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UPMC HEALTH SYSTEM
Western Psychiatric Institute and Clinic
3811 O'Hara Street
Pittsburgh, PA 15213-2593

CONSENT TO ACT AS A PARTICIPANT IN A RESEARCH STUDY

Title of Study: In vivo imaging of corticotropin-releasing factor-nociceptin receptor interactions

PRINCIPAL INVESTIGATOR:
Rajesh Narendran, M.D.
Associate Professor of Radiology and Psychiatry
B-938 PUH, PET Facility
200 Lothrop Street
Pittsburgh, PA 15213
(412) 647-0736

CO-INVESTIGATORS

James M. Mountz, Ph.D.
Professor of Radiology
B-938 PUH, PET Facility
200 Lothrop Street
Pittsburgh, PA 15213
(412) 647-0736

N. Scott Mason, Ph.D.
Associate Professor of Radiology
B-938 PUH, PET Facility
200 Lothrop Street
Pittsburgh, PA 15213
(412) 647-0736

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Why is this research being done?
This study is being done to examine an interaction between two proteins in the brain--corticotropin-releasing hormone (CRH) and nociceptin. CRH and nociceptin are used by the brain to pass messages between brain cells. Both these proteins seem to play an important role in regulating pain, stress, and reward function. Studies have reported abnormalities in both these proteins in animal models of addiction. Thus, we are interested in developing a methodology to study this interaction in humans.

Positron emission tomography (PET) is a nuclear medicine medical imaging technique that produces 3-dimensional images of the body. PET scanning will be used to examine nociceptin receptor levels in your brain after the injection of the radiotracer [^{11}C]NOP-1A. The PET scan works by measuring a very small amount of this radioactive substance in your brain. PET scans need to be corrected for the partial blockage of signal caused by body tissues. The PET signal correction can be measured by a low radiation dose computed tomography (CT) scan. A CT scan is a method to take pictures of your brain using X-rays. You will undergo two CT scans and two [^{11}C]NOP-1A PET scans in this study. In addition, following the first [^{11}C]NOP-1A PET/CT scan, you will be given an intravenous injection of hydrocortisone before undergoing the second [^{11}C]NOP-1A PET/CT scan. Hydrocortisone increases the amount of CRH in the brain. It is used in this study so that we can examine the effect of CRH on nociceptin receptors. By comparing the two [^{11}C]NOP-1A PET/CT scans (before and after hydrocortisone) done in the same day, we can understand more about how CRH and nociceptin interact in the brain. This interaction is likely critical to one's ability to manage stress and experience anxiety symptoms.

Who is being asked to take part in this research study?
You are being asked to participate in this study because you are a healthy individual. Participants in this study may be males or females, 18 – 40 years of age. Females cannot be pregnant or breast feeding an infant. This study is being performed on a total of 20 healthy individuals at this medical center.

What procedures will be performed for research purposes?
All study procedures, assessments, and clinical research evaluations are done for research purposes. If you decide to take part in this study, you will undergo the following research procedures that are not part of your standard medical care:

Screening Procedures:
Procedures to determine if you are eligible to take part in a research study are called "screening procedures". This will require you to come to the PET Facility (UPMC Presbyterian Hospital, B-wing 9th floor) for approximately 6 hours. For this research study, the screening procedures include:

1. You will receive a comprehensive psychiatric and physical evaluation before entering the study. The psychiatric evaluation will include several standard questions, computerized

tasks, and open-ended questions about your mental health. The physical evaluation will include a physical exam, heart tracing (electrocardiogram), urinalysis, and blood tests (approximately 35 ml or 2.5 tablespoons). The blood test will make sure your body chemistry is normal and if you are pregnant (women only). The urine analysis will check if there are drugs of abuse in your system. You may also be asked questions pertaining to the medical and psychiatric history of your family members without specific identifying information. The physical exam will be done by one of our doctors.

2. If you are a woman who could possibly be pregnant, you will need to have a pregnancy test prior to participation on the study day. A blood sample will be taken for this pregnancy test at screening and a urine sample on the PET scan day. Pregnant women, or women who are currently breast-feeding an infant, will not be allowed to take part in this study.

