are not currently receiving any treatment for OCD and are interested, referrals for external treatment providers will be given."

Eligible subjects who have finished other studies in the Anxiety Disorders Clinic will be offered participation if they are eligible. These protocols will include:

IRB#6628 Attaining and maintaining wellness in OCD
IRB#7000 Control and Reward Circuits in OCD
IRB#7127 Toward Precision Medicine for OCD
IRB#7059 Pilot study of personalized-computerized inhibitory control training for OCD
IRB#6837 Internet Based Treatment for OCD (iCBT)
IRB#7239 Cannabinoid Medication for Adults with OCD
IRB#7572 Feasibility, Acceptability and Preliminary Efficacy of a Mobile App (nOCD) for OCD

Inclusion/Exclusion Criteria

Name the subject group/sub sample
Adults with OCD
Create or insert table to describe the inclusion criteria and methods to ascertain them

1. Patient must be 21-55 years of age at the time of consent	Clinical interview
2. Patient must be physically healthy male or non-pregnant female. Females of childbearing potential must comply with contraceptive restrictions noted in the protocol.	Clinical interview by trained M.D. or Ph.D., physical examination by M.D., ECG, and blood tests
3. Patients must fulfill DSM 5 criteria for OCD, OCD being the principal disorder (i.e., currently the most severe and needing of treatment), and have had OCD for at least one year with near-constant symptoms.	Clinical Interview by trained M.D. or Ph.D. and results of SCID
4. Patients with a Y-BOCS score of greater than or equal to 16 prior to entering trial.	Clinical interview and assessment by trained rater
5. Patient has smoked marijuana at least once in the past and did not experience intolerable side effects.	Clinical Interview
6. Patient has not smoked marijuana more than once per day over the preceding 8 weeks.	Clinical Interview and urine toxicology
8. Each patient must have a level of understanding sufficient to provide written informed consent to all required study tests and procedures.	Clinical interview
9. Women who are practicing an effective form of birth control (e.g. hormonal contraception or barrier methods).	Clinical interview

Create or insert table to describe the exclusion criteria and methods to ascertain them

1. First degree relative with schizophrenia	Psychiatric evaluation
2. Presence of psychotic symptoms or lifetime history of schizophrenia, bipolar disorder, substance-induced psychotic disorder, or psychosis due to a general medical condition.	Psychiatric evaluation/SCID
3. Current, eating disorder	Psychiatric

	evaluation
4. Major Depressive Disorder or other current psychopathology requiring medical intervention	Psychiatric evaluation
5. Severely depressed patients with HDRS (Hamilton Depression Rating Scale) score greater than 25 or judged clinically to be at risk of suicide	Psychiatric evaluation/SCID and HDRS
6. Female patients who are either pregnant or nursing	Clinical interview, medical examination, and blood pregnancy test
7. Patients planning to commence cognitive-behavioral therapy during the period of the study or those who have begun cognitive-behavioral therapy within 8 weeks prior to enrollment	Clinical interview
8. Patients receiving psychotropic medication other than clomipramine or selective SRIs. Patients taking clomipramine or a selective SRI must be on a stable dose for 6 weeks prior to study entry and must not plan to alter their regimen during the period of the study.	Clinical interview
9. Patients who report using any illicit substances other than marijuana within 3 months prior to study entry or who have a urine toxicology screen positive for any substance other than marijuana.	Clinical interview
10. Presence of significant medical illness (e.g. diabetes, cardiovascular disease, hypertension, clinically significant laboratory abnormalities, LFTs>1.5x upper limit of normal), resting blood pressure >140/90	Medical history, physical examination, laboratory tests, 12-lead ECG, Mantoux test
11. History of heart disease	Clinical interview, abnormal ECG
12. Current parole or probation	Self-report during interview
13. History of violence	Self-report during interview
14. Patient is seeking treatment for marijuana use	Self-report during interview
15. Request for drug treatment	Self-report during interview

Waiver of Consent/Authorization

Indicate if you are requesting any of the following consent waivers
Waiver of consent for use of records that include protected health information (a HIPAA waiver of Authorization)
No
Waiver or alteration of consent
No
Waiver of documentation of consent
No
Waiver of parental consent
No

Consent Procedures

Is eligibility screening for this study conducted under a different IRB protocol?
Yes
Indicate NYSPI IRB #
6112R
Describe Study Consent Procedures
1) Initial telephone screening interviews will be carried out through the Anxiety Disorders Clinic and Hispanic Treatment Program Screening and Evaluation Process (IRB #6112R). After initial determination of eligibility, volunteers will come into the laboratory for their first screening visit. They will be asked to sign our screening and evaluation consent form, allowing us to collect questionnaire data, conduct interviews, and obtain medical information. Patients will receive a physical exam, routine blood work, urinalysis, EKG, pregnancy test, and urine drug screen at this time. Participants will be told that they will be taking part in a study investigating the effects of smoked marijuana on OCD symptoms.

