Protocol Title: PET Imaging of the Dopaminergic and Serotonergic Systems in Treated HIV Positive Subjects

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PRINCIPAL INVESTIGATOR: Dima Hammoud, M.D.

STUDY TITLE: PET Imaging of the Dopaminergic and Serotonergic Systems in Treated HIV Positive Subjects

STUDY SITE: Clinical Center

Cohort: Standard

Consent Version: 09/30/2021

WHO DO YOU CONTACT ABOUT THIS STUDY?

Principal Investigator: Dima Hammoud, MD, 301-402-3041, hammoudd@cc.nih.gov

Study Coordinator: Amanda Wiebold, RN, 301-594-5194, amanda.weibold@nih.gov

Study Coordinator: Tracy Cropper, RN, BSN, 301-402-6132, tcropper@nih.gov

This consent form describes a research study and is designed to help you decide if you would like to be a part of the research study.

You are being asked to take part in a research study at the National Institutes of Health (NIH). Members of the study team will talk with you about the information described in this document. Some people have personal, religious, or ethical beliefs that may limit the kinds of medical or research treatments they would want to receive (such as blood transfusions). Take the time needed to ask any questions and discuss this study with NIH staff, and with your family, friends, and personal health care providers. Taking part in research at the NIH is your choice.

IT IS YOUR CHOICE TO TAKE PART IN THE STUDY

You may choose not to take part in this study for any reason. If you join this study, you may change your mind and stop participating in the study at any time and for any reason. In either case, you will not lose any benefits to which you are otherwise entitled. However, to be seen at the NIH, you must be taking part in a study or are being considered for a study. If you do choose to leave the study, please inform your study team to ensure a safe withdrawal from the research.

WHY IS THIS STUDY BEING DONE?

The purpose of this research is to learn how human immunodeficiency virus (HIV) affects two chemicals in the brain, serotonin and dopamine.

BACKGROUND

Serotonin is a brain chemical that is important in mood changes, mainly depression. We do not understand yet why some people with HIV have high levels of depression and other mood problems. The serotonin system in the brain may have a connection to those problems. Previous imaging research has shown the serotonin system to be different in HIV compared to healthy uninfected subjects, especially in HIV patients who are depressed.

Dopamine is another brain chemical that is involved in movement, memory and thinking. We also do not understand yet why some people with HIV have some memory and thinking problems. The

dopamine system in the brain may have a connection to those problems. Previous imaging research has shown the dopamine system to be especially sensitive to the effects of HIV in the brain.

In this study, we will look at serotonin and dopamine in the brain of people with HIV and compare the findings to those in people without HIV. We will look at the serotonin system by positron emission tomography (PET) scan using a radioactive drug called 11C-DASB. We will look at the dopamine system by doing a PET scan using another radioactive drug called 18F-FDOPA. You may do one of those PET scans or both in this study.

STUDY POPULATION

As many as forty five people with HIV, and seventy people without HIV, will take part in this study.

PROCEDURES

Screening

If we think you can be included in this study and you are willing and able to take part, you will be asked to come to the NIH for the screening.

1. Physical Exam, if needed
2. Blood testing, if needed.
3. MRI scan, if needed
4. Client Diagnostic Questionnaire, if needed

If you had a physical exam under protocol another NIH protocol less than three months before the day of the PET scan, you will not have a repeat the exam.

If you had blood tests under another NIH protocol less than three months before the day of the PET scan, you may or may not need to repeat those tests. Blood will be drawn through a needle in your arm. We will draw no more than two teaspoons of blood during the entire study.