3. The screening evaluations (6 hours) will need to be completed prior to the actual PET scanning studies. The investigators will spread this 6-hour screening evaluation over multiple days, if necessary, to accommodate your schedule.

Experimental Procedures:
Once you qualify to take part in this research study, you will be required to come in to UPMC Presbyterian University Hospital (PUH) a minimum of 2 times to complete the imaging related experimental procedures: Once for MRI, which will take 2 hours, and once for PET/CT scans, which will take 8 hours. If you prefer, an effort will be made by the research team to complete the MRI and PET/CT scans in a single day. However, completing both the MRI and PET/CT scans in a single day will increase the duration of this visit to 10 hours. You will undergo the following imaging-related experimental procedures: As alcohol, drugs, and some medications (over the counter or prescription) may alter your brain chemistry and interact with hydrocortisone, you will be required not to use any of them 48 hours prior to the PET study. If you do use alcohol, drugs, or medications, please notify the research investigators. You will be required to pass a urine drug test on the day of the PET scan.

<u>MRI scan day</u>
The MRI scan will be done at the UPMC PUH MR Research Facility. A structural magnetic resonance imaging (or MRI) system will be used to take pictures of your brain before the PET scanning is done. MRI is a diagnostic test that produces pictures that look very much like x-ray pictures. A MRI machine, or scanner, uses a large magnet with no radioactive substances. The MRI scanner is a large tunnel-like machine. You will receive a urine pregnancy test to confirm that you are not pregnant for women who could possibly be pregnant. You will lie on a table that will move you into the tunnel for about 30 minutes. You will be required to lie still during the scan. The scanner makes loud, banging sounds during the study, but you will still be able to talk to and hear responses from the technician who is performing the test. MRI is routinely used in medical practices.

Because of the powerful magnet, you will be instructed to remove all jewelry and any other objects that might contain metal before entering the scan room. You will also be asked, by a nurse in the MR center, a list of questions about earlier activity that may put you at risk for having metal in your body. If there is a possibility of metal being present in your body, you will not be able to participate in this study. The MRI scan will require your lying on a narrow table that slides into a small tunnel. Because you must lie with your head and neck inside the tunnel, it is possible that you might become anxious and frightened in the enclosed space. Some people might have had such reactions of anxiety and fear in similar situations that involved enclosed spaces in the past. Should you become anxious or frightened during the study, or for any reason feel that you cannot remain in the scanner, the study will be stopped and you will be removed from the scanner.

PET/CT and hydrocortisone scan day

You will undergo the PET studies with [^{11}C]NOP-1A before and after the administration of hydrocortisone on this day. These procedures will be done at the UPMC PUH PET Research Facility.

PET scanning of the brain works by measuring a small amount of radioactive chemical (radiotracer) in different parts of the brain. You will be given the radiotracer before each PET scan. The amount of radiotracer is measured in “mCi” amounts (as a drink is measured in ounces). You will be given 12 mCi or less of the radiotracer for each scan. The radiotracer [^{11}C]NOP-1A used in this study is not currently approved by the FDA (Food and Drug Administration); however, its use in this research study is considered to be generally safe and effective and is approved by the University of Pittsburgh Radioactive Drug Research Committee in accordance with FDA regulations (21 CFR 361.1). You will receive two [^{11}C]NOP-1A PET/CT scans as part of this research study, once before and once after you are injected with hydrocortisone.

Hydrocortisone is measured in "milligrams, mg". The amount of hydrocortisone you receive will be adjusted according to your body weight (measured in kilograms, Kg). You will be injected with 1 mg/kg body weight of hydrocortisone via an intravenous (IV) line. Although IV hydrocortisone is currently approved by the FDA for the treatment of severe allergic reactions, severe asthma, adrenal gland insufficiency, certain infections, etc., it is not approved for the use proposed in this research study. You will receive one IV injection of hydrocortisone 1 mg/kg as part of this research study.

You will undergo the following procedures on this day:

- On arrival for the PET scanning procedures, you will receive a urine pregnancy test to confirm that you are not pregnant (for women who could possibly be pregnant); and a urine drug test and alcohol breath-analyzer to ensure you have not used any street drugs

or alcohol prior to the scan. Your blood pressure and heart rate will be checked to ensure that you are safe to receive hydrocortisone before you undergo any scan procedures.