2) A study clinician will conduct interviews regarding OCD symptoms and drug use, and will provide a detailed explanation of the procedures outlined in the consent form.

3) Medical and psychiatric interviews will be conducted by one of the study physicians (Drs. Kayser, Simpson, Campeas, Sanchez-LaCay), and will include a physical examination and review of all medical results and study inclusion/exclusion criteria. Volunteers who pass this screening will have the study described to them again by the study physician. Based on the results of clinical interviews, physicians will confirm whether volunteers have major current psychopathology (e.g. major depressive disorder, bipolar disorder, schizophrenia, suicide risk) requiring medical intervention. The physician will discuss this protocol with the volunteer and document their consent to the research study. The physician and volunteer will then sign the study consent form.

4) Study procedures will begin after the study physician verifies that the participant meets inclusion/exclusion criteria, understands the medical risks of participation, and is capable of providing informed consent. Dr. Simpson, the senior study physician, will settle any disagreements among the study team as to a volunteer's eligibility, and will make the final decision as to study participation.

Indicate which of the following are employed as a part of screening or main study consent procedures
✓ Consent Form

Persons designated to discuss and document consent

Select the names of persons designated to obtain consent/assent
Campeas, Raphael, MD
Haney, Margaret, PHD
Kayser, Reilly, MD
Sanchez-Lacay, jose, MD
Type in the name(s) not found in the above list

Study Procedures

Describe the procedures required for this study
Screening Interviews:
1) All screening interviews (both initial telephone screening and subsequent in-depth in-person screening) will be carried out through the Anxiety Disorders Clinic and Hispanic Treatment Program Screening and Evaluation Process (IRB #6112R). After initial determination of eligibility via telephone screening, volunteers will come into the laboratory for their first screening visit. They will be asked to sign our screening and evaluation consent form, allowing us to collect questionnaire data, conduct interviews, and obtain medical information. Patients will receive a physical exam, routine blood work, urinalysis, EKG, pregnancy test, and urine drug screen at this time. Participants will be invited to participate in a study investigating the effects of smoked marijuana on OCD symptoms.

2) A study clinician will conduct interviews regarding OCD symptoms and drug use, and will provide a detailed explanation of the procedures outlined in the consent form.

3) Medical and psychiatric interviews will be conducted by one of the study physicians (Drs. Kayser, Simpson, Campeas, Sanchez-LaCay), and will include a physical examination and review of all medical results and study inclusion/exclusion criteria. Volunteers who pass this screening will have the study described to them again by the study physician. Based on the results of clinical interviews, physicians will confirm whether volunteers have major current psychopathology (e.g. major depressive disorder, bipolar disorder, schizophrenia, suicide risk) requiring medical intervention. The physician will discuss this

protocol with the volunteer and document their consent to the research study. The physician and volunteer will then sign the study consent form.

4) Study procedures will begin after the study physician verifies that the participant meets inclusion/exclusion criteria, understands the medical risks of participation, and is capable of providing informed consent. Dr. Simpson, the senior study physician, will settle any disagreements among the study team as to a volunteer's eligibility, and will make the final decision as to study participation. Behavioral observations and testing will be carried out by one of the study clinicians. In the event of an emergency, one of the study physicians will be available by phone. Dr. Haney and other psychologists, nurses, and physicians are around the corner or down a corridor from the outpatient laboratory. We do not test research participants unless we are sure that a physician is available by telephone or by pager in the event of an emergency. A set of emergency procedures, including a list of physicians, telephone and pager numbers is posted in the outpatient laboratory.

Medication: Patients will be administered smoked marijuana at one of the following concentrations: High THC (5-10%)/Low CBD (<1%), Low THC (<1%)/High CBD (>10%), or placebo (0% THC and CBD). The order in which they receive each concentration will be randomized. Participants will complete 1 or 2 sessions per week depending on timing and subject availability. Because of cannabidiol's long terminal half-life (21-33 hours), we are allowing time for drug clearance in between sessions (at least 3 days) to avoid potential carryover effects (Consroe et al., 1991).

