Official Title: SNIFF Multi-Device Study 2 - Study of Nasal Insulin to Fight Forgetfulness
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Wake Forest®
School of Medicine

DEPARTMENT/SECTION OF INTERNAL MEDICINE/GERONTOLOGY & GERIATRIC MEDICINE
ROENA B. KULYNYCH CENTER FOR MEMORY AND COGNITION RESEARCH

STUDY OF NASAL INSULIN TO FIGHT FORGETFULNESS
SNIFF Multi - Device Study 2

Informed Consent Form to Participate in Research
Suzanne Craft, PhD Principal Investigator

SUMMARY

You are invited to participate in a research study. The purpose of this research is to determine the ability of three different devices that deliver medications through the nose (Aptar CPS, VP7 and the UDSI device) to deliver insulin to the brain effectively. These devices have not received approval from the FDA for how they will be used in this study.

You are invited to be in this study because you have expressed an interest in participating in a research study. Your participation in this research will involve 3 visits and last about 2 – 3 hours each over approximately the next 2 months.

Participation in this study will involve using one device to administer insulin through your nose (intra-nasally). All research studies involve some risks. A risk to this study that you should be aware of is a drippy nose. There is no benefit to you from participating in this study.

Your participation in this study is voluntary. You do not have to participate in this study if you do not want to. There may be other choices available to you. Some other choices may include not participating in this study and to continue to follow up with you doctor. You will not lose any services, benefits, or rights you would normally have if you choose not to participate.

The remainder of this form contains a more complete description of this study. Please read this description carefully. You can ask any questions if you need help deciding whether to join the study. The person in charge of this study is Dr. Suzanne Craft. If you have questions, suggestions, or concerns regarding this study or you want to withdraw from the study her contact information is: [redacted].

If you have any questions, suggestions or concerns about your rights as a volunteer in this research, contact the Institutional Review Board at [redacted] or the Research Subject Advocate at Wake Forest at [redacted].

INTRODUCTION

You are invited to be in a research study because you are a healthy adult with no signs of memory impairment or because you have mild cognitive impairment or MCI. Research studies are designed to gain scientific knowledge that may help other people in the future. Your participation is voluntary. Please take your time in making your decision as to whether or not you wish to participate. Ask your study doctor or the study staff to explain any words or information contained in this informed consent document that you do not understand. You may also discuss the study with your friends and family.

WHY IS THIS STUDY BEING DONE?

Insulin is a hormone that is produced in the body. It works by lowering levels of glucose (sugar) in the blood.

During this study, we will determine the effects of 20 and 40 International Units of insulin on memory, blood and cerebral spinal fluid administered intra-nasally using either the CPS, VP7 or UDSI Aptar device. Spinal fluid is a clear, colorless fluid which protects your brain and spinal cord.

Insulin is approved by the US Food and Drug Administration (FDA). However, using it in this way is experimental.

HOW MANY PEOPLE WILL TAKE PART IN THE STUDY?

A total of 30 people, 15 healthy individuals with no memory impairment and 15 individuals with mild memory impariment will take part in this study here at Wake Forest Baptist Health. In order to identify the 30 subjects needed, we may need to screen as many as 50 people because some will not qualify to be included in the study.

WHAT IS INVOLVED IN THE STUDY?

You will be randomized to receive either 20 or 40 International Units during your baseline study visit and you will receive the opposite at visit 3.

Insulin will be administered with either the CPS, VP7 or UDSI Aptar device. You will be randomly assigned to a device. The device assigned will not change during your participation. For example, if you are assigned the CPS device at baseline, the CPS device will be used at visit 3.

Randomization means that you are put into a group by chance. It is like flipping a coin: you will have a one in two chance of being placed in either group. In this study you will receive both, 20 and 40 International Units of insulin. However, you and the study team will not know which dose you receive first or second.

Neither you nor the investigator will know which dose you are receiving. This is done so that a fair evaluation of results can be made. This information is available to the researchers if needed in an emergency.

