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Cover page

Official Title of Study: Impact of Cannabis on Pain and Inflammation Among Patients with Rheumatoid or Psoriatic Arthritis

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BROWN UNIVERSITY
CONSENT FOR RESEARCH PARTICIPATION

Impact of Acute Cannabis Administration on Pain Symptomology and Inflammatory Markers among Patients with Rheumatoid or Psoriatic Arthritis

Project CANMID

Version 3, 11/16/2021

KEY INFORMATION:

You are invited to take part in a Brown University research study. Your participation is voluntary.

- PURPOSE: The study is about determining whether cannabis can reduce pain and inflammation associated with inflammatory rheumatic diseases, such as rheumatoid and psoriatic arthritis.
- PROCEDURES: For all study sessions, you will be asked to avoid drinking alcohol for 24 hours before sessions, and for the experimental sessions to also avoid caffeine and eating for 2 hours before your sessions. You may not use any marijuana outside the study sessions for the duration of your participation. You will be asked to breathe into a tube to test for alcohol and carbon monoxide in your lungs. You will also be asked to provide a urine sample, which will be tested for recent drug use, and if you are able to become pregnant, the urine will also be tested for pregnancy. You will be asked to use a highly effective birth control method during study participation. You will be asked to complete questionnaires and interviews about your medical history, complete computer tasks, have your height and weight measured, and complete a physical exam with our study physician or nurse practitioner. You will have blood drawn and vaporize marijuana as well.
- TIME INVOLVED: The first study session will take 3-4 hours (baseline session) and the other 2 sessions will be 5-6 hours each (experimental sessions) for a total up to 16 hours of participation. The experimental sessions will occur at least two days apart from each other to ensure that no cannabis remains in your system from the previous experimental session.
- COMPENSATION: You will receive compensation for participating in the study. You will receive $300 (if completing all 3 sessions). If eligible, you will receive $50 after completing the baseline session (including physical exam). You will receive $10 cash if found ineligible. After completing each of the experimental sessions, you will receive $100. Lastly, you will receive a $50 bonus after completing the second experimental session.

- RISKS: You may feel uncomfortable responding to questionnaires or tasks, experience discomfort or pain from blood draws, impaired judgment or motor coordination, inhalation of particulate matter during vaporization, and other potential adverse reactions to marijuana.
- BENEFITS: We cannot and do not guarantee or promise that you will receive any benefits from this study. You will have a chance to contribute to a scientific study that may help people in the future.
- ALTERNATIVES TO PARTICIPATION: This is a research study and your participation is completely voluntary.

1. Researcher(s):

Elizabeth Aston, Ph.D., Center for Alcohol and Addiction Studies, Brown University School of Public Health, Box G-S121-5, Providence, RI 02903. Co-investigator: Dr. Anthony M. Reginato, M.D., Brown Medicine Division of Rheumatology, Brown Physicians Patient Center.

2. What is this study about?

You are being asked to take part in a Brown University research study. The researcher will explain the purpose of the project. He or she will explain how the project will be carried out and what you will be expected to do. The researcher will also explain the possible risks and possible benefits of being in the project. Please read the form and ask the researcher any questions you have about any of these things before you decide whether you wish to take part in the study. This process is called informed consent.

We are interested in learning whether vaporizing marijuana may reduce pain and inflammation among individuals with rheumatic diseases. This project is sponsored by the National Institutes of Health.

Biospecimens (i.e., blood) collected from you for this research may be used to develop new tests or devices. Researchers, their organizations, and other entities, including companies, may potentially profit from the use of the data, biospecimens or discoveries from this research. You will not have rights to these discoveries or benefit financially from them.

You are being asked to be in this study because you reported that you: are between the ages of 18 and 65 and are diagnosed with active rheumatoid or psoriatic arthritis.

3. What will I be asked to do?

Participants who complete the online or telephone pre-screening survey (and appear eligible to proceed to the baseline screening and physical exam) will be asked to meet with research staff for a brief, approximately 15-minute Zoom videocall to complete the informed consent and HIPAA Authorization form. We will then schedule your baseline study session.