- You will not be able to smoke during the study. However, you can drink water or non-caffeinated beverages. Light snacks will be provided during the study.

- Trained medical personnel will use a needle to place a small plastic tube in a vein in your arm. (called an "IV"). This small plastic tube will be used to inject the radiotracers and hydrocortisone during the study.

- Following this, an anesthesiologist will place another plastic tube in the artery in your wrist (called an "arterial line") so that the blood can be drawn during the study. Before inserting the plastic tube, the doctor will first use an anesthetic (lidocaine) to numb your wrist area.

- A Empatica E4 wrist band that resembles a watch will be placed on your wrist that does not have the arterial line. The purpose of this E4 wrist band is to monitor various measures of stress that affect your body (for example, heart rate and rhythm variations, skin electrical variations, etc.) during scan procedures.

- You will be asked to lie on your back and remain very still on a PET scanner table during the scan.

- After you are positioned on the scanning table as comfortably as possible, a low-dose CT scan will be performed in a few minutes.

- [^{11}C]NOP-1A will then be injected into your body through the tube in your vein.

- [^{11}C]NOP-1A PET scan #1 (baseline condition) will begin at the time of radiotracer injection and last approximately 70 minutes.

- After this scan, you will be allowed to take a short break to get out of the scanner (approximately 5-10 min).

- You will be connected to an automated blood pressure machine that will monitor your blood pressure and heart rate.

- You will then be injected with hydrocortisone 1 mg/kg through the IV line. After the administration of hydrocortisone, your blood pressure and heart rate will be recorded every ten minutes for the first 60 minutes and then every 15 minutes (for 2 hours). In addition, you will be asked several questions about how you are feeling while on

hydrocortisone.

- You will be asked to lie back in the PET scanner and we will perform another low-dose CT scan identical to the first CT scan (approximately 3.5 hours after hydrocortisone).

- This will be followed by [^{11}C]NOP-1A PET scan #2 (post-hydrocortisone condition), which will be identical to the first PET scan (approximately 70 minutes) and occur approximately 3.5 hours after you were administered the hydrocortisone.

- Blood samples will be drawn for the entire time (20 samples during the first 2 minutes and another 15 samples during the next 70 minutes) that you are in the PET scanner for each PET scan. No more than 130 mL (about 9 tablespoons) of blood will be taken from your body. The samples will be used to determine the amount and fate of the radiotracer in blood over time (how much sticks to protein, how much broken down by the body). These samples will also be used to measure stress hormones such as cortisol that are present in your blood.

- Following the completion of the hydrocortisone and scan procedures, you will receive a physical exam and a mental status exam. These exams, as well as your blood pressure, heart rate and heart tracing (electrocardiogram), will need to be within an acceptable safe range prior to your discharge home.

- You will be asked to avoid activities that require strain on your wrist for 36 hours. This is to prevent bleeding from the area where the tube in your artery was placed.

- You will be asked to avoid the use of alcohol or drugs for 36 hours, because it may interact with the hydrocortisone.

Follow-up Procedures:
A follow-up telephone call will be made to you by the research team approximately 2-7 days after the last scan to inquire about any adverse events you may have encountered related to the scans or the hydrocortisone.

What are the possible risks, side effects, and discomforts of this research study?
As with any experimental procedure, there may be adverse events or side effects that are currently unknown and certain of these unknown risks could be serious or life threatening. Possible risks of this research study may be due to the hydrocortisone, the arterial catheter, the radiation exposure from the PET and CT scan, the [^{11}C]NOP-1A, the venous catheter and blood sampling, study questions and breach of confidentiality.

Risk of hydrocortisone: Hydrocortisone is similar to a natural hormone produced by your adrenal glands. It is a corticosteroid drug used to relieve inflammation (swelling, heat, redness and pain).

Common side effects of hydrocortisone include headache, nausea, vomiting, dizziness, insomnia, restlessness, depression, anxiety, unusual moods, increased sweating, increased hair growth, reddened face, acne, thinned skin, easy bruising, tiny purple spots, and irregular (or absent) menstrual periods. Typically, these symptoms tend to be mild and go away with time.