General Design: There will be three 4-hour laboratory sessions, which will occur between 0900 and 1300 hr, testing the effect of smoked marijuana on OCD symptoms. Sessions will occur once or twice per week over a period of approximately 3 weeks depending on each participant's availability.

Laboratory Sessions: Participants will be instructed that they should not smoke either marijuana or cigarettes on the morning of a session (beginning at midnight). We will do a carbon monoxide (CO) test upon their arrival in the laboratory to verify nothing was recently smoked. Participants will also be given a breathalyzer test to ensure that they did not drink alcohol prior to arrival. At each visit, urine samples will be tested for drug use, and, for women of child-bearing age, for pregnancy. Subjects who are found to be pregnant will be discontinued from the study, but will receive payment for those procedures that they have already completed. Participants with high COs or those testing positive for drugs other than marijuana will be re-scheduled and possibly excluded from further participation. Patients will then receive either high THC (5-10%)/low CBD (<1%) marijuana, low THC (<1%)/high CBD (>10%) marijuana, or placebo (0% THC and CBD). The marijuana used in the study will be provided by the NIDA. We will guide participants through smoking individual puffs of marijuana using cue-dosing procedures until 50% of the cigarette has been smoked. Specifically, for each puff, participants will be instructed to inhale for 5 seconds and hold each puff in the lungs for 10 seconds. There will be approximately a 40-second interval between each puff. For the first hour after marijuana administration, clinical ratings, scales, and BP/HR will be obtained every 20 minutes. During the second hour, these measures will be repeated once every half-hour, and then again at the conclusion of the third hour (see Table 1). The session will end after the third hour. Participants will be allowed to leave the facility when they pass the field sobriety test, and will be instructed not to drive a car or use other drugs or alcohol for at least 8 hours after marijuana administration.

Table 1. Session Schedule

TIME (min)	EVENT
-50	CO, collect urine, breathalyzer, start breakfast
-30	Finish breakfast (set timer for 30 min), balance, TLFB, BP/HR, VAS, YBOCCS, STAI
0	Marijuana administration
20	BP/HR, VAS, YBOCCS, MRF, STAI
40	BP/HR, VAS, YBOCCS, MRF, STAI
60	BP/HR, VAS, YBOCCS, MRF, STAI
90	BP/HR, VAS, YBOCCS, MRF, STAI
120	BP/HR, VAS, YBOCCS, MRF, STAI
180	BP/HR, VAS, YBOCCS, MRF, STAI, Field Sobriety Test, participant discharge

** BP/HR = blood pressure and heart rate; VAS = Visual Analogue Scale; YBOCCS = Yale-Brown Obsessive-Compulsive Challenge Scale; MRF = Marijuana Rating Form; STAI = State/Trait Anxiety Inventory; TLFB = Marijuana Timeline Followback

Patients will be required to take public transportation to and from the laboratory each session, for which they will be reimbursed. Study clinicians will conduct the Field Sobriety Test. After confirming that the participant has passed the Field Sobriety Test, the patient will be allowed to leave the laboratory. If a participant is still impaired at the end of the session, she or he will be asked to remain in the laboratory until the effects wear off, and will be paid extra (i.e. $10 per hour for any additional time in the laboratory). In the event that the impairment does not resolve in a timely manner, a study physician will determine whether the person can leave the laboratory or if further action is needed. It is worth noting that in our experience, it is exceedingly rare (<1% of all participants) for marijuana smokers to remain intoxicated several hours after smoking marijuana in the laboratory.

Laboratory Facility: Experimental sessions will be conducted in the Substance Use Research Center (SURC) located on the 3rd floor of the NYS Psychiatric Institute.

Safety Measures: Vital signs (heart rate and blood pressure) will be monitored in each session. If SBP > 180 mmHg, DP > 110 mmHg, or HR > 120 bpm, these measures will be taken 2 additional times at 2 min intervals: A physician will see the participant immediately if blood pressure or heart rate remain above these levels for 3 continuous readings.