Client Diagnostic Questionnaire

If needed, we will ask you about your current mental health and your mental health history. We will ask you about your mood. We will ask you if you have had scary past experiences and how they have affected you. We will ask you about your history of taking drugs for fun and how much alcohol you drink. These answers will be kept strictly confidential. (No need to be repeated if performed at NIH within 3 months of planned PET scan)

Neuroimaging with Brain MRI

If needed, we will obtain a Magnetic resonance imaging (MRI) scan on your brain. MRI uses a very strong magnet and radio waves to take pictures of your brain. The MR scanner is a large long metal tube. You will lie still on a table that slides into the MR tube. You will be in the MRI scanner for about 45 minutes. While in the scanner you will hear loud knocking noises, and you will be fitted with earplugs or earmuffs to muffle the sound. You will be able to communicate with the MR staff at all times during your scan, and you may ask to be moved out of the machine at anytime.

An MRI from another NIH study might be acceptable as per the investigators' discretion. You may not need to repeat it for this study.

PET scan (either 18F-FDOPA or 11C-DASB)

After we complete screening procedures and you are found to be eligible for this study we will do PET scan (either 18F-FDOPA or 11C-DASB) for one visit. If you are eligible and decide to participate in both parts of this study (18F-FDOPA and 11C-DASB), you might have both scans on the same day or you might be asked to come for an additional visit. The scanning will be done in the PET department at the Clinical Center. Each visit will include:

1. Urine testing.
2. Blood testing, if needed.
3. Updated history and physical exam, if needed.
4. PET scan.
5. Neuropsychological testing, if needed

Urine Testing:

To determine if you are eligible for this study, we will test your urine for illegal drugs (urine toxicology). If your drug test is positive, you will be told and you might not be included in the study. The results of the drug testing will be in your NIH medical record. If you do not want this information in your medical record, you should not participate in this study. Your medical record can only be released with your written agreement. However, insurance companies may require you to release these records and may not give you insurance if you refuse.

Pregnancy Testing:

The radioactive drug used in this study can harm a developing fetus. Participants who are physically able to become pregnant will have a pregnancy test before the PET scan. You will not be able to participate if the pregnancy test is positive.

The urine pregnancy and toxicology screening results are required prior to proceeding to the PET scan. Other test results are not required before initiating scan.

Blood Testing

If you had blood tests under another NIH protocol or this protocol less than three months before the day of the PET scan, you may or may not need to repeat those tests.

PET Scan:

The PET scan gives information on brain chemistry and function. For the 18F-FDOPA PET scan, you will be asked to fast for 4-6 hours prior to the scan. If you are diabetic and taking oral medications or long acting insulin, we will ask you to take your medications as usual. If you take short acting insulin before meals, we will ask you to not take the insulin until your meal after the scan. If you feel your sugar is low at any point during the fasting period, we will check your blood sugar levels. The maximum fasting time will be seven and a half hours, which includes the time in the scanner. One hour before the scan begins you will receive one pill (carbidopa) which helps direct the 18F-FDOPA tracer to your brain. You can eat normally after the end of the scan.

For the 11C-DASB scan you will not be asked to fast.

The PET scanner is shaped like a doughnut. You will lie on a bed that slides in and out of the scanner.

You will have an intravenous (IV) catheter placed for either PET scan.A needle will be used to guide a thin plastic tube (catheter) into one of your arm veins. The needle will be removed, leaving only the catheter in the vein. The catheter will be taped to the skin to hold it in place. The IV will be used to inject the 11C-DASB or 18F-DOPA tracers. The scan duration after either injection will be an hour and a half.

Once the scan is over, we will ask you to empty your bladder and drink a lot of fluids. We will also ask you to empty your bladder every two hours thereafter for the rest of the day.