Your participation will involve coming to the Sticht Center for Healthy Aging and Alzheimer's Prevention at Wake Forest Baptist Medical Center up to 3 times over the next 6 weeks. During this time, you will complete the series of measurements below. If you have had an evaluation with the Sticht Center within 12 months, you may only need to attend two visits. During your visits you will be asked to:

- Give blood samples (up to 3 times)
- Have a physical exam (1 time)
- Take tests of memory/thinking and answer questions about your daily activities (up to 3 times)
- Undergo a lumbar puncture (LP) (2 times)
- Have an electrocardiogram (ECG) (1 time). An ECG measures the electrical signals from your heart

As a part of the study, we will provide you with ECG and blood test results that you may give to your physician. These tests can reveal more information about your heart, blood sugar, cholesterol levels, liver function, and kidney function. We will advise you to consult with your physician if your tests suggest that you have a medical problem.

In the future, research on your specimen may involve whole genome sequencing.

DESCRIPTION OF STUDY VISITS

The following procedures will be completed during your screening visit: safety labs, screening cognitive testing, ECG, physical exam, collection of demographics, medications and medical history. If you have participated in a research study with the Alzheimer's Disease Research Center at Wake Forest School of Medicine within the last 12 months, you may not have to repeat all of the screening procedures. Data used during the completion of the previous study will be used in order to avoid duplicating those procedures. Other procedures that occur during and upon completion of the SNIFF Device Study will be completed as described.

You will be asked to fast (no food or drinks except water) for 8 hours prior to 2 visits during your participation in this study.

During your participation, we may need to request medical records from your primary care doctor. We will ask you to sign a medical records release form giving us permission to request these records if needed.

SCREENING VISIT

After review of this consent form, you will have the opportunity to ask questions about this study. After your questions have been answered, you will be asked to sign this consent form.

If this information has not previously been collected within the past 12 months, we will complete the following:

- Memory screening
- Collection of demographic information
- Collect a list of current medications
- Medical history
- Vital signs - such as pulse, heart rate and blood pressure
- Height and weight will be measured
- Physical exam, including a nasal examination
- Electrocardiogram (ECG) will be completed
- About 2 teaspoons of blood will be drawn

Blood Collection: Approximately 2 ½ teaspoons of blood will be drawn from a vein for routine laboratory tests to ensure that there are no other medical conditions that might interfere with your participation. In the event any of your lab results fall just outside of the required range, you may be asked to return to the clinic for a repeat blood collection. About 1 teaspoon will be drawn for optional DNA storage and to determine your apolipoprotein (ApoE) genotype.

Previous studies have shown that the ApoE gene may be linked to how well some people do on memory tests and can also identify volunteers who may have an increased risk of developing AD. However, this test alone does not predict who will or will not develop AD as there are many other factors involved. The ApoE test is for research purposes only; you will not receive the results and they will not become part of your medical record.

This visit will last between 3 and 4 hours.

BASELINE VISIT 2

This visit will take approximately 2 hours to complete. You will be asked to fast for 8 hours prior to this visit.

Visit 2 includes the following:

- A nasal exam will take place
- You will receive a dose of 20IU insulin or 40IU insulin administered with one of the three Aptar devices
- We will review your current medications and any changes in your health since your last visit
- A brief memory test will be completed
- About 3 teaspoons of blood will be collected
- A lumbar puncture will be performed

Study staff will call you the following day after your baseline visit to see how you are.

VISIT 3

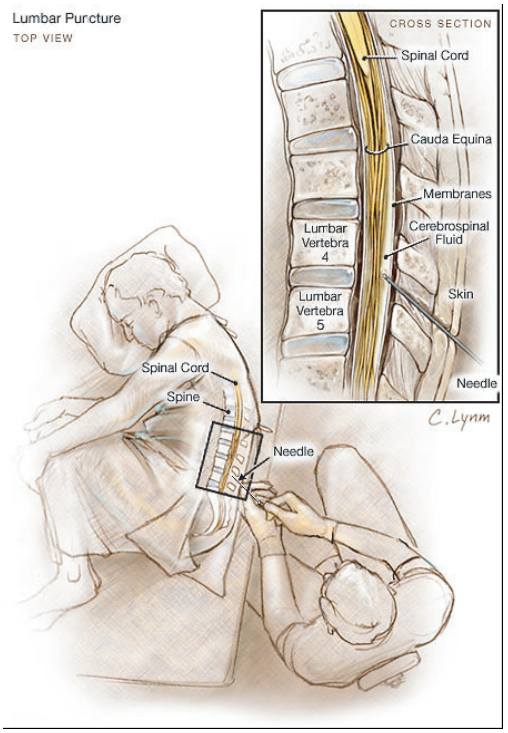
This visit will take approximately 2 hours to complete and will occur from 2 to 6 weeks after Visit 2. You will be asked to fast for 8 hours prior to this visit.

