Official Title: Using Cannabinoids to Enhance Opioid Analgesic Effects in Humans

NCT: 02901275

Informed Consent Date: November 13, 2017

If you are using Epic for this study, fax a copy of the signed consent form to 410-367-7382.

Patient I.D. plate

RESEARCH PARTICIPANT INFORMED CONSENT AND PRIVACY AUTHORIZATION FORM

Protocol Title: **Enhancing Medication-based Analgesia in Humans**

Application No.: **IRB00097937**

Sponsor: **National Institute on Drug Abuse (NIDA)**

Principal Investigator: **Kelly Dunn, Ph.D.**
5510 Nathan Shock Drive
Baltimore MD 21224
Phone: 410-550-2254; Fax: 410-550-0030

1. What you should know about this study:

- You are being asked to join a research study. This consent form explains the research study and your part in it. Please read it carefully and take as much time as you need. Ask your study doctor or the study team to explain any words or information that you do not understand.
- You are a volunteer. If you join the study, you can change your mind later. There will be no penalty or loss of benefits if you decide to quit the study.
- During the study, we will tell you if we learn any new information that might affect whether you wish to continue to participate.
- If we think your participation in this study may affect your clinical care, information about your study participation will be included in your medical record, which is used throughout Johns Hopkins. Doctors outside of Johns Hopkins may not have access to this information. You can ask the research team to send this information to any of your doctors.
- When Johns Hopkins is used in this consent form, it includes The Johns Hopkins University, The Johns Hopkins Hospital, Johns Hopkins Bayview Medical Center, Howard County General Hospital, Johns Hopkins Community Physicians, Suburban Hospital, Sibley Memorial Hospital and All Children's Hospital.
- Biospecimens will be collected in this study. Biospecimens may include any of the following: blood, tissue, saliva, urine, bone marrow, cells, etc. Most biospecimens contain DNA, which is the genetic code for each person.
- 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.
- If you would like to review the information for this study, or a summary of the results, ask the study team doctor for the ClinicalTrials.gov study registration number.

- During this study, you will not have access to certain medical information and test results collected for study purposes. If an emergency occurs while you are in the study, medical information needed for your treatment can be made available to your study physician and other physicians who treat you. When the study is completed, all the information in your medical record will be available to you.

2. Why is this research being done?

This research is being done to evaluate whether combining two medications can make the medications more effective at reducing pain.

Though all the medications being used in this study are approved by the U.S. Food and Drug Administration (FDA), their use in this study is investigational because we are using them in a way that the FDA has not yet approved. The FDA is allowing the use of these study medications for this study.

People with who are over 18 years old and healthy may join this study.

How many people will be in this study?

This study is aiming to have 60 people (30 men and 30 women) complete the study.

3. What will happen if you join this study?

If you agree to be in this study, we will ask you to do the following things:

Screening Visit 1:

You will be completing the first Screening visit today.

The goal of this Screening visit is to make sure that you are eligible for the study and healthy, so that participating in this study will not put you at risk.

During this visit, we will ask you a series of questions and will collect a blood sample (no more than 2 tablespoons) and urine sample from you to ensure it is safe for you to be enrolled into the study. You will also complete an electrocardiogram (ECG) to make sure your heart is healthy.

At some point either today or before the beginning of your 1st study session (see below) you will also meet with a medical staff member to complete a brief history and physical.

Study Sessions:

If you are determined to be eligible after completing the Screening Visit then you will be asked to complete 5 study sessions. Each session will last all day (around 8 hours). You are welcome to spend the night before each session in our clinical research unit, which is located on our same hospital campus. If you prefer not to spend the night, you may arrive the morning of the session. However, since we cannot be sure how you will feel after taking the study medications, we will ask you to not drive to the sessions and will pay for a taxi to bring you to and from the sessions if needed.