Hydrocortisone can also cause skin rash, swollen feet, ankles, legs, vision problems, eye pain, muscle pain and weakness, black tarry stools, unusual bleeding and severe depression. These symptoms could be indicative of severe allergic reaction (anaphylaxis), heart problems (abnormal heart rhythm, heart attacks, heart failure, etc.,), serious skin problems, precipitation of diabetes, kidney and liver problems (fluid retention, abdominal distension, bowel/bladder problems etc.,), seizure disorder, fractures of hip and shoulder bones, seizure disorder, psychiatric problems and eye problems (glaucoma, exophthalmos).

Hydrocortisone can also dampen your immune system. Thus, it is necessary for you not to undergo vaccination and avoid exposure to medical procedures that may increase your risk fungal or viral infections immediately before and after the hydrocortisone infusion.

A study physician will be available at all times to help you during and after you are injected with hydrocortisone. If you experience minor complications following the hydrocortisone injection, the study physician will manage your symptoms. This may involve administering intravenous fluids to manage your blood pressure, administering lorazepam for anxiety, etc. If you develop or experience any of the serious or extremely serious side effects to the hydrocortisone, you will be taken to the UPMC Presbyterian ER for medical treatment.

Hydrocortisone has been shown to interact with several prescription and non-prescription medications. Therefore, it is important that you inform the study investigators of any medications you take before and immediately after the study.

Lorazepam is an anti-anxiety medication. This may be used as a rescue-medication in this study if you experience increased anxiety symptoms following the hydrocortisone challenge. The most commonly noted adverse events associated with lorazepam are sedation , dizziness, weakness, and unsteadiness. Rarely, a serious allergic reaction may occur which would include: rash, itching, swelling, severe dizziness, trouble breathing.

Risk of arterial catheters: There is a very rare risk of complication from the arterial line, including slight pain, swelling, bruising at the puncture site, dizziness, fainting, bleeding, infection, or blood clot. The formation of such blood clots as a solid swelling (hematoma) in the nearby skin, soft tissue or muscle in your wrist could sometimes lead to pain. In most cases,

these hematomas resolve by themselves and are manageable with over the counter pain meds and warm compresses. However, in rare cases, they may need to be surgically removed to alleviate this pain. There is also a very rare risk of cutting off circulation to your hand, which could result in the need for surgical repair or, in rare instances, could result in the loss of use of part or all of the hand. These complications are rare and usually occur in medically ill patients who have the arterial line in their wrists for several days. In contrast, the arterial line will remain in your arm for several hours for this study. You should also be aware that repeated placements of IVs or arterial lines can increase the risk of discomfort or complications.

Lidocaine, an FDA-approved local anesthetic (numbing medicine), will be used to decrease the discomfort of having the arterial line placed. The use of Lidocaine may result in mild reactions including a metallic taste, ringing in the ear, and rarely allergic reactions. If you know you are allergic to Lidocaine or Novocain, commonly used in dental procedures, please tell the investigator. The symptoms of an allergic reaction would include excessive pain, redness or swelling near the site of injection, a body rash after injection, or wheezing and difficulty breathing after injection.

No more than 165 ml (about 12 tablespoons) of blood will be drawn during the entire study. This total amount of blood drawn is less than a typical blood donation and unlikely to cause any serious health risks.

Placement of arterial lines for PET research at the University of Pittsburgh has been performed over 1000 times without serious complications such as ischemia (decrease in blood supply) or permanent injury. Only experienced medical personnel place these arterial lines to minimize these risks.

Risks of Radiation Exposure: The study procedures will result in exposure to radiation from the CT component of the PET/CT scans and from the two injections (12 mCi/injection) of the [C-11]NOP-1A. The total amount of radiation exposure that you will receive from the PET scan procedures is equivalent to a uniform whole body dose of 0.42 rem (a unit of radiation exposure). This dose is less than 10 % or 1/10th of the annual whole body radiation exposure (5 rems) permitted for radiation workers by federal regulations. Each additional CT scan, if required, will result in a uniform whole body radiation dose of 0.016 rem. There is no known minimum level of radiation exposure that is recognized as being totally free of the risk of causing genetic defects (cellular abnormalities) or cancer.