Visit 3 includes the following:

- A nasal exam will take place
- You will receive a dose of 20IU insulin or 40IU insulin administered with one of the three Aptar devices
- We will review of your current medications and any changes in your health since your last visit
- A brief memory test will be completed
- About 3 teaspoons of blood will be collected
- A lumbar puncture will be performed

Study staff will call you the following day to see how you are.

LUMBAR PUNCTURE



An LP is a procedure in which a small amount of the fluid that surrounds the brain and spinal cord is removed from the lower back. You will be asked not to eat or drink anything other than water for at least 8 hours before the lumbar puncture visit. However, because you will need to be well hydrated, please drink plenty of water. You will be positioned sitting up and bent forward or lying on your side and your lower back will be cleaned with antiseptic. Local anesthetic (lidocaine, 1%) will be injected into the skin of your lower back. When the area is numb, a very thin needle will be inserted into the spinal canal in the lower back, well below the level where the spinal cord ends, and about 25 milliliters (less than 2 tablespoons) of fluid will be removed. Your body replaces this spinal fluid within 1-2 hours. After the LP is complete, you will remain in the clinic while resting quietly for about half an hour. You will be given something to eat and drink and detailed instructions on self-care after the LP will be provided. Specifically, you will be asked to avoid any strenuous physical activity for 24 hours.

MEMORY ASSESSMENTS

You will be asked to do several tasks, such as remembering stories and lists of words. You may choose not to answer any questions or items in any assessment.

BLOOD COLLECTION

Approximately 10 teaspoons of blood will be drawn from a vein during your participation. Your blood will be used for routine laboratory tests and stored for future research.

APTAR DELIVERY DEVICES

The three intranasal delivery devices to be investigated in this study have been developed and extensively tested by Aptar Pharmaceuticals, a company specializing in drug delivery.

-  The CPS pump is an advanced preservative free device.
-  The VP7 pump is adapted with a long tipped Actuator.
-  The UDS pump is a single use, disposable device.

Aptar Pharma has a wide range of nasal spray devices used for the administration of allergy, cough & cold and intra-nasally administered vaccinations.

How Long Will I Be in the Study?

You will be in the study for about 2 months. You can stop participating at any time. If you decide to stop participating in the study, we encourage you to talk to the investigators or study staff first to learn about any potential health or safety consequences.

What Are the Risks of the Study?

Being in this study involves some risk to you. You should discuss the risk of being in this study with the study staff. Risks and side effects related to your participation in this study are outlined below:

Nasal Insulin Administration

No serious adverse reactions to insulin given through the nasal passages have been observed in similar studies. Insulin given in this manner has not been associated with low blood sugar in our previous studies.

A few subjects in previous studies complained of "drippy nose" after being given the study drug, but these symptoms did not persist beyond the initial use of the study drug. As with any drug, there may be unexpected side effects that we are not aware of.

Risks associated with use of the nasal devices

There are risks that may occur from use of the nasal device, although these are not expected to be serious, as the study nurse will be present to assist if needed. Risks may include discomfort to your eyes, face and/or nose. These risks are not long lasting and will subside without medical treatment.

Blood Collection

Removal of blood by a needle and syringe poses a small risk of pain or bruising at the site of the needle stick, but this is temporary. Some people may experience fainting or dizziness, and there is also a slight risk of infection at the site of the needle stick. To minimize these risks, experienced medical personnel will collect all blood and sterile conditions will be maintained. About 10 teaspoons of blood will be taken during the entire course of this study and your body will readily produce new blood to make up for the loss.