Before we begin each session, we will collect a urine sample that will be tested for recent drug use. If you are female, we will also test you for pregnancy and will collect a blood sample from you that we will test to determine your hormone status. It is possible that the staff member may cancel your study session if your urine results indicate recent drug use or pregnancy. If your study session is canceled, you will not receive payment for that visit and will have to reschedule your visit. If you are eligible for the study session, then a staff member will escort you to the clinical research unit to stay the night. Depending on what time you arrive, you may be provided with dinner while on the research unit.

Each morning you will be provided with a calorie-controlled breakfast before the session begins. Study sessions are expected to last all day. During the session you will first be asked to complete some questionnaires that ask you about how you feel and to complete some pain testing procedures (these are described in more detail below). You will then receive capsules that contains the study medications for you to swallow. The medications you receive may contain a prescription stimulant, a prescription cannabinoid (related to the active ingredient in cannabis or marijuana), a benzodiazepine (e.g., anti-anxiety medication), an opioid (e.g., a pain medication), an over-the-counter medication, or a placebo (contains no medication, like a sugar pill). Neither you nor the staff member will know what combination of medications you have received.

After you receive the study medications, we will ask you to continue completing questionnaires, computerized tasks, and pain testing procedures at regular intervals throughout the session day. We will also collect information about how your body is responding to the study medications, by collecting your blood pressure, heart rate, pupil diameter, and other measures of biological response. At the end of the session, we will provide you with a taxi ride home.

You will be asked to complete 5 of these study sessions. Each session will be identical and we ask you to complete them about 1 week apart.

Pain Testing Procedures:

We will ask you to complete some pain testing procedures as part of this study. These tests help us to understand whether combining medications can reduce pain, and these data will help us learn whether there are new and better ways for the medical community to be treating pain in their patients.

We will be using well-validated pain-testing procedures that are used by several other laboratories throughout the world. Some of the pain testing will include the application of a topical cream.

It is important that you know that even though each procedure may produce some level of pain, we expect the pain to be relatively mild, and you will be able to end the procedure at any time with no consequences. We are conducting several different pain procedures because they all activate different pain pathways, however the pain they produce is brief and none of these procedures are expected to produce any lasting pain or damage to you. Specifically, you will be asked to place your arm and/or hand into cold water. This may be mildly painful, however you will be able to remove your arm/hand whenever you want. A staff member will also place a small device on some of your muscles, which will make you feel some pressure on those muscles. This procedure may also be mildly painful, and you will be able to end the procedure whenever you wish. We will also tap a place on your hand or elsewhere with some pencil-like objects. These may also be mildly painful, but again you will be able to stop the task whenever you want. Finally, we rub a cream on your hand that contains capsaicin, which is the chemical that makes some peppers hot. We will then use a machine that generates heat to evaluate your response to temperature-induced pain. A staff member will introduce you to these procedures during the Screening visits, so you will be able to make an informed decision about whether you'd like to participate in this study.

Request to re-contact you for future research:

We would also like to store the information that you provide to us so that we may re-contact you in the future to ask if you'd like to learn about additional research opportunities. This does not mean you would have to participate in any additional research, that is a separate decision that you would make at another time. Rather, it will give us permission to contact you about research for which we believe you may be interested and/or eligible, based on the responses that you provide to us during *this* study. You are free to chose whether we can contact you or not, and your choice will not impact your ability to be enrolled into this study.

Would you like us to contact you in the future regarding new research opportunities?

YES ☐ _____ NO ☐ _____

Signature of Participant Signature of Participant

Optional genetic testing:
You will be asked give about 1-2 tablespoons of blood for genetic testing. Your sample may be stored for future genetic testing that study how genes may impact response to medications or respond to painful stimuli or possibly other diseases may be studied. The samples will not be used for purposes other than research. The results will not be given to you. To protect your confidentiality, all exploratory samples will be disguised using labels with a unique code number. Only the investigator and designated study staff have the key to link the code to you. The analysis results will not be linked to you. All genetic research information obtained from your samples will be kept strictly confidential.

