University of Pittsburgh

Continence Research Unit
Division of Geriatric Medicine
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CONSENT TO ACT AS A SUBJECT IN A RESEARCH STUDY

TITLE: Investigation of brain mechanisms involved in the Urinary Continence mechanism associated with aging

PRINCIPAL INVESTIGATOR:

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If you have any questions about your rights as a research subject or wish to talk to someone other the research team, please call the University of Pittsburgh Human Subjects Protection Advocate toll-free at 866-212-2668.

SOURCE OF SUPPORT: NIH (National Institute on Aging)

If you have any emergency medical concerns arising from this study outside of office hours please call Dr Tyagi at 412-715-6280 (available 24 hours).

Key Information:

- You are being asked to take part in a research study. Research Studies include only people who choose to take part. The study team members will explain the study to you and will answer any questions you might have. You should take your time to make your decision
- This is a 2-visit study to better understand the brain's role in bladder control, each lasting 2-3 hours for which you are paid
- You will undergo a full health history, short physical exam, ultrasound bladder scan and bladder catheterization during an MRI scan
- Risks include potential for Urinary tract infection (UTI) due to catheter insertion, and potential side effects from antibiotics given to prevent a UTI
- There will be no direct benefit to you from participating in the study. However, this study will help researchers learn more about the brain's role in bladder control and it is hoped that this information will help in the treatment of future patients with conditions like yours.
- If you decide not to participate in this research, your other choices may include:
    - Getting treatment or care for Urgency Urinary Incontinence without being in a study
    - Taking part in another study
    - Getting no treatment

Study summary

We would like to better understand the brain's role in bladder control in both continent (able to control the bladder) and incontinent (unable to control the bladder), younger and older, adult women. We hope that knowledge gained from this study will enable development of novel therapies for treatment of Urinary Urge Incontinence.

We will enroll 220 women, aged 18-45 and 65+ years old, who have urgency urinary incontinence (a sudden strong urge to urinate that is hard to stop and results in urine leakage). and those who do not have urgency urinary incontinence.

Your Study Involvement

If you agree to participate, and are eligible, you will be asked to come to our office 2 times over the next 2-4 weeks.

Because we are committed to educating the next generation of clinicians and researchers, health sciences students who have received appropriate instruction about

privacy and confidentiality of medical information may attend study visits as observers, but you may refuse to have these observers present.

Here we describe the research procedures which will be carried out at each study visit:

Visit 1 (1-2 hours):

Steps 1-3 may be conducted over the phone or in the office, dependent on COVID restrictions. Steps 4-6 will be conducted in our office. You will complete step 7 at home between visits.

1. Informed consent: An introduction to the study, and how you will participate and we will ask you to sign these consent forms.
2. Health and bladder history: Collect information about you, your medical history, and your bladder habits or problems. We also will ask questions to test your mental ability.
3. MRI screen: We will ask about medical implants and anything else that might prevent you from getting an MRI.
4. Uroflow and dip: You will empty your bladder into a special toilet that measures how much urine you pass and how fast. We will measure what remains in the bladder by ultrasound and test for infection (infection is the invasion and multiplication of microorganisms such as bacteria, viruses, and parasites that are not normally present within the body) and pregnancy using a dipstick (a thin, plastic stick with strips of chemicals on it is placed in the urine to detect abnormalities). Pregnancy testing will only be done during this visit if you suspect there is a possibility you may be pregnant. If the pregnancy test determines you are pregnant, you will be excluded from the study.
    - Ultrasound: Gel will be applied to your abdomen and the researcher will press a small device on your abdomen to capture images of your bladder to measure what remains in the bladder
5. Urinalysis (conditional): If the dip procedure indicates or suggests infection, a catheterization specimen (urine collected through a tube that has been placed into your bladder, which may cause brief discomfort) will be sent for urinalysis and culture. If positive, you will be advised to see your PCP for treatment.
6. Physical examination: A short physical examination by a nurse or physician, including height, weight, and blood pressure measurement. If you report significant prolapse (a bulge occurring between the legs when muscles and tissues supporting the pelvic organs [the uterus, bladder, or rectum] become weak or loose) beyond the vaginal opening you will not be eligible for the study. If

you are unsure, with your permission, the research nurse will visually inspect the extent of the prolapse.

7. Voiding diary: We will ask you to keep a record of every time you urinate or lose control of your urine for 3 days between visits. We will also give you a set of weighed pads in Ziploc bags, to wear for 24 hours, changing them (and replacing used pads in their bags) when you go to the bathroom. You will bring these back with you to visit 2.

