University of Illinois at Chicago
Research Information and Consent for Participation in Biomedical Research
"Neurologic Biomarkers of Smoking Behavior"

You are being asked to participate in a research study. The study team is required to provide a consent form such as this one to tell you about the research, to explain that taking part is voluntary, to describe the risks and benefits of participation, and to help you to make an informed decision. Feel free to ask a member of the study team any questions you may have.

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Sponsor: University of Illinois at Chicago

Why am I being asked?

You are being asked to be a subject in a research study about the effects of intranasal insulin on brain activity.

You have been asked to participate in the research because you have been identified as either a cigarette smoker or non-smoker between the ages of 21-40 years old.

Your participation in this research is voluntary. Your decision whether or not to participate will not affect your current or future dealings with the University of Illinois at Chicago. **If you decide to participate, you are free to withdraw at any time without affecting that relationship.**

Approximately 120 subjects may be involved in this research at UIC.

What is the purpose of this research?

This research is being done to better understand the effect of intranasal insulin on brain activity in smokers and non-smokers. Understanding this outcome may lead to drug development that is not only patient-specific, but possibly more effective than currently available smoking cessation aids. Although there are several FDA-approved treatments on the market, only approximately

6% of an estimated 40 million smokers successfully quit. Taking a more individualized approach to resolving this healthcare concern may lead to higher quit rates amongst smokers.

The insulin treatment used in this study is not FDA approved and is therefore investigational.

What procedures are involved?

This research will be performed at the UIC Center for Clinical and Translational Science (CCTS) located on 914 South Wood Street Chicago, IL 60612. Participants will complete screening and testing in a private clinic room in CCTS.

Before participating in the study, you will be asked to complete several screening tests to determine if you are eligible for the study. The screening session (i.e. today) will take approximately 3 hours. The screening tests will include the following:

1. Urine drug and pregnancy screens – All subjects will be required to have **a negative drug screen** during screening (i.e. today) and subsequent testing sessions to continue participation in the study. In addition to urine drug screens, female participants will also be asked to complete a urine pregnancy test. Female participants will be required to have **a negative pregnancy test** during screening (i.e. today) and subsequent testing sessions to continue participation in the study.
2. Shipley IQ Test – The Shipley IQ Test is a brief measure of cognitive functioning. The test will include a 40 question vocabulary test on word meaning. You will be asked to complete the test in 10 minutes.
3. Breath Alcohol Test – The breath alcohol test will measure your breath alcohol level to rule out recent alcohol intake. **Drinking alcohol up to 48 hours before your appointment (either screening or testing session) is not permissible for the purpose of this study.** You will be asked to take a deep breath and blow into the mouthpiece of the breath alcohol device to test your levels.
4. Point-of-care glucose check – You will be asked to provide a blood sample. A nurse will take a drop of blood from your finger and measure your plasma glucose levels to ensure that your blood glucose levels are within the normal range.
5. Carbon Monoxide Monitor – The purpose of measuring the CO level is to classify you as either a smoker or a non-smoker.
6. Baseline Demographics - You will be asked basic demographic questions in a survey.
7. Fagerstrom Test for Nicotine Dependence (FTND) – If you are a cigarette smoker, you will be asked questions about your level of nicotine dependence.
8. Substance Use History – You will be asked detailed questions about your substance use history in this survey. This survey will ask you very personal questions about your drug use history. This study has a Certificate of Confidentiality issued by the government to protect the privacy of participants involved in this research. The Certificate of Confidentiality allows the research team to refuse to disclose identifying information about you in any civil, criminal, administrative, legislative, or other proceeding, whether at the federal, state, or local level.
9. Structured Clinical Interview – You will be asked detailed questions about your mental health. This interview will take approximately 30 minutes.

10. Hair – You will be asked if you have thick, braided hair. If your hair is in tight braids, it may be difficult for the study coordinator to establish a clear signal from your scalp to the EEG cap with gel. You will have to unbraid your hair prior to the beginning of the study. If you are unsure of whether your hair needs to be unbraided for the experiment, please contact the CEDAR Lab.

If you are eligible to participate in the study after completing the in-person screening procedures, you will be asked to schedule appointments for 2 testing sessions. You will need to come to the study site on 2 separate days separated by approximately 1 week.

You will need to abstain from any illicit drug intake during the course of this study. Drinking alcohol 48 hours prior to each study session is not permissible for the purpose of this study. Each of those visits will take 4 hours. If you are a smoker, you will be allowed to resume smoking at the end of the 4-hour session.

If you are a smoker, you may smoke the normal amount of cigarettes that you usually smoke within the first 30 minutes of waking prior to each session. After the first 30 minutes, you must refrain from smoking for the rest of the morning. It is important that you smoke the same amount of cigarettes prior to both sessions. For example, if you usually smoke 2 cigarettes upon waking, you should smoke 2 cigarettes prior to the first session and 2 cigarettes prior to the second session.