The Genetic Information Nondiscrimination Act (GINA) may help protect you from health insurance or health-related employment discrimination based on genetic information.

The law provides that health insurance companies and group health plans

- may not ask for genetic information from this research and
- may not use genetic information when making decision about eligibility or premiums

The law will not stop health insurance companies from using genetic information to decide whether to pay claims. The law does not apply to other types of insurance (such as life, disability or long-term care).

Despite the GINA protections and the best efforts of the research team to protect your information, you may still be at risk if information about you were to become known to people outside of this study.

Genetic information is unique to you and your family, even without your name or other identifiers. Johns Hopkins follows procedures to prevent people who work with your DNA information from being able to discover it belongs to you. However, new techniques are constantly being developed that may in the future make it easier to re-identify genetic data, so we cannot promise that your genetic information will never be linked to you.

No information will be provided to family members, third persons or organizations. **This sample is completely voluntary and will not impact whether you are eligible for the primary study.**

Will you allow us to collect a blood sample to be stored for future genetic testing?

YES ☐ _____ NO ☐ _____

Signature of Participant Signature of Participant

Request to collect and store biospecimens for future research:
As part of this research study, we would like to ask you to let us store your biospecimens and health information for future research. This research could include other diseases. The study doctor can provide you with additional information if you have questions. Also, further information about our use

of your biospecimens can be found in this consent document under the heading *What happens to Data and Biospecimens that are collected in the study?*

Will you allow us to store the biospecimens we collect for this study for use in future research?

YES ☐ _____ NO ☐ _____
Signature of Participant Signature of Participant

How long will you be in the study?
You will be in this study for 6 visits (1 screening visit and 5 session visits). We expect this to take about 8-10 weeks to complete all the study visits.

4. What are the risks or discomforts of the study?

Study Drugs:
The largest risk of this study is associated with the medications you will receive. Side effects of the medications you will be receiving are expected to be mild and short-lived. You will be screened before enrolling in the study to ensure you are at a low risk of experiencing any study medication-related side effects.

It is important that you understand the potential side effects that you could experience from the study medications. These medications have been administered to people previously either as treatments for different medical illnesses or in other experimental studies. Below is a list of side effects that have been reported by some people who have taken these medications, however it is important to remember that some of these side effects may be related to the medical illnesses being treated and not a result of the medication itself. Side effects are also more likely to happen when the medications are taken for several days in a row, which is different from how you will be taking the medications in this study.

- Dermatologic: Reddening of the face (2% of people), Itchy skin (1-8% of people)
- Gastrointestinal: Constipation (7-31% of people), Nausea (3-28% of people), Vomiting (3-14% of people), Abdominal Pain (3%-10% of people), Dry Mouth (38%-50% of people)
- Cardiovascular: Low blood pressure (less than 2% of people), Fainting (less than 2% of people), and High blood pressure, Heart Palpitations, Fast heart beat, or Widening of blood vessels (more than 1% of people).
- Neurologic: Weakness or Dizziness (1-11% of people); Headache (1-12% of people); Sleepiness (3-10% of people); Coma, Jerking of Muscles, and Increased Intracranial Pressure (less than 2% of people); Amnesia or Memory Los, Loss of Control of Body Movements, Confusion, Coordination Problems, and Vertigo (more than 1% of people in all cases)
- Psychiatric: Feeling High Euphoria (3-10% of people); Suicidal thoughts (less than 2% of people); Anxiety, Feelings of Persecution, Loss of Sense of Self, Depression, or Hallucinations (more than 1% in all cases)
- Respiratory: Brief Stop in Breathing, Stopping Breathing (less than 2% of people)
- Other: Drug dependence/Addiction or Drug Withdrawal (less than 1% of people)

It is important for you to know that, in extreme cases, these medications may cause your breathing to slow down or stop. They could also cause a severe allergic reaction or even death. You will undergo extensive medical testing during the Screening visits to determine whether you have any of the risk factors that would increase the likelihood that you would have an extreme reaction to the study medication and will not be enrolled into the study if we have any reason to believe that the study medication would put you at undue risk.