For all study sessions, you will be asked to avoid drinking alcohol for 24 hours and stop eating or consuming any caffeinated beverages 2 hours before your scheduled appointment on all experimental study days. You may not use any marijuana outside the study sessions for the duration of your participation. During all study sessions, we will ask you to put your cellphone/personal technology device away at certain points to maintain confidentiality and so that the study tasks are not interrupted.

For all study sessions: (a) you will be asked to breathe into a tube that will measure the amount of carbon monoxide in your lungs and this information will be used to confirm that you have avoided all smoking prior to today's session. If the test suggests you have smoked within the past 15 hours, you will not be able to complete the session and will be given one more opportunity to come in for a session without smoking; (b) you will be asked to blow into a machine that will tell us whether you drank any alcohol before coming in. If there is alcohol in your breath, we will have to re-schedule the session; and (c) you will also be asked to give a urine sample, which will be tested for recent drug use. If you are able to become pregnant, the urine will also be tested for pregnancy. If you are pregnant, you will not be able to participate. You will be asked to use a highly effective birth control method during study participation. In the event of a positive urine test for illicit drugs, you may reschedule the session once.

If you are found to be ineligible for the study based on the interview, repeated positive urine drug test, or found to be pregnant, you will be paid $10 for your time and effort.

You will be asked questions about your substance use and medical and psychiatric history. Some of the questions may be of an embarrassing or sensitive nature and may make you uncomfortable. Therefore, you are free not to answer any questions you do not wish to answer.

In order to establish full eligibility and proceed to the baseline session, participants must have a current diagnosis of active rheumatoid arthritis or psoriatic arthritis, as confirmed to us by your healthcare provider or via your medical record in your possession. If you were not directly referred to us by your doctor, we will ask you for your permission so that we can request your physician release this information to us. They would confirm your rheumatoid/psoriatic arthritis diagnosis with us. They may also share bloodwork results or medical test results relevant to your arthritis, if applicable. You may also be able to share this information with us directly via your personal medical record in your possession. All information we obtain in the study is kept confidential, and all study data will not be stored with your name.

Baseline (1st study visit)
In order to confirm your eligibility for the study, you will be asked to complete several brief questionnaires and interviews about your medical, psychiatric, and substance use history. You will complete some tasks on a computer. You will also do some paper and pencil tasks. We will measure your height and weight.

If you still appear eligible after the interview, you will complete a physical exam with our study physician or nurse practitioner (hereafter referred to as the "study physician"). You will have blood samples drawn (~ 4 - 5 tablespoons total) during this session. An electrocardiogram (EKG) will be conducted. An EKG is a non-invasive method of measuring the electrical activity of your heart. We will attach ten electrodes to your chest and limbs using adhesive pads. We may need to shave a portion of hair from your chest and/or limbs in order to achieve sufficient adhesive and reading. There are minimal risks associated with the use of the EKG. There is a small possibility that you may experience some tenderness or reddening of the skin where the electrodes are placed. You may also feel slight irritation from the gel solution. These symptoms commonly dissipate soon afterwards.

We may learn things about your health that require medical attention as part of the research physical exam. If this happens, this information will be provided to you at the time of the physical exam. You may need to meet with a medical professional with expertise to help you learn more about your research results and/or provide necessary treatment. The study team/study will not cover the costs of any follow-up consultations or actions.

Following the physical exam, you will be asked to complete two experimental study sessions. Each experimental session should be completed at least two days apart from the previous experimental session. In order for this project to have scientific value, we will make every effort to contact you with reminders and confirmations of the scheduled experimental sessions. Study staff will contact you via telephone and email for appointment reminders and information; you may also opt in to receive text message appointment reminders if you would like.

Experimental Sessions (2 study visits)
At each experimental session, you will inhale vaporized marijuana. Each session, you will vaporize marijuana of a different strength ("Dose A" and "Dose B") using a specialized device. These two doses vary in their concentrations of delta-9-THC in the low to moderate potency range from session to session. The marijuana will be provided by the National Institute of Drug Abuse. We will have your blood pressure and heart rate monitored before, during, and after vaporization. You will have 3 blood samples drawn (~ 5 - 6 tablespoons total at each session) at each session, before and after vaporization, for analysis of cannabinoid and hormone levels. A trained phlebotomist, nurse, nurse practitioner, or physician will draw the blood samples from a vein/s in your arm each time.