Withdrawal Plan: If you're currently taking anticholinergic/beta-3 agonists, in order to participate you need to be willing to go off these medications for 4 weeks prior to your second (MRI) visit. There's no problem going off these medications and you can stop them immediately—it does not require a taper. You will be able to restart this medication (if you so wish) immediately after the visit. You are free to discuss this with your PCP, if you wish, before stopping the medication.

In the event of a positive pregnancy test, you will be excluded from the study.

Visit 2 (approximately 3 hours)

You will be asked to come back to the Continence Research Unit at Montefiore where you will be screened by a short MRI screening questionnaire and have your urine tested for infection; if you have a urinary infection you will not be able to continue until it is treated. We will have you put on a gown and using a lubricating jelly, two small soft tubes will be passed side-by-side into your bladder, secured by tape to your legs (these will be used to fill and empty the bladder and to measure pressure). Following this you will be escorted to the Magnetic Resonance Research Center (MRRC) at Presbyterian University Hospital through an indoor connecting tunnel. The following will be performed:

- MRI screening: The MRRC will perform their final screening procedures (similar to the questions in the first study visit).
- MRI scan: You will lie in the scanner and be given a squeeze ball to let us know if you want to exit the scanner. You will also have a pushbutton to communicate if your bladder is full or uncomfortable. We can talk to you via intercom.
    - We will first scan your brain with an empty bladder (around 25 minutes).
    - We will then fill your bladder until you let us know that it feels full.
    - We will then scan your brain while your bladder is filled and emptied with a small amount of extra fluid 4 times in the course of about a minute. *If you signal that you are uncomfortable we will pause, or stop the whole*

procedure if necessary. Then we will ask you about what sensations you felt in your bladder.

You will be in the scanner for about an hour, and no more than 75 minutes.

- End of visit: The catheters will be withdrawn and you will get up and go to the bathroom in the usual way, emptying your bladder into a measuring container in the toilet. Your bladder will then be checked by ultrasound to ensure it is empty. We will also ask you if you felt anxiety in the scanner.

Medication: You will receive an antibiotic pill (i.e. ciprofloxacin or trimethoprim/ sulfamethoxazole nitrofurantoin or cephalexin) before the scan and a dose for the following day to protect you from any subsequent infection. You may not be allowed to continue with the study if you do not want to take this medication.

Three days after this visit we will contact you by telephone to make sure that you are emptying your bladder normally and comfortably and that you are experiencing no other problems that might be related to the study.

The whole procedure will take approximately 3 hours.

Study Risks

The possible risks of this research study may be due to the drugs used in the study and/or the bladder tests (urodynamics).

As with any investigational study, there may also be adverse events or side effects that are currently unknown and it is possible that certain of these unknown risks could be permanent, serious or life threatening.

Medications

All of the drugs used in this study are Food and Drug Administration (FDA) approved for use in standard medical care and are administered in standard doses. None of them are experimental. For all medications, however, there is a rare risk of an allergic or anaphylactic reaction. Early symptoms of this may include flushing (warmth and redness of the skin), itching (often in the groin or armpits), and hives. These symptoms are often accompanied by a feeling of anxiety and sometimes a rapid, irregular pulse. Symptoms of rhinitis or asthma may occur causing a runny nose, sneezing, and wheezing, which may worsen the breathing difficulty. Vomiting, diarrhea, and stomach cramps may develop. Throat and tongue swelling may occur resulting in hoarseness, difficulty swallowing, and difficulty breathing. There may be a drop in blood pressure, lightheadedness, or even loss of consciousness. Such risks are rare; other risks for each medication are outlined below.

Nitrofurantoin (Macrobid/Macrodantin)

- **Common – nausea, headache**
- **Rare – hepatitis, – pulmonary hypersensitivity (cough, chills, fever)**
- **Rare – clostridium difficile diarrhea. If this occurs, it can be treated with an antibiotic.**

Trimethoprim/sulfamethoxazole (Bactrim)

- Common – rash, itching
- Infrequent – muscle and joint aches
- Rare – clostridium difficile diarrhea. If this occurs, it can be treated with an antibiotic.