Cognitive Testing

Memory tests may be slightly frustrating or produce fatigue and boredom.

Lumbar Punctures (LP)

During and after the procedure, you may have temporary pain or discomfort at the insertion site in your back. You may feel faint. You may experience a mild headache, backache or sore muscles in your neck from the positioning required for the procedure. Rarely, a low pressure headache may develop after the procedure due to leakage of spinal fluid. If this headache persists it may require additional treatment. Uncommonly a blood patch (injection of some of your blood into the puncture site to patch the spinal fluid leak) may be required. This typically relieves the headache immediately. Because we use a very small, specialized needle in our study, the risk of a low pressure headache after a lumbar puncture is less than 1-2%.

Although very rare, it is possible that you may have an allergic reaction to the local anesthetic (lidocaine l%) used for the LP. This would cause swelling and a rash on your skin where the anesthetic was injected. Please tell us if you have ever had a reaction to local anesthetic before (such as when you were visiting the dentist). Potential but very rare risks of an LP include infection of the skin or in the spinal fluid space (meningitis), bleeding, or damage to nerves in your back. The risk of these is very small. To minimize these risks, the LP procedure will be performed by experienced medical professionals who are specifically trained to carry out this procedure.

OTHER POTENTIAL RISKS

There also may be other side effects that we cannot predict. You should tell the research staff about all the drugs, vitamins and supplements you take and any medical conditions you have. This may help avoid side effects, interactions and other risks.

CONFIDENTIALITY

Taking part in this research study may involve providing information that you consider confidential or private. Efforts, such as coding research records, keeping research records secure and allowing only authorized people to have access to research records, will be made to keep your information safe. We will do our best to protect your confidential information.

FUTURE RESEARCH & STORAGE OF BIOLOGICAL SAMPLES

If you agree to participate in this study, blood and spinal fluid will be stored and used for future research to learn more about other diseases. Your samples will be obtained in the Sticht Center at Wake Forest Baptist Medical Center. The samples will be stored at Wake Forest Baptist Medical Center. Your samples may be shared with other researchers when that is the best way to advance scientific knowledge and public health. The National Institutes of Health (NIH) and other central repositories have developed special data (information) banks that collect the results of genetic studies, especially when the research looks at all or large sections of individual's genetic code. This is often called whole genome sequencing. Genomic information relates to the structure and function of all of the genetic material in the body. These central banks will store your genetic information and give them to other qualified and approved researchers to do more studies. The data that we share with federal repositories will be coded in such a way that you would not be able to be identified. We will not share your name, birth date, or any other information that could directly identify you. The link to the code would be kept securely at the Wake Forest Baptist Health. Even so, there is a possibility that when your genomic information is combined with other information available to researchers, either now or in the future, they may be able to identify a group you belong to (like an ethnic group or a disease population) or, less likely, you personally. NIH prohibits people from trying to identify individuals whose genomic information is in an NIH-designated repository.

Your blood and spinal fluid samples will be used only for research and will not be sold. The findings from this research may result in the future development of products that are of commercial value. There are no plans to share any of the profits with you which may occur as a result of the research.

We do not think that there will be further risks to your privacy and confidentiality by sharing your genetic information with these banks. However, we cannot predict how genetic information will be used in the future. The genetic data could be used to study a wide variety of diseases.

ARE THERE BENEFITS TO TAKING PART IN THE STUDY?

If you agree to take part in this study, there may or may not be direct benefit to you. We hope the information learned from this study will benefit other people in the future. Potential benefits of participating in this study are insulin administered intra-nasally may enhance your memory performance. The results of the study will be used to guide the development of future studies of intranasal insulin as a therapy for Alzheimer's disease and memory loss.

WHAT OTHER CHOICES ARE THERE?

This is not a treatment study. You may choose not to participate.

WHAT ABOUT MY HEALTH INFORMATION?

In this research study, any new information we collect from you about your health or behaviors is considered Protected Health Information. Some of the information we will collect for this research study includes**:**

- demographic information
- social security number (required in order to receive travel reimbursement)
- emergency contact information
- medical record release form (required if we need to request your medical records)

If this research study involves the diagnosis or treatment of a medical condition, then Protected Health Information collected from you during this study may be placed in your medical record, and may be used to help treat you, arrange payment for your care, or assist with Medical Center operations.

