

CONSENT FOR RESEARCH
The Pennsylvania State University

Testing the Effect of ENDS Flavors on Neurotransmission

Principal Investigator: Andrea L. Hobkirk, PhD

Address: 500 University Drive Hershey PA 17033

Telephone Numbers: Weekdays: 8:00 a.m. to 5:00 p.m. (717) 531-7279.

Subject's Printed Name: _____

We are asking you to be in a research study.

Whether or not you take part is up to you. You can choose not to take part. You can agree to take part and later change your mind. Your decision will not be held against you, and there will be no penalty or loss of benefits to which you are entitled.

This form gives you information about the research. Please ask questions about anything that is unclear to you and take your time to make your choice.

KEY INFORMATION

The following is a short summary of this study to help you decide whether or not to be a part of this research. More detailed information is provided later in this form. If you have any questions, be sure to ask the study team.

Why am I being invited to take part in this research study?

We are asking you to take part in this voluntary research study because you use tobacco such as vapes or electronic cigarettes (e-cigarettes).

What is the purpose of this research study?

The purpose of this voluntary research is to study the effects of different e-cigarette flavoring chemicals on brain activity.

How long will the research study last?

Your participation in study will last about 11 days, depending on your availability for two in-person visits.

What will I need to do?

You will be asked to complete a remote eligibility screen to answer questions and provide survey responses that help us determine if you qualify for the study. If you are eligible, you will attend two laboratory visits at the Milton S. Hershey Medical Center in Hershey, PA. The laboratory visits will happen before and after you use a study e-cigarette for 10 days at home and record information about your e-cigarette use on a study phone app. During the laboratory visits you will answer interview questions, complete surveys, rate your experience while you puff on e-cigarettes, and play a computer game to earn puffs of e-cigarettes. If you are interested and eligible to complete the neuroimaging scan, you will puff on e-cigarettes and play a computer game during functional magnetic resonance imaging (MRI) or near-infrared spectroscopy. You will be asked to abstain from using any nicotine for 14 hours before the laboratory visits.

What are the main risks of taking part in the study?

For this study, the main risks are: discomfort from using an e-cigarette (dry mouth, sore throat, nausea) and loss of confidentiality.

What are the possible benefits to me that may reasonably be expected from being in the research?

There are no benefits to you from taking part in this research. The results of the study may benefit other people in the future by helping us learn more about how flavors in e-cigarette liquids influence the brain.

What happens if I do not want to be in this research?

Participation in research is completely voluntary. You can decide to participate or not to participate. You may choose not to take part in this research study at any time during the study.

DETAILED INFORMATION

The following is more detailed information about this study in addition to the information listed above.

1. Why is this research study being done?

This research is being done to find out if certain e-cigarette flavor chemicals influence brain reward function. The results have the potential to inform our understanding of electronic nicotine device addiction, which may assist in tobacco product regulation decisions, addiction prevention efforts, and better treatments for smoking and e-cigarette cessation.

Approximately 120 people will take part in this research study at Penn State.

2. What will happen in this research study?

You will complete two in-person laboratory visits at the Milton S. Hershey Medical Center in Hershey, PA and use a study e-cigarette for 10 days at home over the course of the study.

- Laboratory Visit Procedures (In-Person) – This visit will occur twice; at the start and end of the 10-day e-cigarette use. You will need to abstain from using any nicotine for 14 hours prior to each Laboratory Visit. At the visit you will do the following:
 - Complete Written Consent form
 - Provide an exhaled breath carbon monoxide measurement using a hand-held monitor and provide urine for nicotine analysis and pregnancy testing if appropriate.
 - Receive hands-on training on how to use and store the study e-cigarette.
 - Laboratory Testing
 - E-cigarette Ratings
 - You will be asked to puff on three e-cigarettes with varying flavor combinations and provide subjective ratings of the e-cigarettes (e.g., intensity, familiarity, sweetness, liking, satisfaction, etc.).
 - Computer Task
 - On a computer, you will choose between puffs of a flavored or unflavored e-cigarette by clicking on the pictures with the mouse.
 - Complete surveys that will ask about your demographics, medical history, nicotine use history, nicotine withdrawal symptoms and cravings.
- At Home E-cigarette Use –
 - You will be given a study e-cigarette and e-liquid pods to use at home for 10 days. You will be asked to puff on the e-cigarette at least 10 times a day and to record the number of puffs you take on the MyCap phone application or a paper log each

day. You do not need to stop using your usual tobacco products during the 10-days. You will be asked to return bring the pods to the next laboratory visit.