Cephalexin (Keflex)

- Infrequent -nausea, diarrhea, vomiting, heartburn, stomach pain, rectal or genital itching, dizziness, extreme tiredness, agitation, confusion, headache, joint pain
- Rare - watery or bloody stools, stomach cramps, or fever during treatment or for up to two or more months after stopping treatment, rash, itching, hives, swelling of the face, throat, tongue, lips, and eyes, difficulty breathing or swallowing, wheezing, a return of fever, sore throat, chills, or other signs of infection, hallucinations (seeing things or hearing voices that do not exist)

Ciprofloxacin (Cipro)

- Infrequent – nausea, diarrhea
- Rare – clostridium difficile diarrhea. If this occurs, it can be treated with an antibiotic.

MRI scanning

The MRI scanner uses a large magnet and radio signals to take pictures of your brain. No harmful radiation is involved. There are no known risks from the MRI. Some people may experience a mild twitching sensation. You will not be able to participate if any of the following risk factors are present or suspected:

- Claustrophobia (a fear of tight enclosed spaces which affects 2-5% of the population). If you experience this in the scanner, the scan can be stopped immediately, and you can be removed from the scanner in a short amount of time if necessary.
- interference with devices such as pacemakers
- metallic prostheses, aneurysm clips or any other metal objects in the body

The Magnetic Resonance Research Center is in Presbyterian Hospital with standard

emergency equipment and access to other hospital facilities.

Earplugs are used for all participants to minimize the noise, which sounds like a loud banging.

Catheterization

During fMRI two urethal catheters are inserted to measure bladder pressure and to fill and empty the bladder. There is a low likelihood of urinary tract infection and transient bacteremia (bacteria in the blood stream). Both are uncommon but must be treated to avoid severe consequences. We will therefore follow the protocol used in our unit for >15 years with an excellent safety record, documenting only two urinary tract infections possibly related to urodynamics in over 600 studies.

Urodynamic monitoring during MRI

Urodynamic monitoring is routinely used to investigate lower urinary tract (the bladder and urethra which is the tube that carries urine from your bladder out of the body) function. This study is different from normal urodynamics as we are monitoring while we scan your brain and we are filling your bladder in different ways by testing one long fill against several short fills. The examination is conducted by an experienced investigator, with a nurse or a physician present throughout.

Common risks:

- A small amount of blood in the urine for a brief amount of time after the test.
- A feeling of burning or stinging sensation when you pass urine, for a few hours or one or two days after the test (one in ten people).
- Discomfort on inserting the catheter (this take a few seconds). To minimize the risk we use lubricant jelly to pass the bladder catheter

Rare risks:

- Introduction of a urine infection into the bladder (less than one in one hundred); minimized by using strictly sterile (germ-free) conditions and giving you prophylactic antibiotics.
- Introduction of an infection into the blood stream; minimized by using strictly sterile (germ-free) conditions and giving you antibiotics.
- Fainting during the test.

Text Messages and Emails:

- You may receive text messages and/or emails for this study. Text messages and emails may not be encrypted or secure during their transmission or storage and it is possible they could be intercepted and used by others not associated with this study.

Questionnaire Completion

Answering questionnaires may cause you to feel uncomfortable.

Breach of Confidentiality

Paper-based records are kept in a secure location and are accessible only to personnel involved in the study. Computer-based files will be made available only to personnel involved in the study through the use of access privileges and passwords. Prior to being granted access to any study-related information, personnel will be required to sign statements agreeing to protect the security and confidentiality of such information. Whenever feasible, identifiers will be removed from study-related information. Precautions are in place to ensure that the data is secure through the use of passwords.

Data storage

Since we store all the information that we have collected from you in these visits, there is a risk of breach of confidentiality. To protect against this, paper-based records are kept in a secure location and are accessible only to personnel involved in the study. Computer-based files will be made available only to personnel involved in the study through the use of access privileges and passwords. Prior to being granted access to any study-related information, personnel will be required to sign statements agreeing to protect the security and confidentiality of such information, and adhere to HIPAA (Health Insurance Portability and Accountability Act) guidelines. Whenever feasible, identifiers will be removed from study-related information.

Study Benefits to You

There are no direct benefits to you from taking part in the study. You may experience some satisfaction from taking part in a study that may ultimately improve understanding and treatment of incontinence. Sometimes examining incontinence

patterns in detail can help you better implement strategies to cope with leakage. This is not a treatment study. Please consult your physician for treatment options.

You will be promptly notified if any new information we learn during this research study may cause you to change your mind about continuing to participate in the study.

Compensation

You will be compensated for taking part in this research study as follows.

- Visit 1: $40
- Visit 2: $150
- Transportation (up to $10) and parking each visit

The study team will discuss the payment options with you.