We will make every effort to keep your Protected Health Information private. We will store records of your Protected Health Information in a cabinet in a locked office or on a password protected computer.

Your personal health information and information that identifies you ("your health information") may be given to others during and after the study. This is for reasons such as to carry out the study, to determine the results of the study, to make sure the study is being done correctly, to provide required reports and to get approval for new products.

Some of the people, agencies and businesses that may receive and use your health information are the research sponsor; representatives of the sponsor assisting with the research; investigators at other sites who are assisting with the research; central laboratories, reading centers or analysis centers; the Institutional Review Board; representatives of Wake Forest University Health Sciences and North Carolina Baptist Hospital; representatives from government agencies such as the Food and Drug Administration (FDA) or the Office of Human Research Protections (OHRP), the Department of Health and Human Services (DHHS) and similar agencies in other countries.

Some of these people, agencies and businesses may further disclose your health information. If disclosed by them, your health information may no longer be covered by federal or state privacy regulations. Your health information may be disclosed if required by law. Your health information may be used to create information that does not directly identify you. This information may be used by other researchers. You will not be directly identified in any publication or presentation that may result from this study unless there are photographs or recorded media which are identifiable.

Monitors, auditors, IRB or other regulatory agencies will be granted direct access to the participant's original medical record for verification of clinical trial procedures or data, without violating confidentiality of the participant and to the extent permitted by other applicable laws.

If required by law or court order, we might also have to share your Protected Health Information with a judge, law enforcement officer, government agencies, or others. If your Protected Health Information is shared with any of these groups it may no longer be protected by federal or state privacy rules.

Any Protected Health Information collected from you in this study that is maintained in the research records will be kept for an indeterminate period of time. This authorization does not expire. You will not be able to obtain a copy of your Protected Health Information in the research records until all activities in the study are completely finished.

You can tell Dr. Suzanne Craft that you want to take away your permission to use and share your Protected Health Information at any time by sending a letter to this address:

Dr. Suzanne Craft
[redacted]

However, if you take away permission to use your Protected Health Information you will not be able to be in the study any longer. We will stop collecting any more information about you, but any information we have already collected can still be used for the purposes of the research study.

By signing this form, you give us permission to use your Protected Health Information for this study.

If you choose to participate in this study, your medical record at Wake Forest University Baptist Medical Center will indicate that you are enrolled in a clinical trial. Information about the research and any medications or devices you are being given as a participant may also be included in your medical record. This part of the medical record will only be available to people who have authorized access to your medical record. If you are not a patient at this Medical Center, a medical record will be created for you anyway to ensure that this important information is available to doctors in case of an emergency.

A description of this clinical trial will be available on http://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 Web site at any time.

Laboratory test results and other clinically relevant medical reports created as a result of your participation in the research study may be entered into the computer systems of Wake Forest University Health Sciences and North Carolina Baptist Hospital. These will be kept secure, with access to this information limited to individuals with proper authority, but who may not be directly involved with this research study.

A North Carolina Baptist Hospital (NCBH) medical record will be created for all study participants.
Information about your participation in the study will be placed in the NCBH medical record, along with any routine medical test results that were obtained at NCBH as part of this study.

WHAT ARE THE COSTS?

There are no costs to you for taking part in this study. All study costs, including any study drugs and procedures related directly to the study, will be paid for by the study. Costs for your regular medical care, which are not related to this study, will be your own responsibility.

WILL YOU BE PAID FOR PARTICIPATING?

You will receive $100 for the completing the Baseline Visit 2 and $100 for completing Visit 3 for a total of $200.

To receive payment, you must provide your social security number, name and address so that we can comply with IRS (Internal Revenue Service) reporting requirements. When payments are reported to the IRS we do not let them know what the payment is for, only that you have been paid. If you do not wish to provide this information you can still take part in this study but you will not be paid.

WHO IS SPONSORING THIS STUDY?