If you are eligible and you agree to participate in both studies, both scans might be done on the same day or on separate days:

- If the scans are scheduled on the same day, we will ask you to fast for 4-6 hours before the second scan (18F-FDOPA). Your blood tests (if needed) and urine tests will be performed only once. You will have the first scan early in the day (11C-DASB). At the end of the first scan, we will ask you to empty your bladder. You can then take a break until one hour before the second scan. At that time, you will receive one pill (carbidopa) which helps direct the 18F-FDOPA tracer to your brain. One hour later you will have the second scan (18F-FDOPA). At the end of the second scan, we will also ask you to empty your bladder again and every two hours thereafter for the rest of the day. You can eat normally after the end of the second scan.
- If the scans are scheduled on separate days, you will then follow the instructions for each scan separately. You will only have to fast for the 18F-FDOPA scan. We may not repeat your blood studies if you had the required blood studies done as part of this protocol (18-CC-0117) or as part of 13-N-0149 (ALL HANDS protocol) within three months from the date of the second scan.

Neuropsychological Testing:

If needed, we will test your memory, attention, concentration, and thinking. We may ask you about how you feel. You will be interviewed, complete questionnaires, take pen and paper or computerized tests, and perform simple actions. The testing can take up to 4 hours. If you have had these tests within one year, we might be able to use those results instead of repeating the tests. However, we may need to repeat some or all of the tests if the outside tests are different from ours or if your thinking has changed since the testing was done.
Your neuropsychological testing data will be entered into a research database. If other NIH investigators want to study your neuropsychological testing data, the NIH study team may send your results to them. The study team may share information such as your gender, age, health history, or ethnicity when necessary.

STORAGE AND SHARING OF SAMPLES AND DATA

A. Your blood and urine test results, your imaging data and your neuropsychiatric data will be stored securely on the NIH campus. Your name and identifying information will not be on the test results and data. The test results and data will either have a code that links to your identifying

information or will be stored without a code linking them to you. If they are coded, the key to the code will be kept at NIH in a separate, secure area and will not be shared.

B. Your blood and urine tests results, your imaging data and your neuropsychiatric data may be shared with others, including those not at NIH. Your data may be sent to a repository for storage and may be released for research purposes. Some repositories restrict access to the samples and data they contain to researchers and projects they approve. Some repositories permit unrestricted access. The samples and data may be used for other research projects, including those not related to HIV. If you do not want your samples and data used for other projects, you should not participate in this study. Research using data from this study may lead to new tests, drugs, or devices with commercial value. You will not receive any payment for any product developed from research using your data.

C. If you withdraw from this research study before it is done, we will keep and continue to use samples and data that have already been collected. Your privacy will be protected as much as possible.

Banking and Sharing of Identified Samples or Data:

If you are enrolled in other studies, your imaging data and results from your blood, urine and neuropsychiatric tests may be shared with investigators of those studies. The test results and imaging data may be shared with your name and identifying information. Sharing these data and samples will help minimize your need to repeat procedures if data or samples are already collected.

RISKS, INCONVENIENCE AND DISCOMFORTS

History and Physical Examination:

There is minimal medical risk or discomfort from the physical exam.

Urine Sample:

There is minimal medical risk or discomfort from giving a urine sample

Intravenous Line:

You may have some discomfort and bruising from the needle insertion. Some people feel light-headed or faint. The risks of an intravenous catheter also include bleeding, infection, or inflammation of the skin and vein with pain and swelling. These will be treated if they occur.

Carbidopa administration prior to 18F-FDOPA scan:

There are no reports of adverse events when carbidopa is given once at the dose used in this PET scan (18F-FDOPA).

Radiation Safety:

This research study involves exposure to radiation from one PET scan with up to 20 millicuries of radioactive 11C-DASB. This radiation exposure is not required for your medical care and is for research purposes only. The amount of radiation you will receive in this study is 0.52 rem which is below the guideline of 5 rem per year allowed for research subjects by the NIH Radiation Safety Committee. If you complete all the studies that require radiation in the referring protocol and participate in the other PET study in this protocol (18F-FDOPA), your maximum total radiation

exposure will be 1.4 rem, which is also below the guideline of 5 rem per year allowed for research subjects by the NIH Radiation Safety Committee. The average person in the United States receives a radiation exposure of 0.3 rem per year from natural sources, such as the sun, outer space, and the earth's air and soil. If you would like more information about radiation, please ask the investigator for a copy of the pamphlet, An Introduction to Radiation for NIH Research Subjects.