If you are unable to complete a visit (i.e. detected UTI) you will be given the transportation and parking reimbursement. If you participate in research procedures (i.e. catheterization/MRI) you will be fully reimbursed regardless of successful completion of the visit (e.g. if you find the procedure too uncomfortable).

Since you are being compensated for your participation in this study, your name, address, and social security number will be released to the Accounting Office. If the total reimbursement for your participation in research is greater than $600 in a year, this will be reported to the Internal Revenue Service (IRS) as income.

Payment for Procedures

Neither you nor your third-party insurance provider will be billed for any of the research procedures. The study will pay for all research services and procedures, including MRI, laboratory tests of urine, urodynamic monitoring, and medications administered for the purposes of the study.

Privacy and Confidentiality

Where is the data kept?

All information we collect will be stored in research records (not your medical records). It will be accessible to the investigators listed on the first page of this form and their research study staff. All written and printed records about your involvement in this research study will be stored in a file cabinet in a locked room in the continence research unit. Electronic records will be accessed using password-protected computers and saved on a central server, all of which are protected by UPMC/ University of Pittsburgh firewalls and data safety regulations. Only de-identified data will be used for analysis.

When we publish the results of the study, the publications will not include any information that would make it possible to identify you.

Who will have access to the data?

In addition to the investigators listed on the first page of this consent form and their research staff, the following individuals will or may have access to your identifiable medical record information related to your participation in this research study:

- Authorized representatives of the University of Pittsburgh Office of Research Protections may review your identifiable medical record information for the purpose of monitoring the appropriate conduct of this research study.
- Authorized representatives of the UPMC hospitals or other affiliated health care providers may have access to your identifiable medical record information in the event of an emergency.
- In unusual cases, the investigators may be required to release your identifiable research information (which may include your identifiable medical record information) in response to an order from a court of law. If the investigators learn that you or someone with whom you are involved is in serious danger or potential harm, they will need to inform, as required by Pennsylvania law, the appropriate agencies.
- Authorized representatives of the sponsor of the study, National Institutes of Health, may review or obtain your identifiable information (which may include identifiable medical record information) for the purpose of monitoring the accuracy and completeness of the research data and for performing required scientific analyses of the research data. While the NIH understands the importance of maintaining the confidentiality of your identifiable medical record information, UPMC and the University of Pittsburgh cannot guarantee the confidentiality of this information after it has been obtained by the NIH.
- Data from this study may be shared with other investigators, but no personal identifiers will be shared.
- We may use your baseline and MRI data from STUDY19090167: Trospium-MRI brain-bladder if you have already participated in that other research study.

The investigators may continue to use and disclose, for the purposes described above, identifiable information (which may include your identifiable medical

information) related to your participation in this research study for as long as it may take to complete this research study.

We are also requesting your authorization or permission to review your medical records in order to determine if you are eligible for the study. Only records pertaining to the participant's eligibility to have an MRI and nothing will be placed in the medical record. This identifiable medical record information will be made available to members of the research team for an indefinite period of time.

How long will the data be kept?

Per University of Pittsburgh, policy all research records will be maintained for at least 7 years following final reporting or publication of a project.

Can I access the data?

You are permitted access to information resulting from your participation in this research study that is contained in your research file. This will include such data as the questionnaires you have filled out, results of urine testing and your MRI scan.

Your research information may be shared with investigators conducting other research. This information may be identifiable.

Your information and biospecimens (even if identifiers are removed) may be used for commercial profit; however, you will not retain any property rights, nor will you share in any money that the investigators, the University of Pittsburgh, or outside agencies may receive.

You will not be notified of any individual research results.

De-identified data may be shared with other investigators with similar interests in the future.

Certificate of Confidentiality

This research is covered by a Certificate of Confidentiality from the National Institutes of Health. This means that the researchers cannot release or use information, documents, or samples that may identify you in any action or suit unless you say it is okay. They also cannot provide them as evidence unless you have agreed. This protection includes federal, state, or local civil, criminal, administrative, legislative, or other proceedings. An example would be a court subpoena. There are some important things that you need to know. The Certificate DOES NOT stop reporting that federal, state or local laws require. Some examples are laws that require reporting of child or elder abuse, some communicable diseases, and threats to harm yourself or others. The Certificate CANNOT BE USED to stop a sponsoring United States federal or state government agency from checking records or evaluating programs. The Certificate DOES NOT stop disclosures required by the federal Food and Drug Administration (FDA). The Certificate also DOES NOT prevent your information from being used for other research if allowed by federal regulations. Researchers may release information about you when you say it is okay. For example, you may give them permission to release information to insurers, medical providers or any other persons not connected with the research. The Certificate of Confidentiality does not stop you from willingly releasing information about your involvement in this research. It also does not prevent you from having access to your own information.