3. What are the risks and possible discomforts from being in this research study?

E-cigarette use:

- There may be some unknown risks related to the use of e-cigarettes though these risks are not considered to be greater than risks associated with use of smoked tobacco products.
- The most common side effects associated with using e-cigarettes are changes in taste, dehydration, mucus in throat/sinus, dry mouth, dry cough, throat irritation, mouth irritation, sore throat, mouth ulcers, dizziness, headache, and nausea.
- If stored improperly (in pocket or where the e-cigarette device can turn on accidentally), overheating of the device may occur, which presents a minor burn risk.
- E-cigarette liquids contains vegetable glycerin, propylene glycol and flavorings. Participants with known allergies to these substances will be excluded in the study. The most common reported allergic reaction to these substances is contact dermatitis.

Nicotine addiction: You will be asked to inhale e-cigarette aerosols that contain nicotine, which is an addictive substance. The amount of nicotine you receive from this product depends on what product you are given and how you use it.

Nicotine withdrawal symptoms: Using less tobacco than you typically do may result in nicotine withdrawal symptoms (e.g. irritability, anxiety, restlessness, depressed mood, increased appetite, fatigue, difficulty concentrating).

Loss of confidentiality: There is a risk of loss of confidentiality if your information or your identity is obtained by someone other than the investigators, but precautions will be taken to prevent this from happening. The confidentiality of your electronic data created by you or by the researchers will be maintained as required by applicable law and to the degree permitted by the technology used. Absolute confidentiality cannot be guaranteed.

Questionnaires: It is possible that some of the questions in the questionnaires may make you uncomfortable. You are free to skip any questions that make you uncomfortable.

Randomization: You will be assigned to a condition by chance. The condition you receive may have more side effects than the other condition.

Magnetic resonance imaging (MRI): Risk of injury is very low during an MRI scan. However, MRI is not safe for everyone. It may not be safe for you to have an MRI scan if you have any metal containing iron in or on your body. This is because metal containing iron can pose a safety risk when in the presence of strong magnetic fields. Radio waves may also heat the body and metallic objects within or on the body, possibly resulting in burns. Before you are allowed in the scanner room, you will be asked a set of questions to determine if it is safe for you to have an MRI scan at this time. For example, it may not be safe to have an MRI scan if you have a cardiac pacemaker, aneurysm clips, an intrauterine device (IUD), etc. For your safety, it is very important that you answer all questions truthfully.

Near-infrared spectroscopy (NIRS): There are no known risks of imaging with near-infrared light; however, you may experience discomfort on your head and scalp from the cap during use. This discomfort should go away after the cap is removed.

4. What are the possible benefits from being in this research study?

4a. What are the possible benefits to me?

There are no direct benefits to you as part of your participation in this research study.

4b. What are the possible benefits to others?

Medical science may gain a further understanding about how certain e-cigarette flavor chemicals influence brain activity. The results have the potential to inform our understanding of e-cigarette addiction, which may assist in tobacco product regulation decisions, addiction prevention efforts, and better treatments for smoking and e-cigarette cessation.

5. What other options are available instead of being in this research study?

You may choose not to be in this research study.

6. How long will I take part in this research study?

If you agree to take part, it will take you about 11 days to complete this research study. You will be asked to visit the research site 2 times at the start and the end of your trial. Your total participation time will depend on your availability to complete the laboratory visits.

7. How will you protect my privacy and confidentiality if I decide to take part in this research study?

7a. What happens to the information collected for the research?

Efforts will be made to limit the use and sharing of your personal research information to people who have a need to review this information. Reasonable efforts will be made to keep the personal information in your research record private. However, absolute confidentiality cannot be guaranteed, and there may be situations where disclosure is required by law. In our research files at The Milton S. Hershey Medical Center (HMC) and Penn State College of Medicine (PSU) we will include these identifiers: your name, address, phone number, date of birth, email address, and a code number.