The study procedures for each visit is as follows.

1. The study session will begin at 8a.m. You will be asked to provide a urine drug sample, alcohol breath sample, and carbon monoxide breath sample at the beginning of each testing session.
2. At 8:30a.m., you will be instructed to take a chewing gum break. **If you are a smoker**, a member of the research team will provide a strip of Nicorette® nicotine gum. As per the instructions given by Nicorette, you will chew the gum slowly until you experience a tingling sensation, then place the gum between your cheek and gum until the tingle subsides. You will repeat this procedure until most of the tingle is undetectable (20-30 minutes). **If you are a non-smoker**, you will be given a piece of generic (non-nicotine) gum and can chew at your own pace.
3. At 8:50a.m., a study nurse will take a blood sample from your arm to establish your baseline blood nicotine level. The nurse will place a needle in a vein in your arm, and a 4mL blood sample will be taken from it to determine your baseline nicotine blood levels. This step is important to ensure that nicotine levels can be compared between testing sessions.
4. At 9:00a.m., a study nurse will conduct a POC blood glucose check by taking a drop of blood from your finger to examine your blood glucose level.
5. At 9:05a.m., a study nurse will conduct a physical examination of the nares (nostrils). This examination will be conducted to ensure that the condition of your nares is suitable for intranasal administration of insulin.
6. From 9:15 to 10:00a.m., you will be allowed to relax. We will supply magazines and books for you to choose from.

7. The nasal spray administration will start at 10:00a.m. You will either receive insulin or placebo nasal spray. You will not know which treatment you have received. You will spray once in each nostril every 3 minutes for a total of 6 sprays (2 sprays at 10:00a.m., 2 sprays at 10:03a.m., and 2 sprays at 10:06a.m.). During treatment, you will be given a questionnaire to rate spray effects. If you receive insulin in the first session, you will receive placebo in the second session, and vice versa.
8. At 10:10a.m., a member of the research team will set up the electroencephalography (EEG) equipment. The EEG is a non-invasive device which will track and record your brain wave patterns during several tasks in the testing session. EEG equipment includes a cap that you will wear on your head, an EEG device that will record your brain activity, and 32 cords connecting the cap to the EEG. The equipment will also be connected to a laptop for the study team to analyze your brain waves in real-time. The EEG setup will be completed by 10:30a.m.
    - You will be asked to brush your hair to ensure accurate EEG data collection.
    - The study coordinator will put the EEG cap on your head. The EEG cap is non-invasive and will be placed on your head similar to a hat.
    - Next, the study coordinator will put electrolyte gel in each of the 32 electrode slots on the EEG cap. This process involves using a syringe with a blunt needle to insert gel between each electrode and your scalp. In order to ensure a clear signal, the study coordinator will move some of your hair with the blunt needle using a gentle scratching motion. The gel will likely get in your hair during this step but can be washed out with water and shampoo after the study session is complete.
9. At 10:30a.m., you will complete a task on a computer while study coordinators observe your brain activity through the EEG recording. You will be instructed to respond as quickly and accurately as possible. In the task, you will be given instructions on what specific keyboard buttons to press in response to seeing specific letters and shapes on the screen.
10. At 11:40a.m., the study coordinator will wrap up the testing session. At the end of the session, you will be asked to complete a form asking if you experienced any side effects or discomfort from your participation in the session. In addition, you will be given the instructions for the next study session, or for the completion of the study, depending on whether the end of the session occurs after the first or the second session. A member of the study team will answer any questions you may have or address any concerns related to the study procedure.
11. At 11:40a.m., a study nurse will conduct a POC blood glucose check by taking a drop of blood from your finger to examine your blood glucose level.
    - The possibility of experiencing low glucose (i.e. hypoglycemia) is very low. However, if your blood glucose levels are below the euglycemic level (<70 mg/dL) you will be treated for hypoglycemia.
    - You will be given 15 grams of glucose (4 oz of orange juice) and your glucose level will be rechecked in 15 minutes. The process will be repeated if you are still hypoglycemic.
    - Once treated, you will be given a snack (a granola bar) to eat in order to prevent recurrence. You will then engage in a light activity such as reading for an hour.
    - Following this hour, you will drink 4 ounces of orange juice and eat a granola bar.

- At this time, we will retest your blood glucose levels. Upon confirmation that you are still euglycemic, you will be discharged and compensated for your time spent in the session.

12. If you are not treated for hypoglycemia (i.e. are euglycemic), the testing session will end at 12:00p.m. If you are treated for hypoglycemia, the testing session will end at 1:00p.m.