Your physician may be involved as an investigator in this research study. Before agreeing to participate, or at any time during your study participation, you may discuss your care with another doctor who is not associated with this research study. You are not under any obligation to participate in any research study offered by your physician.

Voluntary Participation

Your participation in this research study is entirely voluntary. You may want to discuss this study with your family and friends and your personal physician before agreeing to participate. If there are any words you do not understand, feel free to ask us. The investigators will be available to answer your current and future questions.

Whether or not you provide your consent for participation in this research study will have no effect on your current or future relationship with the University of Pittsburgh. Whether or not you provide your consent for participation in this research study will have no effect on your current or future medical care at a UPMC hospital or affiliated health care provider or your current or future relationship with a health care insurance provider.

Withdrawal from the Study

You can, at any time withdraw from this research study; you can also withdraw your authorization for us to use your identifiable medical information for the purposes described above. This means that you will also be withdrawn from further participation in this research study. Any identifiable research or medical information obtained as part of this study prior to the date that you withdrew your consent will continue to be used and disclosed by the investigators for the purposes described above.

To formally withdraw from this research study, you should provide a written and dated notice of this decision to the principal investigator of this research study at the address listed on the first page of this form.

Your decision to withdraw from this study will have no effect on your current or future relationship with the University of Pittsburgh or on your current or future medical care at a UPMC hospital or affiliated health care provider or your current or future relationship with a health care insurance provider.

It is possible that you may be removed from the research study by the researchers. You may be withdrawn if 1) related or not related to study procedures, your health status changes during study and makes you clinically unstable (i.e. acute cardiac or respiratory failure, diagnosis of cancer, major depression etc.). 2) a serious illness (cardio-respiratory failure, cancer or else) is diagnosed during the study and medical intervention is necessary; you may be able to continue the study after treatment of some adverse effects or reversible conditions e.g., urinary tract infection. 3) non-compliance with study procedures (i.e. completing bladder diary, taking meds).

Compensation for Injury

University of Pittsburgh investigators and their associates who provide services at UPMC recognize the importance of your voluntary participation to their research studies. These individuals and their staff will make reasonable efforts to minimize, control, and treat any injuries that may arise as a result of this research.

If you believe that the research procedures have resulted in an injury to you, immediately contact the Principal Investigator who is listed on the first page of this form. Emergency medical treatment for injuries solely and directly related to your participation in this research study will be provided to you by the hospitals of UPMC. Your insurance provider may be billed for the costs of this emergency treatment, but none of those costs will be charged directly to you. If your research-related injury requires medical care beyond this emergency treatment, you will be responsible for the costs of this follow-up care. At this time, there is no plan for any additional financial compensation. You do not, however, waive any legal rights by signing this form.

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.

VOLUNTARY CONSENT

The above information has been explained to me and all of my current questions have been answered. I understand that I am encouraged to ask questions, voice concerns or complaints about any aspect of this research study during the course of this study, and that such future questions, concerns or complaints will be answered by a qualified individual or the study coordinator, Kandy Newell at 412-647-1271.

I understand that I may always request that my questions, concerns or complaints be addressed by a listed investigator. I understand that I may contact the Human Subjects Protection Advocate of the IRB Office, University of Pittsburgh (1-866-212-2668) to discuss problems, concerns, and questions; obtain information; offer input; or discuss situations that occurred during my participation.

By signing this form I agree to participate in this research study and provide my authorization to share my medical records with the study team. A copy of this consent form will be given to me.

_____	_____
Participant's Name (Printed)	Location (phone/in-person)
_____	_____
Participant's Signature (phone consent)	Date
_____	_____
Participant's Signature (in person)	Date

CERTIFICATION of INFORMED CONSENT

I certify that I have explained the nature and purpose of this research study to the above-named individual(s), and I have discussed the potential benefits and possible risks of study participation. Any questions the individual(s) have about this study have been answered, and we will always be available to address future questions as they arise. I further certify that no research component of this protocol was begun until after this consent form was signed.

_____	_____
Printed Name of Person Obtaining Consent	Role in Research Study
_____	_____
Signature of Person Obtaining Consent	Date