- A list that matches your name with your code number will be kept in a secure database.
- Your research records will be labeled with your code number and your initials and will be kept in a safe area in Dr. Hobkirk's research offices.

This research is covered by a Certificate of Confidentiality from the National Institutes of Health. This means that the researchers cannot disclose information that identifies you to anyone not connected with the research. This protection also prevents this information from being used or disclosed for legal proceedings, such as being accessed through a court order. The Certificate of Confidentiality however does not prevent disclosures required by law, such as information about child abuse or neglect and harm to yourself or others. Also, your information may be disclosed in accordance with any consent you provide, including for your medical treatment or use in other research. For additional information ask the principal investigator or a member of the study team or contact the Human Research Protection Program at (814) 865-1775.

In the event of any publication or presentation resulting from the research, no personally identifiable information will be shared.

We will do our best to keep your participation in this research study confidential to the extent permitted by law. However, the following people/groups may check and copy records about this research.

- The Office for Human Research Protections in the U. S. Department of Health and Human Services
- The research study sponsor, National Institute on Drug Abuse

- The Penn State Institutional Review Board (a committee that reviews and approves human research studies) and the Penn State Human Research Protection Program
- The investigator, Penn State study staff, and other Penn State professionals who may be evaluating the study or need this information to do their jobs (such as for treatment, payment (billing), or health care operations)
- People or groups that we hire to do work for us, such as data storage companies, insurers, and lawyers
- Organizations that provide independent accreditation and oversight of hospitals and research
- Public health and safety authorities (for example, if we learn information that could mean harm to you or others, we may need to report this, as required by law)

Sometimes a Principal Investigator or other researcher moves to a different institution. If this happens, your identifiable information and samples may be shared with that new institution and their oversight offices. Data will be shared securely and under a legal agreement to ensure it continues to be used under the terms of this consent and authorization.

The research team may use your past, present, and future medical information and records for the purpose of your participation in the research study specifically identified in this authorization. Information that will be disclosed may include information that identifies you and your medical condition, as well as information developed as a result of the research study. Your authorization will remain in effect until you revoke it. You may change your mind and revoke (take back) this authorization at any time and for any reason. However, any information previously disclosed under this authorization may not be retrieved and may no longer be protected by federal or state privacy laws. To revoke this consent and authorization, contact the Principal Investigator using the information found on the first page of this form. Revocation of, or refusal to sign, this consent and authorization will not impact the care you receive at Penn State that is not related to the research, however, you will be excluded from participation in this research study if you do not provide this consent and authorization.

7b. What will happen to my research information and/or samples after the study is completed?

We may use your research information and your biological samples in future studies or may share your information or biological samples with other investigators for future research without your additional informed consent. Before we use or share your information or samples we will remove any information that shows your identity.

Researchers can do studies that are more powerful when they share with each other the data or information they get from research studies. They share this information with each other by putting it into scientific databases. Your coded research information may be put in one or more databases and used for future research. Your information stored in these databases will not include any identifying information such as your name, address, telephone number, or social security number. Your research data will only be available to researchers who have received approval from data access committees and/or Institutional Review Boards. Some of these databases are maintained by Penn State, some are maintained by the federal government, and some are maintained by private companies and other institutions.

8. What are the costs of taking part in this research study?

8a. What will I have to pay for if I take part in this research study?

For costs of tests and procedures that are only being done for the research study:

- You and/or your insurance company will not be charged for the cost of any tests or procedures that are required as part of the research and are outside the standard of care (what is normally done) for your condition.
- Examples of research-related tests and procedures that may be provided at no cost to you may include: visits to the study site, procedures and/or questionnaires. Talk to the study team about which items and procedures this includes.

If you have any questions about costs and insurance, ask the research study doctor or a member of the research team.

8b. What happens if I am injured as a result of taking part in this research study?

It is possible that you could develop complications or injuries as a result of being in this research study. If you experience a side effect or injury and emergency medical treatment is required, seek treatment immediately at any medical facility. If you experience a side effect or injury and you believe that emergency treatment is not necessary, you should contact the principal investigator listed on the first page of this consent form as soon as possible and the principal investigator will arrange for medical treatment. You should also let any health care provider who treats you know that you are in a research study.