This study is being sponsored by the Sticht Center for Healthy Aging and Alzheimer's Prevention at Wake Forest School of Medicine.

WHAT HAPPENS IF YOU EXPERIENCE AN INJURY OR ILLNESS AS A RESULT OF PARTICIPATING IN THIS STUDY?

Should you experience a physical injury or illness as a direct result of your participation in this study, Wake Forest University School of Medicine maintains limited research insurance coverage for the usual and customary medical fees for reasonable and necessary treatment of such injuries or illnesses. To the extent research insurance coverage is available under this policy the reasonable costs of these necessary medical services will be paid, up to a maximum of $25,000. Wake Forest University Baptist Medical Center holds the insurance policy for this coverage. It provides a maximum of $25,000 coverage for each claim and is limited to a total of $250,000 for all claims in any one year.

The Wake Forest University School of Medicine, and the North Carolina Baptist Hospitals, Incorporated does not assume responsibility to pay for these medical services or to provide any other compensation for such injury or illness. Additional information may be obtained from the Medical Center's Director of Risk and Insurance Management, at [redacted].

If you are injured, the insurer may require information such as your name, social security number, and date of birth in order to pay for your care. This is because the insurer is required by law to report any payments made to cover the care of any persons who are members of a government insurance plan to the Department of Health and Human Services.

You do not give up any legal rights as a research participant by signing this consent form. For more information on medical treatment for research related injuries or to report a study related illness, adverse event, or injury you should call Dr. Suzanne Craft at [redacted] (after hours number [redacted], ask for the Geriatrician on call and reference the SNIFF Multi-Device 2 study).

WHAT ARE MY RIGHTS AS A RESEARCH STUDY PARTICIPANT?

Taking part in this study is voluntary. You may choose not to take part or you may leave the study at any time. Refusing to participate or leaving the study will not result in any penalty or loss of benefits to which you are entitled. If you decide to stop participating in the study, we encourage you to talk to the investigators or study staff first to learn about any potential health or safety consequences. The investigators also have the right to stop your participation in the study at any time. This could be due to unexpected reactions to the study drug, failing to follow instructions or if the study is stopped early.

Information that identifies you may be removed from the data or specimens that are collected as part of this study and could be used for future research or shared with other without additional consent.

Clinically relevant research results will be disclosed to you. Results may include ECG results and routine laboratory results.

You will be given any new information we become aware of that would affect your willingness to continue to participate in the study.

WHOM DO I CALL IF I HAVE QUESTIONS OR PROBLEMS?

For questions about the study or in the event of a research-related injury, contact the study investigator, Dr. Suzanne Craft at [redacted] (after hours number [redacted], ask for the Geriatrician on call and reference the SNIFF Multi-Device 2 study).

The Institutional Review Board (IRB) is a group of people who review the research to protect your rights. If you have a question about your rights as a research participant, or you would like to discuss problems or concerns, have questions or want to offer input, or you want to obtain additional information, you should contact the Chairman of the IRB at [redacted].

You will be given a copy of this signed consent form.

SIGNATURES

I agree to take part in this study. I authorize the use and disclosure of my health information as described in this consent and authorization form. If I have not already received a copy of the Privacy Notice, I may request one or one will be made available to me. I have had a chance to ask questions about being in this study and have those questions answered. By signing this consent and authorization form, I am not releasing or agreeing to release the investigator, the sponsor, the institution or its agents from liability for negligence.

We can send copies of your test results to your personal physician. Even if you do not wish to have any of your medical information sent to your physician, you can still participate in this research study.

Do you request that we send important medical findings from your study ECG and/or laboratory tests to your personal physician?

[ ] Yes [ ] No _____Initials_____

Subject Name (Printed):_____

Subject Signature: _____ Date: _____Time:_____ am pm

Person Obtaining Consent:_____ Date:_____ Time:_____ am pm

Legally Authorized Representative Name (Print):_____

Relationship to the Subject:_____

Legal Representative Signature: _____ Date:_____ Time:_____ am pm

The above named Legally Authorized Representative has legal authority to act for the research subject based upon (specify health care power of attorney, spouse, parent, etc.)