Studies involving radiation are discouraged during pregnancy because of potential risk to the fetus. Hence, it is important that you not become pregnant within a few days prior to your participation in the PET scanning procedures (which would not be detected by a pregnancy test) or during your participation in the PET scanning procedures (if performed over multiple days). Avoiding sexual activity is the only certain method to prevent pregnancy. However, if you choose to be sexually active, you should use an appropriate “double barrier” method of birth

control (such as female use of a diaphragm, intrauterine device (IUD), or contraceptive sponge, in addition to male use of a condom) or the female should be using prescribed "birth control" pills, injections, or implants at least two weeks prior to the PET/CT scans. At screening and the day of the PET scan, women must have a pregnancy test showing negative results. Women who are currently nursing will not be permitted to participate in this study.

The risk associated with the amount of radiation exposure you will receive during this research study is considered low and comparable to everyday risks. Because the investigators assume that this study represents the only research exposure to radiation that you will be exposed to, it is important that you inform the investigators if you have participated in other research studies during the past year or if your job results routinely in exposure to radiation.

Risk of [11C]NOP-1A: There is a rare risk you may experience an allergic reaction such as rash, shortness of breath and itching from the radiotracer injection of [^{11}C]NOP-1A.

Risks of venous catheter and venous blood sampling: There is a rare risk associated with the chance of infection and a more common risk of slight bruising, bleeding, soreness, dizziness and fainting associated with taking blood from a vein.

Risks of MRI: If you are known to have metal inside your body, e.g., aneurysm clips or pacemakers, you will be excluded from the study because the magnet in the MR scanner can cause these to move. Participants with dental fillings can be studied without risks. Infrequently, heart rhythm disturbances can arise in those who have previous heart rhythm abnormalities. Infrequently people become claustrophobic (highly fearful of the small space) while in the machine. If you experience such sensation, the staff will stop the procedure immediately and you will be quickly removed from the scanner. During the MRI, you will be in voice contact with the staff at all times.

Risks of the Study Questions: We will be asking you many questions concerning your feelings, emotions, and behaviors at different stages of the study (i.e., screening day and PET/CT scan day). Assessments are done so that we can monitor your physical and emotional states during the study. The only infrequent risk to you from these questions is that sometimes people can feel uncomfortable about discussing their personal issues. On the other hand, most people find this process to be a very positive experience. However, if for any reason you do not want to share your feelings and emotions on certain issues during the study, let the interviewers know and they will stop asking further questions.

Risks of Breach of Confidentiality: Breaches in confidentiality could impact future insurability, employability if there is a medical or psychiatric illness that you may have that may be exposed inadvertently during the screening process. To minimize these risks, a study code number will be assigned to you so you will not be identified by your name. This will ensure your

confidentiality. The study code will be used to identify your data. All data collected will be kept in locked file cabinets in a locked and secured area.

What are possible benefits from taking part in this research study?
You will not receive any direct benefit from your participation in this research study. It is possible the imaging methods developed in this study will be used to study brain chemistry in psychiatric and neurological illnesses in the future.

If I agree to take part in this research study, will I be told of any new risks that may be found during the course of the study?
You will be promptly notified if any new information develops during the conduct of this research study, which may cause you to change your mind about continuing to participate.

Will my insurance provider or I be charged for the costs of any procedures performed as part of this research study?
None of the services and/or procedures (MRI, PET Scan, blood tests, hydrocortisone or examinations) you receive during this research study will be billed to you or your health insurance. If you get a bill or believe your health insurance has been billed for something that is part of the study, notify a member of the research team or UPMC Patient Billing Services.

Will I be paid if I take part in this research study?
You may receive up to $1100 for taking part in this study. If you have completed all of the written assessments, the interview with the physician, the physical exam, laboratory screening with blood work, EKG and then ruled as not eligible for continued participation in the study or you decide to discontinue your participation in the study, you will be paid $100 for your time. You will receive $50 for completion of the structural MRI. You will receive $100 for completion of the arterial line. You will receive $150 for completion of the hydrocortisone. You will receive $250 for the completion of each PET scan in this study. You will receive a $200 bonus for completion of all the above listed procedures. In addition, you will be reimbursed for any parking fees related to your participation in this study.