You will be asked to complete behavioral tasks and fill out some brief questionnaires every few minutes. Next, you will complete some of the same computer-based tasks and paper-and-pencil questionnaires that you had previously completed. We will test your blood pressure and heart rate a few times during these sessions. You will remain in the laboratory for at least 3 hours after vaporizing marijuana. You will also be evaluated for signs of impairment and

will complete a field sobriety test. Following evaluation of vital signs and successful completion of the sobriety test, you will be permitted to leave. You may not drive yourself or operate any other form of transportation (e.g., a bike, scooter, skateboard, etc.) but you may use other forms of transportation to get home (e.g., designated driver, taxi, rideshare, bus, etc.). You will be reimbursed for any transportation that requires payment home after the session. Assistance with transport to the laboratory for experimental sessions may be provided as needed.

Certain information such as medications will be re-confirmed the morning of experimental sessions to maintain study eligibility.

Your participation in this study may last up to 16 hours.

4. Will I be paid?

The first session will last 3 - 4 hours including time needed for the physical exam. You will be paid $50 for the first session (including the physical exam). The two experimental sessions will last 5 - 6 hours each. You will be paid $100 for each session. If you complete all study sessions, you will receive a $50 bonus at the second experimental session. The total possible payment you may receive for participating in this study will be $300.

You are free to stop the study at any point during the session. If you choose to stop participating before the experimental sessions are complete, you will receive a prorated payment of $10 for the session in which you terminated early.

5. What are the risks?

There are some possible risks to participating in this study. Some of the questions may be of an embarrassing or sensitive nature and may make you uncomfortable. Therefore, you are free not to answer any questions you do not wish to answer. Some of the tasks you complete may be challenging and may cause stress or frustration. You will be asked to vaporize marijuana. There is a very low risk of inhaling some particulate matter. If this occurs, the vaporizer will be reset. The cannabis being administered is a natural plant product such that it may contain some mold, yeast, or bacteria from the environment. The marijuana that will be vaporized could contain low levels of potential organisms that could result in a serious lung infection for vulnerable patients. Chronic heavy use of cannabis can result in the development of a cannabis use disorder. However, this study involves a one-time administration of a single cannabis dose. Having blood drawn may cause redness, swelling, and bruising or brief bleeding. Other risks from standard blood draw procedures may include pain or discomfort, and fainting. Your judgment and motor coordination may be impaired, which is why you will need to stay with us for 3 hours after marijuana vaporization

Other possible adverse reactions to marijuana include (1) injury due to slips, falls, or physical constraint in response to aggressive behavior; (2) fetal damage; (3) adverse interactions

between marijuana and medications for which marijuana use are contraindicated (e.g., psychotropic drugs, antihistamines); (4) exacerbation of medical problems for which marijuana use is contraindicated; (5) aggravation of pre-existing marijuana problems; (6) breach of confidence and embarrassment due to uninhibited behavior after vaporizing marijuana.

Due to potential adverse effects of marijuana on a fetus, it is important for female participants to use a reliable means of contraception if engaging in sexual intercourse with a man during the course of this study. If you are capable of becoming pregnant and want to participate in this study, you must agree to complete a pregnancy test that we will provide and to use a medically accepted means of birth control. Let us know if you change your mind and decide to become pregnant during the study. You are not eligible to participate in the study if nursing your child, due to the medical risks and/or harms it causes to your child during development.

While participating in the study, you cannot be using medications for which marijuana is contraindicated. You are asked to report all prescription and over-the-counter medications during your participation to guard against interaction with the marijuana that is administered in the study. You cannot have any medical conditions for which you should not use marijuana (e.g., heart conditions, neurological disorders). You are required to report these conditions on the medical history form to ensure your safety in the study. We will monitor your heart rate, blood pressure, and your reactions to marijuana at all times during the experimental sessions. If you experience an unpleasant reaction to marijuana, a licensed psychologist or the study physician will talk to you about your reaction. If you have moderately serious or serious unpleasant physical reactions to marijuana, the study physician will evaluate your need for emergency medical services. This study follows best practices for blood draw procedures. Sterile instruments, disinfecting agents, and non-latex materials will be used.