Data Analysis: A between and within-subject repeated measures analysis of variance (ANOVA) with planned comparisons will be implemented to determine the effects of marijuana on OCD symptoms

You can upload charts or diagrams if any

Criteria for Early Discontinuation

Criteria for Early Discontinuation

Participants are free to withdraw from the study at any time for any reason. Study doctors are to discontinue patients from the study if patients:

• Request an early discontinuation or withdraw consent.
• Experience a serious or intolerable adverse event that prevents the patient from continuing.
• In the Investigator's opinion, are experiencing a clinically significant deterioration in OCD (i.e., 4-5 point change on the visual analogue scale for obsessions or compulsions and YBOCS score 10 points greater than their baseline at any time point).
• Commit a protocol violation, including lack of compliance.
• Are "lost to follow-up".
• Encounter other conditions (such as administrative issues or pregnancy).
If a patient discontinues from the study at any time at their own request or at the study doctor's discretion, the reason(s) for discontinuation are to be recorded by the study.

Blood and other Biological Samples

Please create or insert a table describing the proposed collection of blood or other biological specimens
We will perform urine pregnancy tests and urine drug screens prior to each laboratory session.

Assessment Instruments

Create a table or give a brief description of the instruments that will be used for assessment
1. Telephone Interview (10 minutes)
2. General Health Questionnaire (5 minutes)
3. Drug History Interview (30 minutes)
4. Drug History Questionnaire (10 minutes)
5. Medical History Questionnaire (10 minutes)
6. Psychiatric and Physical Examination (60 minutes)
7. Yale-Brown Obsessive Compulsive Scale (Y-BOCS, 15 minutes)
8. Structured Clinical Interview for DSM 5 (SCID, 1-2 hours)
9. 17 Item Hamilton Depression Rating Scale (HDRS-17, 5 minutes)
10. 14 Item Hamilton Anxiety Rating Scale (HARS-14, 5 minutes)
11. Marijuana Timeline Followback (TLFB, 3 minutes)
12. Yale-Brown Obsessive Compulsive Challenge Scale (YBOCCS, 1-2 minutes)
13. State Anxiety Questionnaire (STAI, 3 minutes)
14. Visual Analog Scale (VAS) (2 minutes): Modified from the OCD visual analog scale (Rodriguez et al. 2013) and Mood scale (Bedi et al. 2013) used in previous studies, this is a visual analog scale used to assess both subjective drug effects (physical symptoms, mood, anxiety) and OCD symptoms

15. Marijuana (Cannabis) Rating Form (MRF, 2 minutes): participants rate the strength, liking, desire to take again, good drug effect and bad drug effect of smoked marijuana
16. Qualitative Urinalysis (2 minutes)
17. Heart Rate and Blood Pressure (1 minute)
Please attach copies, unless standard instruments are used

Off label and investigational use of drugs/devices

Choose from the following that will be applicable to your study
✓ Drug
Select the number of drugs used in this study
1

Drug #1

Name of the drug
Marijuana
Manufacturer and other information
1. Generic or chemical name: Marijuana
2. Other name: pot, weed
3. U.S. Government-supplied: IND #131,990 to Margaret Haney, Ph.D.

IND is for marijuana containing a range of concentrations of THC/cannabidiol.

Approval Status
IND is approved
IND#
131,990
Who holds the IND/IND sponsor?
IND is held by PI/CU Investigator
Haney, Margaret, PHD

Research Related Delay to Treatment

Will research procedures result in a delay to treatment?
No
Treatment to be provided at the end of the study
There is no treatment offered at the end of the study. For subjects who are interested, referrals for external treatment providers will be given. We remain in contact with all participants who are interested in external treatment until they have successfully been referred.

Clinical Treatment Alternatives

Clinical treatment alternatives
Subjects do not have to participate in a study to receive treatment for OCD. There are two evidence-based first-line treatments for OCD. The first is a class of medications called Serotonin Reuptake Inhibitors (SRIs). The second is a form of therapy called Cognitive Behavior Therapy (CBT). Subjects will have these treatment options explained to them by the study doctor, and they will be offered the option to receive referrals for one or both of these treatments rather than participating in the study. Subjects who are interested in drug treatment will be provided with referrals for external treatment providers as well.

Risks/Discomforts/Inconveniences

Risks that could be encountered during the study period

Marijuana: One risk of study participation is marijuana intoxication, primarily increased appetite, sleepiness, concentration difficulties, faintness, restlessness, confusion, lightheadedness, loss of coordination, clumsiness, shakiness, dizziness, stomach upset, headache, paleness, flushing, sweating, dry mouth, slurred speech, fatigue, itching, heart pounding, and changes in the pattern of heart beats.