While there is no direct evidence that the amount of exposure received from participating in this study is harmful, there is indirect evidence it may not be completely safe. There may be a very slight increase in the risk of cancer.

Please tell your doctor if you have had any radiation exposure in the past year, either from other research studies or from medical tests or care, so we can make sure that you will not receive too much radiation. Radiation exposure includes x-rays taken in radiology departments, cardiac catheterization, and fluoroscopy as well as nuclear medicine scans in which radioactive materials were injected into your body.

If you are pregnant or breast feeding, you may not participate in this research study. It is best to avoid radiation exposure to unborn or nursing infants since they are more sensitive to radiation than adults.

Neuropsychiatric Testing

You may be uncomfortable talking about how you feel. Portions of the different tests may be somewhat challenging, and answering questions about memory, ability to learn and think, and mood may be difficult for you. The neuropsychological tests are not harmful but may be frustrating or stressful. No one performs perfectly on these tasks we only ask that you try your best. If you get tired or frustrated during the evaluation, you can ask for a break, you may choose not to answer every question, or you may choose to stop the testing all together.

Client Diagnostic Questionnaire

You may feel uncomfortable talking about your feelings and remembering past experiences that make you feel sad or scared. You can choose not to answer questions if you do not want to answer. You can stop the questionnaire at any time.

MRI scan

People are at risk for serious injury from the MR magnet if there is metal present. For this reason, all magnetic objects (for example, watches, coins, jewelry, and credit cards) must be removed before entering the MR scan room. You will not be able to have an MRI if you have a pacemaker or other implanted electrical device. This includes brain stimulators, some types of dental implants, aneurysm clips (metal clips on the wall of a large artery), metallic prostheses (including metal pins and rods, heart valves, and cochlear implants), implanted delivery pump, or shrapnel/metal fragments. You will be screened for these conditions before having any scan. If you are not sure if there is metal present in your body, discuss this with the research team. Those with back problems may have back pain or discomfort from lying in the scanner. The noise from the scanner can be loud enough to damage hearing, especially in people who already have hearing loss. Please discuss any hearing problems with the research team before the MRI. You will be fitted with hearing

protection and if the hearing protection becomes loose during the scan, the radiology staff can help you. There are no known long-term risks of MR scans.
Once you are on the table, we will secure your head with cushions to prevent your head from moving. You can ask us to stop the scan at any time if you feel too uncomfortable. There is no evidence that scanning at high magnetic field strengths is dangerous, but we do not know if there are any long-term effects. Some people become anxious during an MR scan because of being in a small space. If you feel anxious, you can receive lorazepam or a similar medication and you will be monitored in the outpatient clinic until it has worn off and it is safe for you the leave.

You will need to arrange for someone to drive you home or we will provide a taxi for you. Side effects of lorazepam include sleepiness, dizziness, weakness, unsteadiness, hallucinations, confusion, and rarely an allergic reaction causing rash, hives, or swelling.

It is not known if MR is completely safe for the developing fetus. Therefore, all women of childbearing potential will have a pregnancy test performed no more than 1 week before the MRI scan. The scan will not be done if the pregnancy test is positive.

Investigational use of MRI (machine, sequences and/or coils): We will be using the MRI for investigational research. This means that the way the MRI is generating the images may be different from what is normally done in a routine clinical scan. However, all studies done under this protocol will be performed within FDA safety guidelines. We also plan to use research coils (antennae). These are parts of the machine that help generate the image. This use of research tools in the MRI has not been approved by the FDA and is considered investigational. Additionally, some of the MR machines that we use are considered investigational (not yet approved by the FDA for this use) but are used within the FDA safety guidelines

Risks of Storage and Sharing of Samples and Data:

Even though we will remove information that could identify you from Blood and urine tests results and your imaging that are sent to repositories or shared, there is a very small chance that the blood and urine tests results and imaging data could be identified as yours.