Payment received as compensation for participation in research is considered taxable income for a research subject. If payments are more than $600 in any one calendar year, the University of Pittsburgh is required to report this information to the Internal Revenue Service (IRS). Research subject payments exceeding $600 during any calendar year will result in a 1099 (Miscellaneous Income) form being issued to the research subject and a copy will be sent to the IRS.

If the researchers have access to some of your data (for example, a MRI scan) from the recent participation in a research study with them, and decide it does not need to be repeated again, you will not be compensated for these procedures that are not performed (as per payment schedule listed above).

Who will pay if I am injured as a result of taking part in this research study?
University of Pittsburgh researchers and their associates who provide services at the University of Pittsburgh Medical Center (UPMC) recognize the importance of your voluntary participation in their research studies. These individuals and their staffs will make reasonable efforts to minimize, control, and treat any injuries that may arise as a result of this research. If you believe that you are injured as a result of the research procedures being performed, please immediately contact the Principal Investigator or a co-investigator 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 the UPMC. It is possible that the UPMC may bill your insurance provider for the costs of this emergency treatment, but none of these 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 unless otherwise specifically stated below. There is no plan for monetary compensation. You do not, however, waive any legal rights by signing this form.

Who will know about my participation in this research study?
Any information about you obtained from or for this research study will be kept as confidential (private) as possible. All paper records that could identify your involvement in this research study will be stored in a locked file cabinet. All electronic records that could identify your involvement will be stored in password-protected files. All blood samples collected during the scan will be stored in a locked freezer at the PET Facility. These samples that will be identified only by a code number will be stored till completion and analysis of all your study results (less than 2 years). Your identity on these records and any blood samples collected will be indicated by a case number rather than by your name. Your de-identified blood samples may be sent to outside laboratories that perform specialized analysis (such as cortisol assays). Although it is highly unlikely, there is still the possibility that information on your identity could be linked back to your research information. For this reason, additional protections will be taken with the information linking the case numbers with your identity. For example, information linking case numbers to your identity will be kept separate from the research records in locked or password-protected files. Access to your research records will be limited to the researchers listed on the first page of this form and authorized representatives of the University of Pittsburgh. It is also possible that data from this study may be shared with other investigators who are interested in addiction and imaging. You will not be identified by name in any publication of the research results.

Data Sharing and Re-contacting:
Your identifiable data (which include your clinical assessments, MRI, etc) and medical record information (which include your medical and psychiatric diagnosis, lab work, etc.,) will be shared with other imaging studies that you have consented to participate within Dr. Narendran's

research group. The sharing of such data may allow for the researchers to not have to repeat some of these experimental procedures on you again.
The de-identified data (without any information that could identify you) gathered in this study may be combined with other similar de-identified data gathered in separate studies performed here at UPMC or at other research centers in a secure, password-protected database managed by the investigators of this study. This combined, de-identified data and (without any information that could identify you) may form the basis of scientific publications and may be shared in the future with researchers within or outside of UPMC who are interested in studying neuroimaging in relation to neuropsychiatric disorders.

Will this research study involve the use or disclosure of my identifiable medical information?
This research study will involve the recording of past, current and/or future identifiable medical information from your hospital and/or other outpatient records. The information that will be recorded will be limited to information concerning your medical history as it relates to inclusion/exclusion, previous MRI or CT scans, and results of any blood tests. This information will be used for the purpose of identifying whether you meet the conditions for participation in this study.

This research study may result in identifiable information that will be placed into your medical records held at the UPMC. The nature of the identifiable information resulting from your participation in this research study that will be recorded in your medical record includes the results of pregnancy tests (for women of childbearing potential) and tests done on blood samples taken during the screening visit.

Who will have access to identifiable information related to my participation in this research study?
In addition to the investigators and funding agency listed on the first page of this authorization (consent) form and their research staff, the following individuals will or may have access to identifiable information (which may include your identifiable medical information) related to your participation in this research study:

- The staff of the University of Pittsburgh Medical Center PET facility and MUH-CTRC will have access to your identifiable research information (which may include your identifiable medical information) for the purpose of performing the PET studies and monitoring done as part of this protocol.

- Authorized representatives of the University of Pittsburgh Research Conduct and Compliance Office may review your identifiable research information (which may include your identifiable medical information) for the purpose of monitoring the appropriate conduct of this research study.