There are also possible side effects following CBD administration. The medication has few psychoactive effects (e.g., Leweke et al., 2000; Fusar-Poli et al., 2009), although there is a report of decreased anxiety and increased sedation (400 mg; Crippa et al., 2004). One placebo-controlled study administered CBD (approximately 700 mg/day) to patients with Huntington's disease for 6 weeks and reported no significant adverse effect from the medication relative to placebo (Consroe et al., 1991). CBD doses up to 1500 mg/day have been given for several weeks to schizophrenic patients with no side effects reported (Zuardi et al., 1995, 2006).

Describe procedures for minimizing risks
All participants are fully informed of these effects, and because all currently smoke marijuana, these effects should be familiar to them.

The risks of marijuana and/or CBD exposure to a developing fetus or newborn are unknown, so women who participate in the study will be required to confirm that they are not pregnant or breastfeeding and are practicing an effective form of contraception (e.g. hormonal contraception or barrier methods) throughout the duration of the study.

In previous studies, participants have not found the study procedures to be stressful or difficult. They are monitored continuously throughout the experimental procedure. Emergency medical equipment is available in our laboratory, which is located in a hospital where a full medical emergency back-up team is constantly available. We anticipate that careful participant selection, dose selection and monitoring will obviate the need for such emergency care.

Methods to Protect Confidentiality

Describe methods to protect confidentiality
Confidentiality will be strictly maintained. Medical charts, standard questionnaires, records, rating scales, and any other recorded information will be kept in a locked file in an office or the record room of the New York State Psychiatric Institute. Confidentiality is further supported by the use of unique ID numbers in coding some records. Data entered into a computer and/or submitted electronically will contain numerical IDs and, in some cases, initials, and will be password-protected. No identifiers (name, address, phone number, etc.) will be used that could allow direct linking of database information to individual participants. Where temporary linking of information with identifiers is necessary, such identifiers will be temporarily attached to the questionnaire, and will immediately be removed after information has been encoded. No identifying information will be used in publications. Only the research team and institutional personnel will have access to such material.
Will the study be conducted under a certificate of confidentiality?
No

Direct Benefits to Subjects

Direct Benefits to Subjects
There are few direct benefits to research volunteers in the proposed study. Prior to study acceptance, all volunteers will have a medical and psychiatric work-up. Referrals will be offered to participants who are interested in treatment for OCD or drug use at any stage of their participation. We repeat our offer for treatment referral at screening and at discharge from the study.

Compensation and/or Reimbursement

Will compensation or reimbursement for expenses be offered to subjects?
Yes
Please describe and indicate total amount and schedule of payment(s).
Include justification for compensation amounts and indicate if there are bonus payments.

Patients will be required to take public transportation to and from the laboratory each session, for which they will be reimbursed. We will pay for mass-transit expenses in cash during each visit in a total of $6.00 per visit (to cover $2.75 subway fare to and from the laboratory). At the end of each laboratory session, study clinicians will conduct the Field Sobriety Test. After confirming that the participant has passed the Field Sobriety Test, the patient will be allowed to leave the laboratory. If a participant is still impaired at the end of the session, she or he will be asked to remain in the laboratory until the effects wear off, and will be paid extra (i.e. $10 per hour for any additional time in the laboratory).

For participating in this study subjects will receive cash for each laboratory session they complete. They will earn $25 for each session, and an additional bonus of $50 if they complete the study. If they withdraw early they will not receive the bonus payment. Session pay will be given in cash at the end **each session.** ~~of~~

~~the third session if all the sessions are completed. If subjects withdraw from the study, they will be given cash for the sessions completed at that time.~~ In total, the pay for study participation will be $125 for completion of all sessions.

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CONSENT FORM

Informed Consent for Participation in Research

Effects of Marijuana on Symptoms of Obsessive-Compulsive Disorder

Purpose and Overview

You are being asked to take part in a research study because you have symptoms of Obsessive Compulsive Disorder (OCD) and these symptoms cause difficulties in your daily activities. Before you choose whether or not to take part, it is important for you to understand why this research is being done, and what it will involve. Please take time to read the following information carefully and ask the study doctor any questions that you may have about this research study.

This research study is designed to examine whether smoked marijuana affects OCD symptoms. Marijuana contains a number of compounds called cannabinoids that are thought to interact with certain regions of the brain that are involved in OCD. The goal of this study is to see how marijuana affects OCD symptoms. It is not designed to provide treatment of your OCD. A total of 20 adults between the ages of 21 and 55 years who have OCD and who are also occasional marijuana smokers will participate in the study. If you are a woman, you will confirm that you are not pregnant and are using an effective form of birth control (for example, condoms or hormonal contraceptives).