ANTICIPATED BENEFITS

There is no direct benefit to you from participating in this research study. However, we hope to learn more about HIV.

RIGHT OF WITHDRAWAL AND CONDITIONS FOR EARLY WITHDRAWAL

You may withdraw from the study at any time and for any reason without loss of benefits or privileges to which you are otherwise entitled. We can remove you from the study at any time if we believe that continuation is not in your best medical interest or if you are unable to comply with the requirements of the study.

RESULTS FROM THIS STUDY

The PET imaging information we obtain from this study will not provide information on your health. You will not receive any individual results from those scans. However, we will inform you of any abnormal test results we get from your blood and urine testing.

ALTERNATIVES TO PARTICIPATION OR TREATMENT

This study does not provide treatment and does not replace any therapy that your own doctor is giving you or your child. You may choose not to participate.

COMPENSATION, REIMBURSEMENT, AND PAYMENT

Will you receive compensation for participation in the study?

Some NIH Clinical Center studies offer compensation for participation in research. The amount of compensation, if any, is guided by NIH policies and guidelines.

You will receive compensation according to the table below for a maximum of $820.

	Pay for inconvenience	Time (h)	Pay for time	Total pay
PET scan (2 possible)	150.00	3	40.00	190.00
Antecubital venous catheter (with each scan)	30.00			30.00
Blood tests (2 possible)	30.00			30.00
MRI	110.00	2	30.00	140.00
Neurocognitive Testing	100.00	4	50.00	150.00
Mental Health Questionnaire	10.00	1	20.00	30.00
Total	**Variable depending on procedures performed. Max compensation is $820**			

Compensation will be prorated for parts completed if you do not complete the study.

Employees and staff who participate during work hours must have permission from their supervisor. NIH employees must either participate outside of work hours or take leave in order to receive compensation.

With few exceptions, study compensation is considered taxable income that is reportable to the Internal Review Service (IRS). A "Form 1099-Other Income" will be sent to you if your total payments for research participation are $600 or more in a calendar year. If you have unpaid debt to the federal government, please be aware that some or all of your compensation may be automatically reduced to repay that debt on your behalf.

This study does not offer reimbursement for, or payment of, travel, lodging or meals.

Will taking part in this research study cost you anything?

NIH does not bill health insurance companies or participants for any research or related clinical care that you receive at the NIH Clinical Center.

CONFLICT OF INTEREST (COI)

The National Institutes of Health (NIH) reviews NIH staff researchers at least yearly for conflicts of interest. This process is detailed in a COI Guide. You may ask your research team for a copy of the COI Guide or for more information. Members of the research team who do not work for

NIH are expected to follow these guidelines or the guidelines of their home institution, but they do not need to report their personal finances to the NIH.

No NIH investigator involved in this study receives payments or other benefits from any company whose drug, product or device is being tested.

CLINICAL TRIAL REGISTRATION AND RESULTS REPORTING

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.

CONFIDENTIALITY PROTECTIONS PROVIDED IN THIS STUDY

Will your medical information be kept private?

We will do our best to make sure that the personal information in your medical record will be kept private. However, we cannot guarantee total privacy. Organizations that may look at and/or copy your medical records for research, quality assurance, and data analysis include:

- The NIH and other government agencies, like the Food and Drug Administration (FDA), which are involved in keeping research safe for people.
- National Institutes of Health Intramural Institutional Review Board

When results of an NIH research study are reported in medical journals or at scientific meetings, the people who take part are not named and identified. In most cases, the NIH will not release any information about your research involvement without your written permission. However, if you sign a release of information form, for example, for an insurance company, the NIH will give the insurance company information from your medical record. This information might affect (either favorably or unfavorably) the willingness of the insurance company to sell you insurance.