Risks from Combining the Study Medications:
Although there is no evidence that combining the study medications results in negative side effects, it is always possible there may be some interactions between these medications that are not yet known. We will carefully monitor emerging medical information about these drugs and will discontinue the study medications if new information indicates these medications should not be combined.

Pain Testing:
You will likely experience some discomfort from the pain testing procedures that are conducted during the study. The pain is expected to be mild and short-lived, and you will be able to end your participation in the pain sessions at any time.

Capsaicin:
Capsaicin is the main ingredient in hot peppers, and is used as an over-the-counter drug for the treatment of pain in products like Icy Hot. The dose of capsaicin we are using is higher than what is available over the counter, although it is less than half of the dose in a single habanera pepper. Capsaicin does cause some pain that is similar to how a hot pepper may feel when it is eaten. Capsaicin may produce some local redness and swelling that generally disappears within a day. The area of skin where the capsaicin is applied could be sensitive for up to 48 hours. Capsaicin may cause a burning feeling in the eyes or other areas of the body if accidentally rubbed onto other skin areas. We will take precautions to make sure this does not happen. We will limit the exposure area to a small square on the back of the hand and will wash the capsaicin off with alcohol after each session. If needed, we can use some ice to reduce any continued discomfort you may experience.

Blood Draw:
We will use a needle to draw blood from you. Taking blood may cause discomfort, bleeding, or bruising where the needle enters the body. In rare cases, it may result in fainting. There is a small risk of infection.

Legal Risks:
It is possible that your urine samples will test positive for medications that could be considered abusable by your employers or law enforcement professionals (e.g., stimulants, cannabinoids, opioids). If this is a concern to you then, with your permission, we can provide you with a letter that confirms your participation in the study and the potential for you to test positive for drugs that could be considered abusable for up to 7 days following a study session.

ECG:
An ECG will be conducted to determine that you heart is healthy enough for study participation. To conduct the ECG you will have electrodes placed on your chest, and you may find these cold or uncomfortable, though they are not expected to produce any pain. It is possible that the ECG may reveal abnormalities in your heart functioning that could be clinically significant. In these cases, the study medical team will inform you of the abnormalities and will provide you with relevant information you need to follow-up with your own doctor.

Study Questionnaires:
You may get tired or bored when we are asking you questions or you are completing questionnaires. You do not have to answer any question you do not want to answer.

Confidentiality:
There is the risk that information about you may become known to people outside this study.

Finally, there may be additional side effects and discomforts that are not yet known.

5. Are there risks related to pregnancy?

This research may hurt an embryo or fetus in ways we do not currently know. To protect against this risk, we will test all women for pregnancy before joining the study and prior to every study session. We also ask all women to practice birth control methods during their 8-10 week participation in the study.

6. Are there benefits to being in the study?

There is no direct benefit to you from being in this study. However, your participation in the study will help us to learn more about how to better treat pain, and whether certain combinations of medications should be used for that purpose.

7. What are your options if you do not want to be in the study?

You do not have to join this study. If you do not join, your care at Johns Hopkins will not be affected.

8. Will it cost you anything to be in this study?

No.

9. Will you be paid if you join this study?

You will be compensated up to $1280 for your time in the study, and your earnings are illustrated in this table. You will receive each session payment at the end of the session.

Visit	Payment
Screening	$30
Session 1	$150
Session 2	$200
Session 3	$250
Session 4	$300
Session 5	$350
Total Possible:	$1,280

You may be required to provide your social security number to be paid for taking part in this study. Federal tax law requires that you report your research payments when you file your taxes. If your total payments from Johns Hopkins exceed $600 per year, Johns Hopkins will report these payments to the Internal Revenue Service and you will receive a 1099-MISC form from us.

10. Can you leave the study early?

- You can agree to be in the study now and change your mind later.
- If you wish to stop, please tell us right away.
- Leaving this study early will not stop you from getting regular medical care.