You are free to stop vaporizing marijuana at any point during the study session. If you choose not to finish the marijuana vaporization, you will not be able to continue in the study, but you will receive compensation for the sessions you did complete and a prorated payment of $10 for the session in which you terminated early.

6. What are the benefits?

We cannot and do not guarantee or promise that you will receive any benefits from this study. You will have a chance to contribute to a scientific study that may help people in the future.

7. How will my information be protected?

Participation in this study and information gathered from the study will be kept confidential. All information obtained from you will be identified only by a code number. A record of your name (with address and telephone number) and your code number will be kept in a separate locked location, available only to the Brown University investigators and employees on this project. Your answers are confidential. To further protect your confidentiality, we will refer to ourselves during all telephone calls as "Brown University" and will not use any other

identifying information. The findings of the study may be published but individual participants will not be identified. We may use or share your research information [including blood samples] for future research studies but it will be de-identified, which means that it will not contain your name or other information that can directly identify you. Future research may be similar to this study or completely different. We will not ask for your additional informed consent for these studies. We may also share your de-identified information and blood samples with other researchers here, and at other institutions in the United States or around the world.

Any reports related to child abuse/neglect or elder abuse will be reported by us to the appropriate authorities. A description of this clinical trial will be available on https://www.clinicaltrials.gov, as required by U.S. Law. This website will not include information that can identify you. At most, the website will include a summary of the results. You can search this website at any time. Because this research involves a substance regulated by the Food and Drug Administration (FDA), the FDA may choose to inspect and copy medical or research records that identify individual research subjects.

We have obtained a Certificate of Confidentiality from the National Institutes of Health, which authorizes us to protect the identity of our research participants from any civil, criminal, administrative, legislative, or other proceedings, whether federal or state and local. We cannot be compelled to reveal the identity of our participants unless 1) you provide us with written authorization to disclose your identity, or 2) such release is required by the Federal Food, Drug, and Cosmetic Act, or 3) the National Institutes of Health requests such information for audit or program evaluation purposes. The certificate does not govern the voluntary disclosure of such information, nor does it represent an endorsement of the research project by the Department of Health and Human Services. Please be aware, however, that the certificate of confidentiality does not protect your identity in the event of your own disclosure of participation in this study. Therefore, it is important that you use your discretion with respect to participation in this study.

Future Contact
We would like to keep your contact information so that we can invite you to participate in other studies. If you agree, we would store your information in a separate, secure file. You would not be enrolled in any studies but may be asked to answer questions to decide if you are interested and eligible for future research projects.

Brown University staff sometimes review studies like this one to make sure they are being done safely and correctly. If a review of this study takes place, your records may be examined. The reviewers will protect your confidentiality.

8. Are there any alternatives to this study?

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This is a research study and your participation is completely voluntary. Your alternatives include not participating in this research study. The decision whether to be in this study is entirely up to you. Participation is voluntary. Also, if you decide now to participate, you will be able to change your mind later and withdraw from the project. There will be no penalty if you decide not to be in the project or withdraw from the project later.

9. What if I want to stop?

You do not have to be in this study if you do not want to be. Even if you decide to be in this study, you can change your mind and stop at any time.

If you refuse to participate in or leave the study, your current or future relationship with Brown University or Lifespan, if applicable, or will not be affected.

10. Who can I talk to if I have questions about this study?

If you have any questions about your participation in this study, you can call the Principal Investigator, Dr. Elizabeth Aston, at (401) 863-6668 or study staff at 401-863-6433. Alternatively, you may email Project-CANMID@brown.edu.

Questions about the study should be directed to Dr. Elizabeth Aston at (401) 863-6668.

11. Who can I talk to if I have questions about my rights as a participant?

If you have questions about your rights as a research participant, you can contact Brown University's Human Research Protection Program at 401-863-3050 or email them at IRB@Brown.edu.

12. Consent to Participate

(Check Yes or No, and sign your initials)

I agree to be re-contacted for future studies: Yes/No _____ (initials)

I agree to have my de-identified blood samples stored for testing for future studies:

Yes/No _____ (initials)

Your signature below shows that you have read and understood the information in this document, and that you agree to volunteer as a research participant for this study.

You will be offered a copy of this form.

Participant's Signature and Date / PRINTED NAME

Research Staff Signature and Date / PRINTED NAME