What are the potential risks and discomforts?

You may have side effects while in the study. Everyone taking part in the study will be followed carefully for any side effects. The study drug, intranasal insulin, has been tested in the healthy population and Alzheimer's disease patients in about 2,000 patients. There have been no serious side effects reported resulting from the treatment. However, this medication has not been tested in solely nicotine dependent individuals, so doctors do not know all the side effects that may happen. The potential toxicity of intranasal insulin in the nasal cavity and other exposed tissues has not been tested in animal studies.

You should report to the investigator any side effects you experience while taking part in the study. There is a potential of developing the following side effects:

- Nasal irritation/runny nose (42%)
- Confusion/inability to complete routine tasks (16%)
- Sweating (11%)
- Nonspecific pain (11%)
- Shaking (11%)
- Anxiety (11%)
- Watering eyes (11%)
- Dizziness (5%)
- Headache (5%)
- Visual disturbances, such as double or blind vision (5%)
- Tingling sensation around the mouth (5%)
- Diarrhea (5%)
- Restlessness (5%)
- Discomfort (5%)
- Menorrhagia/abnormal bleeding at menstruation (5%)
- Anosmia/loss of smell
- Insomnia/trouble sleeping

If you experience any of these symptoms, you should contact the investigator immediately.

Anosmia (loss of smell) may be experienced when zinc (an ingredient in insulin solution) is administered nasally. The concentration of zinc that was found to be toxic is between 0.01% and 0.05%. The concentration of zinc in our study is 0.0007%. Though this is a low concentration, it is not known how likely it is that permanent loss of smell will occur. Insomnia may occur the night following the session, with a stabilization and return to normal sleeping pattern the following night.

Hypoglycemia (low blood sugar) may be experienced with insulin administration. However, the amount of intranasal insulin you will receive (60 IU) is unlikely to cause hypoglycemia, as occurrences of hypoglycemia have not been reported in studies with similar doses. For more information about risks and side effects, ask the investigator.

Other likely risks and discomforts in this study include:

- Possible side effects of blood drawing include discomfort, bruising and/or bleeding at the needle site (>20%); dizziness and infection (<2%).
- The process for putting the EEG head cap on your head. In order to collect accurate data, the research will have to insert gel into each of the 32 electrode slots of the EEG head cap using a plastic syringe. The study team will need to make sure the gel makes contact with your scalp for quality EEG signal readings. This process will require researchers to scratch your scalp using the plastic gel-filled syringe, which may cause discomfort. The research team will make every effort to be as gentle as possible throughout this process. The EEG cap is non-invasive and will be placed on your head similar to a hat.
- The process of putting gel in the EEG head cap. After putting the electrolyte gel into each of the 32 slots of the EEG head cap, you will have gel in your hair. Your hair will be sticky due to the substance of the gel, which may cause discomfort.
- Risk of potential loss of confidentiality. Information that identifies subjects will be used in this study and shared with research staff. However, the research team will make every effort to protect subject's private health information and guard against any loss of privacy.
- Risk of stress, anxiety, or both. Some of the questions asked may cause you to have stress or anxiety. If so, contact the University of Illinois Health system at (312) 996-2200 to request information from UI Health Psychiatric Services.

What are the reproductive risks?

If you are a woman: Participating in this research may involve risks to pregnant women and/ or an unborn baby which are currently unforeseeable. To protect against possible side effects of the study drug, if you are pregnant or nursing a child you may not take part in this study. As part of this study, we will be performing urine pregnancy testing. If you become pregnant, your participation will be stopped.

Will I be told about new information that may affect my decision to participate?

During the course of the study, you will be informed of any significant new research findings (either good or bad), such as changes in the risks or benefits resulting from participation in the research or new alternatives to participation, that might cause you to change your mind about continuing in the study. If new information is provided to you, your consent to continue participating in this study may be re-obtained.

Are there benefits to taking part in the research?

It is hoped that knowledge gained from this research may benefit others who are trying to quit smoking in the future. You will not directly benefit from your participation in this research.

What other options are there?

You have the option to not participate in this study.

What about privacy and confidentiality?

The people who will know that you are a research subject are members of the research team, and if appropriate, your physicians and nurses. No information about you, or provided by you, during the research, will be disclosed to others without your written permission, except if necessary to protect your rights or welfare (for example, if you are injured and need emergency care or when the UIC Office for the Protection of Research Subjects monitors the research or consent process).

Study information which identifies you and the consent form signed by you will be looked at and/or copied for examining the research by:

- Food and Drug Administration (FDA)
- Funding Agency
- UIC Office for the Protection of Research Subjects, State of Illinois Auditors

A possible risk of the research is that your participation in the research or information about you and your health might become known to individuals outside the research.