If you leave the study early, Johns Hopkins may use or give out your health information that it has already collected if the information is needed for this study or any follow-up activities.

11. Why might we take you out of the study early?

You may be taken out of the study if:

- Staying in the study would be harmful.
- You need treatment not allowed in the study.

- You fail to follow instructions or fail to adhere to the session visit schedule.
- You become pregnant.
- The study is cancelled.
- There may be other reasons to take you out of the study that we do not know at this time.

If you are taken out of the study early, Johns Hopkins may use or give out your health information that it has already collected if the information is needed for this study or any follow-up activities.

12. How will your privacy be protected?

We have rules to protect information about you. Federal and state laws and the federal medical Privacy Rule also protect your privacy. By signing this form you provide your permission, called your "authorization," for the use and disclosure of information protected by the Privacy Rule.

The research team working on the study will collect information about you. This includes things learned from the procedures described in this consent form. They may also collect other information including your name, address, date of birth, and information from your medical records (which may include information about HIV status, drug, alcohol or STD treatment, genetic test results, or mental health treatment).

The research team will know your identity and that you are in the research study. Other people at Johns Hopkins, particularly your doctors, may also see or give out your information. We make this information available to your doctors for your safety.

People outside of Johns Hopkins may need to see or receive your information for this study. Examples include government agencies (such as the Food and Drug Administration), safety monitors, other sites in the study and companies that sponsor the study.

We cannot do this study without your authorization to use and give out your information. You do not have to give us this authorization. If you do not, then you may not join this study.

We will use and disclose your information only as described in this form and in our Notice of Privacy Practices; however, people outside Johns Hopkins who receive your information may not be covered by this promise or by the federal Privacy Rule. We try to make sure that everyone who needs to see your information keeps it confidential – but we cannot guarantee that your information will not be re-disclosed.

The use and disclosure of your information has no time limit. You may revoke (cancel) your permission to use and disclose your information at any time by notifying the Principal Investigator of this study by phone or in writing. If you contact the Principal Investigator by phone, you must follow-up with a written request that includes the study number and your contact information. The Principal Investigator's name, address, phone and fax information are on page one of this consent form.

If you do cancel your authorization to use and disclose your information, your part in this study will end and no further information about you will be collected. Your revocation (cancellation) would not affect information already collected in the study, or information we disclosed before you wrote to the Principal Investigator to cancel your authorization.

13. What if there is a Certificate of Confidentiality for this study?

The National Institute on Drug Abuse has given us a Certificate of Confidentiality for this study. This Certificate provides some additional protection for research information that identifies you. The Certificate allows us, in some circumstances, to refuse to give out information that could identify you as

a research subject without your consent, when such information is sought in a federal, state, or local court or public agency action. Still, we may disclose identifying information about you if, for example, you need medical help.

We may also disclose identifiable information about you as described in Section 12 of this form or in other cases. For example, the government may see your information if it audits us, and the research team will voluntarily comply with reporting requirements to the appropriate local or state authorities:

- if they suspect abuse, neglect or abandonment of a child or vulnerable or dependent adult;
- if certain diseases are present; and
- if the team learns that you plan to harm someone. In this case, the team also may warn the person who is at risk.

Even with this Certificate in place, you and your family members must continue to protect your own privacy. If you voluntarily give your written consent for an insurer, employer, or lawyer to receive information about your participation in the research, then we may not use the Certificate to withhold this information.

This Certificate does not mean the government approves or disapproves of this research project

14. What treatment costs will be paid if you are injured in this study?

Johns Hopkins and the federal government do not have programs to pay you if you are hurt or have other bad results from being in the study. However, medical care at Johns Hopkins is open to you as it is to all sick or injured people.

The costs for any treatment or hospital care you receive as the result of a study-related injury that are not covered by a health insurer will be billed to you.

By signing this form you will not give up any rights you have to seek compensation for injury.

15. What other things should you know about this research study?

a. What is the Institutional Review Board (IRB) and how does it protect you?