If we share your specimens or data with other researchers, in most circumstances we will remove your identifiers before sharing your specimens or data. You should be aware that there is a slight possibility that someone could figure out the information is about you.

Further, the information collected for this study is protected by NIH under a Certificate of Confidentiality and the Privacy Act.

Certificate of Confidentiality

To help us protect your privacy, the NIH Intramural Program has received a Certificate of Confidentiality (Certificate). With this certificate, researchers may not release or use data or information about you except in certain circumstances.

NIH researchers must not share information that may identify you in any federal, state, or local civil, criminal, administrative, legislative, or other proceedings, for example, if requested by a court.

The Certificate does not protect your information when it:

1. is disclosed to people connected with the research, for example, information may be used for auditing or program evaluation internally by the NIH; or

2. is required to be disclosed by Federal, State, or local laws, for example, when information must be disclosed to meet the legal requirements of the federal Food and Drug Administration (FDA);
3. is for other research;
4. is disclosed with your consent.

The Certificate does not prevent you from voluntarily releasing information about yourself or your involvement in this research.

The Certificate will not be used to prevent disclosure to state or local authorities of harm to self or others including, for example, child abuse and neglect, and by signing below you consent to those disclosures. Other permissions for release may be made by signing NIH forms, such as the Notice and Acknowledgement of Information Practices consent.

Privacy Act

The Federal Privacy Act generally protects the confidentiality of your NIH medical records we collect under the authority of the Public Health Service Act. In some cases, the Privacy Act protections differ from the Certificate of Confidentiality. For example, sometimes the Privacy Act allows release of information from your medical record without your permission, for example, if it is requested by Congress. Information may also be released for certain research purposes with due consideration and protection, to those engaged by the agency for research purposes, to certain federal and state agencies, for HIV partner notification, for infectious disease or abuse or neglect reporting, to tumor registries, for quality assessment and medical audits, or when the NIH is involved in a lawsuit. However, NIH will only release information from your medical record if it is permitted by both the Certificate of Confidentiality and the Privacy Act.

POLICY REGARDING RESEARCH-RELATED INJURIES

The NIH Clinical Center will provide short-term medical care for any injury resulting from your participation in research here. In general, no long-term medical care or financial compensation for research-related injuries will be provided by the NIH, the NIH Clinical Center, or the Federal Government. However, you have the right to pursue legal remedy if you believe that your injury justifies such action.

PROBLEMS OR QUESTIONS

If you have any problems or questions about this study, or about your rights as a research participant, or about any research-related injury, contact the Principal Investigator, Dima Hammoud, MD, 301-402-3041. Other researchers you may call are: Bryan Smith, MD, 301-451-4585 and Tracy Cropper, RN, BSN, 301-402-6132. You may also call the NIH Clinical Center Patient Representative at 301-496-2626, or the NIH Office of IRB Operations at 301-402-3713, if you have a research-related complaint or concern.

CONSENT DOCUMENT

Please keep a copy of this document in case you want to read it again.

Adult Research Participant: I have read the explanation about this study and have been given the opportunity to discuss it and to ask questions. I consent to participate in this study.

Signature of Research Participant	Print Name of Research Participant	Date

Investigator:

Signature of Investigator	Print Name of Investigator	Date

Witness to the oral short-form consent process only: This section is only required if you are doing the oral short-consent process and this English consent form has been approved by the IRB for use as the basis of translation.

Witness:

Signature of Witness*	Print Name of Witness	Date

***NIH ADMINISTRATIVE SECTION TO BE COMPLETED REGARDING THE USE OF AN INTERPRETER:**

____ An interpreter, or other individual, who speaks English and the participant's preferred language facilitated the administration of informed consent and served as a witness. The investigator obtaining consent may not also serve as the witness.

____ An interpreter, or other individual, who speaks English and the participant's preferred language facilitated the administration of informed consent but did not serve as a witness. The name or ID code of the person providing interpretive support is: _____.