Penn State compensation for injury

- There are no plans for Penn State to provide financial compensation or free medical treatment for research-related injury.
- If an injury occurs, medical treatment is available at the usual charge.
- Costs will be charged to your insurance carrier or to you.
- Some insurance companies may not cover costs associated with research injuries.
- If these costs are not covered by your insurance, they will be your responsibility.

When you sign this form you are not giving up any legal right to seek compensation for injury.

9. Will I be paid to take part in this research study?

You will receive the following compensation for this study paid as you complete each section:

- Remote Screening - \$50
- Pre-Randomization Laboratory Visit - \$75
- At-Home ENDS Use Surveys - \$50
- Post- Randomization Laboratory Visit - \$75

You can earn up to \$250 for completing the main trial and attending all the visits. You will also be provided a study e-cigarette and cartridges as part of your participation.

The payment will be provided by Greenphire ClinCard.

This reimbursement will be issued by an external company called Greenphire. You will be issued a ClinCard, which is a debit card that your funds are loaded onto and can be used at your discretion. The research team will give Greenphire some personal information about you, as described below. Greenphire will only use your personal information to process this reimbursement and will not share it with anyone for any other purpose. Details of the debit card system are explained on an additional sheet. If you lose the card, you will be responsible for the replacement fee.

When a visit is completed, funds will be approved and loaded onto your card. The funds will be available within 2-3 business days. In order to assign a ClinCard to you and load funds onto the ClinCard, Greenphire will need your Study/Subject ID, Name, Address, and date of birth.

You will have the option to receive updates related to payment alerts via text message and/or email message. Standard text messaging rates will apply. In order to send you messages Greenphire will need your Mobile Phone Number and/or E-mail Address.

10. Who is paying for this research study?

The institution and investigators are receiving a grant from the National Institute on Drug Abuse to support this research.

11. What are my rights if I take part in this research study?

Taking part in this research study is voluntary.

- You do not have to be in this research.
- If you choose to be in this research, you have the right to stop at any time.
- If you decide not to be in this research or if you decide to stop at a later date, there will be no penalty or loss of benefits to which you are entitled.

Your research doctor may take you out of the research study without your permission.

- Some possible reasons for this are: continuing the research would be harmful, you did not follow the instructions of the study doctor, you experience serious side effects.
- Also, the sponsor of the research may end the research study early.
- If your participation ends early, you may be asked to visit the research doctor for a final visit.

During the course of the research you will be provided with any new information that may affect your health, welfare or your decision to continue participating in this research.

12. If I have questions or concerns about this research study, whom should I call?

Please call the head of the research study (principal investigator), Dr. Andrea L. Hobkirk at (717) 531-7279 if you:

- Have questions, complaints or concerns about the research.
- Believe you may have been harmed by being in the research study.

You may also contact the Penn State Human Research Protection Program (HRPP) at (814) 865-1775 or visit the HRPP website at <https://www.research.psu.edu/irb/participants> if you:

- Have questions or want information regarding your rights as a person in a research study.
- Have concerns, complaints or general questions about the research.
- Have questions about your privacy and the use of your personal health information.
- You may also call this number if you cannot reach the research team or wish to offer input or to talk to someone else about any concerns related to the research.

A description of this clinical trial will be available on <https://www.ClinicalTrials.gov>, as required by U.S. Law or policy. 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.

Optional part(s) of the study

In addition to the main part of the research study, there is another part of the research. You can be in the main part of the research without agreeing to be in this optional part.

MRI Safety Questionnaire:

You will complete a questionnaire to determine if you can safely complete a MRI scan.

Neuroimaging:

You will inhale e-cigarette aerosols that contain nicotine during a functional magnetic resonance imaging (MRI) or near-infrared spectroscopy (NIRS) scan lasting approximately 45 minutes. Prior to the scan, a respiration sensor will be placed around your chest and the device tubing will be placed near your mouth. You will be asked to breathe at a natural pace—in through your mouth and out through your nose. A series of scans might be conducted depending on timing and availability of equipment, including a high-resolution baseline anatomical scan, a functional scan that includes the aerosol delivery protocol, and a game that asks you to press a button when you see shapes on a display screen to earn or avoid losing hypothetical money. For the aerosol delivery protocol, the aerosols from the e-cigarette device will be delivered via the device tubing orally. Some aerosols will be flavored and some will not. .