Voluntary

Participation in this research study is voluntary. If you decide not to participate, or if you later decide to stop participating, you will not lose any benefits to which you are otherwise entitled. A decision not to participate or withdraw your participation will not affect your current or future treatment at the New York State Psychiatric Institute or Columbia University.

Alternative Treatments/Alternatives to Participation

This is not a treatment study. Information is being collected for research purposes only and to learn more about how marijuana affects OCD symptoms. The study will not provide information that will be medically useful for you. The alternative to participating would be simply not to participate.

You do not have to participate in this study to receive treatment for OCD. Medicines called *Serotonin Reuptake Inhibitors* (SRIs) are available for the treatment of OCD. In addition, there is a form of therapy called *Cognitive Behavior Therapy*, which has been found to be effective in treating OCD. If you decide not to participate in this study, you may choose to be treated with one or more of these therapies (on your own), or not seek further treatment. If you wish, we can provide a list of other doctors, therapists and/or treatment facilities in the community who offer these treatments.

Procedures

Screening: As part of the routine screening done in the Anxiety Disorders Clinic, you have already met with staff of the Anxiety Disorders Clinic to discuss your medical and psychiatric history. You were given an interview and have undergone a complete physical exam, routine bloods, urinalysis, electrocardiogram, pregnancy test (if female), and a urine drug screen sample. If after this screening process, you are eligible to participate in this study and you agree to participate, you will be asked to sign this consent form.

Study Procedures:

The study consists of 3 laboratory sessions, and in each session we will ask you to smoke a marijuana cigarette. The strength of the marijuana you smoke in each session will vary. It will contain different levels of THC, which is the major active ingredient in marijuana, and cannabidiol, another component of the marijuana plant. Neither you nor the research staff will know during the laboratory session which strength of marijuana

you received. We do not tell the strength of the marijuana you will receive in advance, as this knowledge may affect your response.

Laboratory sessions (a total of 3) will be conducted once or twice per week depending on your availability. You will need to arrive at the laboratory in the morning and stay for about 4 hours. You will receive a different strength of marijuana in each session. We will collect data concerning your heart rate and blood pressure, your mood, and your OCD symptoms.

It is important that you do not smoke marijuana the morning before coming in for a session. Thus, if you smoke marijuana the night before a session, you must stop smoking by midnight on the day of the session, so that there will be at least 10 hours between your marijuana use at home and in the laboratory.

We need to confirm that you are free of recent marijuana or alcohol use to ensure the scientific integrity of our study. Therefore, before each session we will ask you to provide a urine sample that may be screened for drug use. You will also have your breath alcohol, carbon monoxide and possibly saliva measured in order to verify that you have not smoked marijuana or had any alcohol shortly before a session, as the presence of these substances may affect your response in the laboratory. If you are a woman, you will also have a urine pregnancy test prior to each session.

You will need to complete the questionnaires at the scheduled times. When you are not filling out questionnaires, you may engage in activities such as reading and homework, as long as these activities do not interfere with the protocol.

At the end of each smoking session, you may or may not still have a drug effect. For your safety, the research staff will evaluate you and decide if you are able to leave. If you are still having a drug effect you may be asked to stay longer until the drug effects wear off; you will be paid at a rate of $10/hour for any extra time. You will not be allowed to drive a car for 8 hours after drug administration so you need to be picked up by a relative or friend, or you will need to take a bus or subway to your destination. We will pay for mass-transit expenses in cash during each visit in a total of $6.00 per visit (to cover $2.75 subway fare to and from the laboratory). Depending on our evaluation of any remaining drug effect, we may also arrange for a taxi to take you to your destination, and we will reimburse you for these expenses when you provide us with a receipt for the taxi fare. These are safety precautions for your benefit. Failure to follow our advice could result in termination from the study.

Risks and Inconveniences

You may experience side effects from the marijuana, which could include: increased appetite, sleepiness, concentration difficulties, faintness, restlessness, confusion, lightheadedness, loss of coordination, clumsiness, shakiness, dizziness, stomach upset, headache, paleness, flushing, sweating, dry mouth, slurred speech, fatigue, itching, heart pounding, and changes in the pattern of heart beats. We will watch you carefully throughout your laboratory sessions to minimize the chance of any serious reactions.