- In unusual cases, the investigators may be required to release identifiable information (which may include your identifiable medical information) related to your participation in this research study 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 of potential harm, they will need to inform, as required by Pennsylvania law, the appropriate agencies.

- Authorized representatives of the U.S. Food and Drug Administration may review and/or obtain identifiable information (which may include your identifiable medical information) related to your participation in this research study because of this agency's oversight of the research use of radiotracers and hydrocortisone. While the U.S. Food and Drug Administration understands the importance of maintaining the confidentiality of your identifiable research and medical information, the University of Pittsburgh and UPMC cannot guarantee the confidentiality of this information after it has been obtained by the U.S. Food and Drug Administration.

- Authorized representatives of the UPMC hospitals or other affiliated health care providers may have access to identifiable information (which may include your identifiable medical information) related to your participation in this research study for the purpose of (1) fulfilling orders, made by the investigators, for hospital and health care services (e.g., laboratory tests, diagnostic procedures) associated with research study participation; (2) addressing correct payment for tests and procedures ordered by the investigators; and/or (3) for internal hospital operations (i.e. quality assurance).

- Authorized representatives of the Sponsor of this research which is the National Institute of Health may review and/or obtain identifiable information (which may include your identifiable medical information) related to your participation in this research study because of this Sponsor's obligation to fund and regulate this research

For how long will the investigators be permitted to use and disclose identifiable information related to my participation in this research study?

The investigators may indefinitely 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. It is University policy that all research records be maintained for a period of at least 7 years following final reporting or publication of a project. After that time, de-identified data, which include PET and MRI images will be secured for long term retention in the PET imaging facility electronic archives.

May I have access to my medical information that results from my participation in this research study?

In accordance with the UPMC Notices of Privacy Practices document that you have been provided, you are permitted access to information (including information resulting from your participation in this research study) contained within your medical records (such as screening lab

results) filed with your health care provider unless otherwise specifically stated below. You will not have access to information generated by this research (such as MRI and PET scans), which is not part of your medical record.

Is my participation in this research study voluntary?
Your participation in this research study, to include the use and disclosure of your identifiable information for the purposes described above, is completely voluntary. (Note, however, that if you do not provide your consent for the use and disclosure of your identifiable information for the purposes described above, you will not be allowed, in general, to participate in the research study.) 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.

May I withdraw, at a future date, my consent for participation in this research study?
You may withdraw, at any time, your consent for participation in this research study, to include the use and disclosure of your identifiable information for the purposes described above. (Note, however, that if you withdraw your consent for the use and disclosure of your identifiable information for the purposes described above, you will also be withdrawn, in general, from further participation in this research study.) Any identifiable research or medical information recorded for, or resulting from, your participation in this research study prior to the date that you formally withdrew your consent may continue to be used and disclosed by the investigators for the purposes described above. Biological samples such as blood samples will be destroyed after you withdraw consent because they cannot be used by the investigators unless you complete the PET/CT scans.

To formally withdraw your consent for participation in 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 your consent for participation in this research study will have no effect on your current or future relationship with the University of Pittsburgh. Your decision to withdraw 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.

If I agree to participate in this research study, can I be removed from the study without my consent?
It is possible that you may be removed from the research study by the investigators if, for example, you are a female and your pregnancy test proves to be positive, if you are unable to

remain abstinent from drugs and alcohol, if you are claustrophobic or can not undergo the MRI scan for any reason, or if your psychological tests indicate you are not appropriate for this study.

Any identifiable research or medical information recorded for, or resulting from, your participation in this research study prior to the date that you were withdrawn from participation may continue to be used and disclosed by the investigators for the purposes described.

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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 by the investigator(s) listed on the first page of this consent document at the telephone number(s) given. 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 Subject 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 in the event that the research team is unavailable. By signing this form, I agree to participate in this research study and provide my authorization to share my medical records with the research team. A copy of this consent form will be given to me.

_____ _____
Participant's Printed Name Participant's Signature

_____
Date

CERTIFICATION OF INFORMED CONSENT:
I certify that I have explained the nature and purpose of this research study to the above-named individual and I have discussed the potential benefits and possible risks of the study participation. Any questions the individual has about this study have been answered, and we will always be available to address future questions, concerns or complaints 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