Additional Risks for the Optional Portion of the Study:

MRI (magnetic resonance imaging) Risks: MRI does not involve radiation and there are no known long-term risks of MRI. You will be assessed for MRI safety at the screening visit and again at the scan visit before entering the scanner. We will be assessing for potential MRI hazards like metal fragments in the body or metal implanted devices that could shift during scanning. You will be instructed to remove all metal from your body and clothing before entering the scanning room. The major discomforts of fMRI scanning include lying still in a supine position for a sustained period of time and hearing loud tapping sound during image acquisition. You may be uncomfortable inside the MRI scanner, especially if you do not like to be in closed spaces (“claustrophobia”). In between scanning sequences, you will be able to talk with the MRI staff through a speaker system. At any time, you can choose to stop the scan by squeezing a “panic” button.

Functional Near Infrared Spectroscopy (NIRS): There is minimal risk to NIRS recording. NIRS is a noninvasive neuroimaging technique that uses light to measure oxygen in the outermost part of the brain, called the cortex. You might experience discomfort on your scalp from the head cap and light sources used for the scan. However, we do not expect discomfort to last following removal of the NIRS equipment.

Incidental Finding: None of the tests carried out in this study are intended to provide diagnoses for clinical purposes, but you will be alerted to findings that should be discussed with a healthcare provider. They are intended solely for research purposes. The investigators for this project are not trained to perform medical diagnosis, and the scans to be performed in the study are not optimized to find abnormalities. On occasion, a member of the research team may notice a finding on a scan that seems abnormal. When a finding is noticed, one of the investigators may consult a physician specialist, such as a radiologist or neurologist, as to whether the finding merits further investigation. If the specialist recommends further follow-up, the investigator or another member of the research team will contact you within 48 hours (via phone) of the recommendation and suggest that you contact your private medical provider for follow-up. To facilitate follow-up care, you will be given a copy of your images via a letter if you would like a copy. Being told about a finding may cause anxiety as well as suggest the need for additional tests and financial costs. Medical insurance may be affected whether or not the finding is ultimately proved to be of clinical significance. Costs for clinical follow-up are not covered in the cost of research. The decision as to whether to proceed with further examination or treatment lies with you.

Compensation for Optional Portion of the Study:

In addition to the compensation from the main portion of the study listed in Section 9, you can earn the following compensation:

- Pre- Randomization MRI or NIRS Scan – \$75
- Post- Randomization MRI or NIRS Scan - \$75 and an electronic file of your 3-D anatomical brain image if you completed MRI (optional)

The compensation will be added to your Greenphire card as described in Section 9. Completing the main trial and optional neuroimaging will result in earning up to \$400 for the entire trial.

You should initial below to indicate what you want regarding the functional neuroimaging. You would receive two neuroimaging scans over the course of the study in addition to the main study visits.

a. I would like to be enrolled in the neuroimaging portion of the study if eligible
_____ Yes _____ No

INFORMED CONSENT TO TAKE PART IN RESEARCH

Signature of Person Obtaining Informed Consent

Your signature below means that you have explained the research to the subject or subject representative, provided the subject or subject representative an opportunity to discuss and consider whether or not to participate in the research, and have answered any questions about the research.

Signature of person who explained this research Date Time Printed Name
(Only approved investigators for this research may explain the research and obtain informed consent.)

Signature of Person Giving Informed Consent and Authorization

Before making the decision about being in this research you should have:

- Discussed this research study with an investigator,
- Read the information in this form, and
- Had the opportunity to ask any questions you may have.

Your signature below means that you have received this information, have asked the questions you currently have about the research and those questions have been answered. You will receive a copy of the signed and dated form to keep for future reference.

Signature of Subject

By signing this consent form, you indicate that you voluntarily choose to be in this research and authorize your information to be used and shared as described above.

Signature of Subject Date Time Printed Name