Some of the marijuana that you smoke will contain higher amounts of cannabidiol relative to THC (the active ingredient in marijuana). Like THC, cannabidiol is a natural part of the marijuana plant, and there is little evidence that it has many direct effects, although it is possible that you may feel sleepy. Cannabidiol is not listed as a carcinogen (a substance that causes cancer) by the International Agency for Research on Cancer. However, exposure to THC or cannabidiol may have a harmful effect on a fetus or a newborn, and therefore you will not be allowed to participate in the study if you are pregnant or breastfeeding during the study. You will be asked to confirm that are using an effective form of birth control while you are participating in the study.

Benefits

This study is not designed to benefit you directly, and we do not know whether or not your symptoms of OCD will improve while in this study. The benefits of this research relate primarily to your participation contributing to our understanding the effect of marijuana on symptoms of OCD in adults.

Confidentiality

Your records will be kept in locked files and will be kept confidential. Records will be available to research staff, and to Federal, State and Institutional regulatory personnel (who may review records as part of routine audits). Your name and other personal identifying information will be stored in an electronically secure database at New York State Psychiatric Institute. All data will be stored separately from any identifying information and will be password protected. Information about you may be transferred through the internet, but only a code number and your initials will be used to identify you. In reporting the results of this study, privacy is protected by reporting group results or by using coding systems that do not reveal the identity of individuals when individual results are reported. Your name or address is never reported.

A description of this clinical trial will be available on http://www.ClinicalTrials.gov, as required by U.S. Law. This Web site will not include information that can identify you. At most, the Web site will include a summary of the results. You can search this Web site at any time.

Study Compensation

For participating in this research you will receive cash for each laboratory session you complete. You will earn $25 for each session, and an additional bonus of $50 if you complete the study. If you withdraw early you will not receive the bonus payment. Session pay will be given in cash at the end of each session. If you do not follow the study protocol, you may be removed from the study. In total, the pay for study participation will be $125 for completion of all sessions. You will also be reimbursed for public transportation after each laboratory session.

In Case of Injury

If you believe that you have sustained an injury as a result of participating in a research study, you may contact the Principal Investigator at (646) 774-6369 so that you can review the matter and identify the medical resources that may be available to you.

Please be aware that:

1. The New York State Psychiatric Institute, Columbia University and New York Presbyterian Hospital will furnish that emergency medical care determined to be necessary by the medical staff of this hospital
2. You will be responsible for the cost of such care, either personally or through your medical insurance or other form of medical coverage.
3. No monetary compensation for wages lost as a result of injury will be paid to you by the New York State Psychiatric Institute, Columbia University or by New York Presbyterian Hospital.
4. By signing this consent form, you are not waiving any of your legal rights to seek compensation through the courts.

New York State Psychiatric Institute and Research Foundation for Mental Hygiene do not provide compensation or payment for treatment of research related injuries. However, you should be aware that you do not give up your legal right to seek such compensation through the court by participating in this research.

Questions

For questions or emergencies, Dr. Reilly Kayser is available to answer your questions about the study at any time. Dr. Kayser can be reached during the day at (646) 774-6369. After 5 P.M. you can page the Anxiety Clinic Doctor on Call at (917) 786-6939.

If you have any questions about your rights as a research participant, want to provide feedback, or have a complaint, you may call the NYSPI Institutional Review Board (IRB). (An IRB is a committee that protects the rights of human subjects in research studies). You may call the IRB Main Office at (646) 774-7155 during regular office hours.

Documentation of Consent

Statement of consent

I have discussed the study described above with _____ to my satisfaction. To the best of my knowledge, I am not pregnant. I understand that my participation is voluntary, and that I can withdraw from the study at any time without prejudice. Signing this form does not waive any of my legal rights. I have read the above, and I voluntarily agree to participate in this research study.

Print name: _____

Signed: _____

Date: _____

Statement of Investigator Obtaining Consent

I have discussed the proposed research with this participant including the risks, benefits, and alternatives to participation (including the alternative of not participating in the research). The participant has had an opportunity to ask questions and in my opinion is capable of freely consenting to participate in this research.