The Johns Hopkins Medicine IRB is made up of:

- Doctors
- Nurses
- Ethicists
- Non-scientists
- and people from the local community.

The IRB reviews human research studies. It protects the rights and welfare of the people taking part in those studies. You may contact the IRB if you have questions about your rights as a participant or if you think you have not been treated fairly. The IRB office number is 410-955-3008. You may also call this number for other questions, concerns or complaints about the research.

When the Johns Hopkins School of Medicine Institutional Review Board (IRB) reviews a study at another site, that site (institution) is solely responsible for the safe conduct of the study and for following the protocol approved by the Johns Hopkins IRB.

b. What do you do if you have questions about the study?
Call the principal investigator, Dr. Kelly Dunn Ph.D. at 410-550-2254. If you wish, you may contact the principal investigator by letter or by fax. The address and fax number are on page one of this consent form. If you cannot reach the principal investigator or wish to talk to someone else, call the IRB office at 410-955-3008.

c. What should you do if you are injured or ill as a result of being in this study?
If you think you are injured or ill because of this study, you may call Dr. Traci Speed, M.D., or Dr. Eric Strain, M.D. at 410-550-0052 during regular office hours.

If you have an urgent medical problem related to your taking part in this study, call Dr. Traci Speed, M.D., or Dr. Eric Strain, M.D. at 410-550-0052 during regular office hours and on weekends.

d. What happens to Data and Biospecimens that are collected in the study?
Johns Hopkins and our research partners work to understand and cure diseases. The biospecimens and/or data you provide are important to this effort.

If you join this study, you should understand that you will not own your biospecimens or data, and should researchers use them to create a new product or idea, you will not benefit financially.

With appropriate protections for privacy, Johns Hopkins may share your biospecimens and information with our research sponsors and partners.

16. What does your signature on this consent form mean?

Your signature on this form means that: You understand the information given to you in this form, you accept the provisions in the form and you agree to join the study. You will not give up any legal rights by signing this consent form.

WE WILL GIVE YOU A COPY OF THIS SIGNED AND DATED CONSENT FORM

Signature of Participant	(Print Name)	Date/Time

Signature of Person Obtaining Consent	(Print Name)	Date/Time

NOTE: A COPY OF THE SIGNED, DATED CONSENT FORM MUST BE KEPT BY THE PRINCIPAL INVESTIGATOR; A COPY MUST BE GIVEN TO THE PARTICIPANT; IF YOU ARE USING EPIC FOR THIS STUDY A COPY MUST BE FAXED TO 410-367-7382; IF YOU ARE NOT USING EPIC A COPY MUST BE PLACED IN THE PARTICIPANT'S MEDICAL RECORD (UNLESS NO MEDICAL RECORD EXISTS OR WILL BE CREATED).

ONLY CONSENT FORMS THAT INCLUDE THE JOHNS HOPKINS MEDICINE LOGO CAN BE USED TO OBTAIN THE CONSENT OF RESEARCH PARTICIPANTS.

DOCUMENTATION OF PHYSICIAN/MID-LEVEL PROVIDER CONSENT

My signature below indicates that I have discussed the risks, benefits, and alternatives, answered any questions, and believe the participant is able to make an informed choice to join the study.

Signature of Physician/Mid-Level Provider	(Print Name)	Date/Time

Signature of Participant	(Print Name)	Date/Time

NOTE: A COPY OF THE SIGNED, DATED CONSENT FORM MUST BE KEPT BY THE PRINCIPAL INVESTIGATOR; A COPY MUST BE GIVEN TO THE PARTICIPANT; IF YOU ARE USING EPIC FOR THIS STUDY A COPY MUST BE FAXED TO 410-367-7382; IF YOU ARE NOT USING EPIC A COPY MUST BE PLACED IN THE PARTICIPANT'S MEDICAL RECORD (UNLESS NO MEDICAL RECORD EXISTS OR WILL BE CREATED).

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