Paper documents will be stored in a locked filing cabinet in the Principle Investigator's lab located in the UIC College of Pharmacy in rooms 117A, 112C, and 115. Access to electronic research data will be limited to Ajna Hamidovic and her designated study team and will be stored in a secure database on password-protected computers.

The research team will be responsible for maintaining files and storing data for all subjects of the study. Researchers will write about the combined data that is gathered from the study. Any talks or papers about this study will not identify the subject. Researchers will make every effort to keep the information collected for this study confidential.

Research personnel will assign participants with a personal identification number (PIN). For the duration of the study, patients will be tracked based on their PIN, not by any personal information. Personal information from participants will be accessed on secure, password-protected electronic databases.

When the results of the research are published or discussed in conferences, no information will be included that would reveal your identity.

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.

To help us protect you and the information we will be collecting from you, this research has been given a Certificate of Confidentiality by the U.S. government. This Certificate means that researchers cannot be forced, even by courts or the police, to disclose any information about you.

The Certificate does not stop you from disclosing, or agreeing in writing to allow researchers to disclose, information about you. For example, if you would like an employer or insurer to know something about you that is documented in this research, you can write and sign a statement telling the researchers it is okay to give your employer or insurance company information.

What if I am injured as a result of my participation?

If you get ill or injured from being in the study, UIC will help you get medical treatment. You should let the study doctor know right away that you are ill or injured. If you believe you have become ill or injured from this study, you should contact Dr. Hamidovic at telephone number 312-996-8838.

You should let any health care provider who treats you know that you are in a research study. If you do seek medical treatment, please take a copy of this document with you because it may help the doctors where you seek treatment to treat you. It will also provide the doctors where you seek treatment with information they may need if they want to contact the research doctors.

You or your health insurance plan will be billed. No money has been set aside to pay the costs of this treatment. Health insurance plans may or may not cover costs of research-related injury or illness. You should check with your insurance company before deciding to participate in this research study. Costs not covered by insurance could be substantial.

UIC has not set aside any money to pay you or to pay for your treatment if you get ill or injured from being in the study. There are no plans for the University to provide other forms of compensation (such as lost wages or pain and suffering) to you for research related illnesses or injuries. The only exception to this policy is if it is proven that your injury or illness is directly caused by the negligence of an UIC employee.

By signing this form, you are not giving up any legal rights to seek compensation of injury.

What are the costs for participating in this research?

There are no costs to you for participating in this research.

Will I be reimbursed for any of my expenses or paid for my participation in this research?

You will receive a cash payment of $100 for completing each study visit. You will receive a total cash payment of $200 for completing both study visits.

You will receive your payment at the end of the study in cash.

Can I withdraw or be removed from the study?

If you decide to participate, you are free to withdraw your consent and discontinue participation at any time without affecting your future care at UIC.

You have the right to leave a study at any time without penalty.

The study team also has the right to stop your participation in this study without your consent if:

- They believe it is in your best interests;
- You were to object to any future changes that may be made in the study plan;
- The sponsor of the research has decided to stop the research,
- If you do not follow the study procedures
- If new information is identified

Who should I contact if I have questions?

Contact Dr. Hamidovic and her research team at 312-996-8838 or cedar@uic.edu

- if you have any questions about this study or your part in it,
- if you feel you have had a research-related injury (or a bad reaction to the study treatment), and/or
- if you have questions, concerns or complaints about the research..

What are my rights as a research subject?

If you have questions about your rights as a research subject or concerns, complaints, or to offer input you may call the Office for the Protection of Research Subjects (OPRS) at 312-996-1711 or 1-866-789-6215 (toll-free) or e-mail OPRS at uicirb@uic.edu.

What if I am a UIC student?

You may choose not to participate or to stop your participation in this research at any time. This will not affect your class standing or grades at UIC. The investigator may also end your participation in the research. If this happens, your class standing or grades will not be affected. You will not be offered or receive any special consideration if you participate in this research.

What if I am a UIC employee?

Your participation in this research is in no way a part of your university duties, and your refusal to participate will not in any way affect your employment with the university, or the benefits, privileges, or opportunities associated with your employment at UIC. You will not be offered or receive any special consideration if you participate in this research

Remember:

Your participation in this research is voluntary. Your decision whether or not to participate will not affect your current or future relations with the University. If you decide to participate, you are free to withdraw at any time without affecting that relationship.

Signature of Subject

I have read (or someone has read to me) the above information. I have been given an opportunity to ask questions and my questions have been answered to my satisfaction. I agree to participate in this research. I will be given a copy of this signed and dated form.

_____ _____

Signature Date

_____

Printed Name

_____ _____

Signature of Person Obtaining Consent Date (must be same as subject's)

_____

Printed Name of Person Obtaining Consent