Print name: _____

Person Designated to Obtain Consent

Signed: _____

Date: _____

New York State Psychiatric Institute (NYSPI)
Authorization to Use or Disclose Health Information during a Research Study

Protocol Number: 7405 **Principal Investigator:** Reilly Kayser, MD

Name of Study: Effects of Marijuana on Symptoms of Obsessive-Compulsive Disorder

Before researchers can use or share any identifiable health information ("Health Information") about you as part of the above study (the "Research"), the New York State Psychiatric Institute (NYSPI) is required to obtain your authorization. You agree to allow the following individuals and entities to use and disclose Health Information about you as described below:

- New York State Psychiatric Institute (NYSPI), your doctors and other health care providers, if any, and
- The Principal Investigator and his/her staff (together "Researchers"). Researchers may include staff of NYSPI, the New York State Office of Mental Health (OMH), Research Foundation for Mental Hygiene, Inc. (RFMH), and Columbia University (CU), provided such staff is a part of the study, and
- Providers of services for the Research at CU, NYSPI and/or RFMH, such as MRI or PET, or Central Reference Laboratories (NKI), if indicated in the consent form**.**

1. The Health Information that may be used and/or disclosed for this Research includes:

☑ All information collected during the Research as told to you in the Informed Consent Form.
☑ Health Information in your clinical research record which includes the results of physical exams, medical and psychiatric history, laboratory or diagnostic tests, or Health Information relating to a particular condition that is related to the Research.
☐ Additional information may include:

2. **The Health Information listed above may be disclosed to:**

☑ Researchers and their staff at the following organizations involved with this Research:
Anxiety Disorders Clinic, NYSPI

☐ The Sponsor of the Research,

and its agents and contractors (together, "Sponsor"); and
☑ Representatives of regulatory and government agencies, institutional review boards, representatives of the Researchers and their institutions to the level needed to carry out their responsibilities related to the conduct of the research.
☐ Private laboratories and other persons and organizations that analyze your health information in connection with this study

☐ Other (family members or significant others, study buddies, outside agencies etc.) Specify:

3. By giving permission to release your Health Information as described above, you understand that your Health Information may be disclosed to individuals or entities which are not required to comply with the federal and state privacy laws which govern the use and disclosure of personal Health Information by NYSPI. This means that once your Health

Information has been disclosed to a third party which does not have to follow these laws (e.g., a drug company or the Sponsor of the Research), it may no longer be protected under the HIPAA or NYS Mental Hygiene Law requirements but is subject to the terms of the consent form and may be subject to other state or federal privacy laws or regulations.

4. **Please note that:**
   - You do not have to sign this Authorization form, but if you do not, you may not be able to participate in the study or receive study related care. You may change your mind at any time and for any reason. If you do so, you may no longer be allowed to participate in the study. If you withdraw this Authorization the research staff and the Sponsor, if this is sponsored research, may still use or disclose Health Information containing identifying information they already have collected about you as needed to maintain the reliability of the research. Any request to withdraw this Authorization must be made in writing to (enter name and contact information below):

     Reilly Kayser, MD
     New York State Psychiatric Institute
     1051 Riverside Drive, Office 1303A
     New York, NY 10032
   - While the Research is going on, you may not be allowed to review the Health Information in your clinical research record that has been created or collected by NYSPI. When this research has been completed you may be allowed to see this information. If it is needed for your care, your Health Information will be given to you or your Doctor.

5. **This Authorization does not have an end date.**

6. **You will be given a copy of this form after you have signed it.**

I agree to the use and disclosure of Health Information about me as described above:

_____ _____

Signature of Participant/ Legal Representative Date

_____

Printed Name of Participant

_____

Relationship of Legal Representative to Participant (if applicable)

We also ask you or your legal representative to initial the statements below:

☐ **I have received a copy of the NYSPI/OMH Notice of Privacy Practices.**

Data Analytic Plan

Demographics: The distribution of demographic variables and baseline clinical characteristics will be examined and described across the sample in terms of means, SDs, proportions, and 95% confidence intervals.

Cannabis Effects: We will use a random-effects linear mixed model to evaluate changes in each continuous outcome (YBOCCS, OCD-VAS, STAI-S MRF, cardiovascular measures) as a function of condition (THC, CBD, placebo), time point, and their interaction. Mixed-effects modeling accounts for clustering of repeated measures within subjects, allows time to be modeled as a continuously rather than categorically, and has been used in similar acute pharmacological challenge studies (Rodriguez et al. 2013). The model will include participants as a random effect, condition and time as fixed within-subjects factors, the interaction between condition and time, and a random intercept. Given that the interval between sessions increases over the course of each session, we will model time as a continuous variable. We will use contrasts within each mixed-effects linear regression model to estimate differences in outcomes between both active cannabis varietals and placebo at different time points. All statistical tests will be conducted using an alpha level of 0.05, two-tailed.

Other Effects: Though we have no a priori hypotheses about the effects of age, gender, comorbid diagnoses (e.g. MDD), or other factors that might influence our participants' response to cannabis, we will nonetheless explore the possibility of such effects by including these factors as covariates in separate analyses.