Study Title: InformationSeekingMesolimbicEngagementStudy1

NCT Number: NCT06257446

Included Documents: Protocol, Statistical Analysis Plan, Results, and Informed Consent

Document Date: February 11th, 2026

Sponsor: Temple University/ Vishnu Murty (murty@uoregon.edu)

Protocol

Background/Objectives

Engagement of the mesolimbic dopamine system—a neuromodulatory system underlying motivation—strengthens hippocampal-dependent encoding and consolidation. In humans, mesolimbic contributions to learning have mainly been studied during reward contexts, focusing on event evoked striatal feedback responses akin to phasic signaling. However, previous work has shown that sustained mesolimbic engagement over entire task contexts is optimized for adaptive memory formation. The connections between VTA and hippocampus engage motivated behaviors for extended periods of time and increase plasticity for salient events encountered during prolonged motivational states. Open questions remain about how sustained and transient mesolimbic signaling prioritizes and stabilizes salient events in long-term memory.

Animal models have shown that information seeking relies on sustained mesolimbic engagement and that information seeking is greatest at moderate forms of uncertainty. Information seeking can be broken into two forms: unguided exploration which occurs in the absence of prior information and hypothesis testing in which individuals use prior knowledge to resolve uncertainty in a directed manner. In hypothesis testing, information seeking during uncertainty increases sustained mesolimbic engagement via hippocampal afferents, which then initiate a series of events resulting in the disinhibition of VTA neurons thus elevating their baseline firing. Information seeking therefore represents a behavior in which mesolimbic engagement facilitates plasticity at multiple time scales, which span multiple components of uncertainty resolution. However, studies have yet to explore how sustained and transient mesolimbic engagement relate to hippocampal-dependent memory encoding and consolidation. Additionally, human research has not yet characterized the memory processes that occur during information seeking. In this study, we propose a model in which VTA engagement during information seeking will bolster immediate memory and consolidation for salient events via interactions with the hippocampus

Design

We used a novel Game Show task, in which the investigators manipulate participant's agency to control their learning environment to specify unguided exploration. In the encoding session, participants play the producer for a game show. On each trial, participants are shown a trial-unique contestant (2s), and then they select one of 3 presented doors to reveal a hidden object (4 seconds). The selected door is then highlighted (2-4s), which is then removed to show a trial-unique object image, which is framed as a prize (2s). On exploration trials, participants actively select which door to open. On control trials, the participant is forced to select a highlighted door, fostering passive rather than active information seeking. Unbeknownst to participants, there is no relationship between selected doors and revealed objects, as objects are pre-selected for each trial. Thus, timing, motor demands, and visual information are fixed across conditions. Participants will complete 3 runs of both the exploration and control condition, with each run containing 20 trials. Temporal jitters are placed between cues and outcomes and between trials, as determined by design optimization software. Run will be pseudo-randomized across participants so no more than 2 runs of the same condition will appear in a row. Following

encoding, participants will complete immediate and delayed item-associative memory test. On each trial of the memory test, participants will view the characters presented during exploration and control trials as well as new foil characters. If a participant indicates that they have previously seen a character before, the participants will be shown three object images encountered during encoding, and decide which item served as a prize for that specific character. In this way, the investigators can resolve memory for contestants (i.e., cues), and associative binding across contestants and prizes (i.e., cue-outcome). Participants memory will be tested for half the stimuli immediately and at a 24-hour delay.

Recruitment Methods

Subjects will be recruited using flyers posted around Temple campus and the Greater Philadelphia area. These flyers will contain QR codes that can be scanned with a smartphone. Scanning this code will bring up a form where interested people can provide contact information for recruitment. The flyer will also include an email address where interested participants can inquire about recruitment. The flyer will include contact information, and exclusion criteria:

Advertisements may also be distributed through listservs, newsletters, and on public transportation. Recruitment materials will only be posted in private spaces (both online and in-person) and only after obtaining the appropriate permissions. Temple students will be recruited through the SONA paid-participation website. All subjects will be verbally instructed about the nature of the research and asked to sign informed consent documents approved by the IRB of Temple University. Prior to participation, each subject will have the study explained to him/her privately, be given the opportunity to read the consent document, and encouraged to ask questions to determine if he/she would like to participate. Only the PI and research assistants certified in human subjects research will obtain informed consent. We will document consent for each subject by having the PI (or research assistant) and subject sign an informed consent form approved by Temple University IRB. All subjects will be informed that they may withdraw their participation in the study at any time without penalty. Compensation for the study will include $15/hr for both in person and online behavioral sessions, and $30/hr for the fMRI sessions. Compensation will be determined by rounding up to the nearest half hour. Participant compensation will range between $30 to $90, depending on the experience and the length of their second session. There are chances for increased earnings for good performance, calculated by rounding to the nearest half hour, using half the hourly rate. In these studies, the bonus will range anywhere between $0.00 to $30.00, in addition to the hourly compensation for participation. Our previous work has suggested that financial bonuses in studies must be higher than the hourly base compensation to successfully manipulate motivation. Bonuses are calculated Subjects will receive their payments in the form of a gift card. Subjects who withdraw before they complete their participation will receive the prorated expense rate.

Inclusion and Exclusion Criteria

Inclusion Criteria: Age 18-45; No history of any neurological or Axis 1 psychiatric diseases; we will not exclude for general Mental Health history in the online study to increase variability in our personality assessments but will exclude individuals with a self-reported diagnosis with a

substance use disorder. Also required are capability of performing the experimental tasks (e.g., can read, can understand instructions, able to cooperate with behavioral and MRI data collection); and informed consent.

Exclusion Criteria: Eligibility requirements will be used for both MRI studies and in-person behavioral studies to keep the study characteristics equivalent and thus making the data more comparable. All participants will be in good medical health and will have no known history of head injury or illness with CNS implications. All participants are required to be free of medications that affect blood flow response or alertness. Smoking and coffee consumption are prohibited within 30 minutes prior to laboratory testing because of established effects on neurophysiology as measured by fMRI. Participants will have at least 20/40 far acuity (either uncorrected or corrected). For the fMRI studies, participants will fulfill these additional criteria: no cardiac pacemaker, aneurysm clip, cochlear implants, pregnancy, IUD, shrapnel, history of metal fragments in eyes, neurostimulators, weight > 250 lbs, or claustrophobia.Inclusion an exclusion criteria will be determined before study participation by using a self-report demographics form. For fMRI studies, a TUBRIC screener form will be used to determine eligibility.

Local Number of Subjects: Total enrollment for the study will be *80* participants.

Statistical Analysis Plan

Power Analyses: To determine the appropriate samples for our studiu we conducted a power analysis estimating a power =.8 and an alpha=.05. Our pilot behavioral data show that to capture a main effect of motivation on episodic memory we will need an n=30 (d=.74). To relate mesolimbic-hippocampal interactions with encoding we will need an n=68 (r^2=0.21). To make sure we have enough data when accounting for bad data quality and drop out, we propose to recruit 80 participants/study.

Behavior: Item memory will be calculated for characters appearing in high versus low motivation trials at the 24-hour memory test using d' metrics, which account for false alarm rates.

Neuroimaging: Data will be analyzed using FSL 5 to estimate task-related activity following standard 1st-level modelling, we will estimate state-based activation using a single prolonged "event" in a univariate model. For the Representational Similarity Analyses to characterize hippocampal-mesolimbic interactions, we will characterize representational similarity within regions of interest by running single-trial analyses and comparing the pattern of activity across trials that are either both from the high motivation condition or both from the low motivation condition. Regions of interest will include a collection of ROIs encompassing the hippocampus as well as Anterior-Temporal largescale networks. Statistical analyses will be implemented on R-software using the lmer function. Neuroimaging analyses will be performed on parameter estimates extracted from relevant ROIs, which avoids problems with multiple comparisons associated with whole-brain analyses.

Temple IRB Approved

01/02/2024

Protocol 29365

Funding: National Institute on Drug Abuse/NIH/DHHS

Title of research: The influence of mesolimbic-hippocampal interactions on episodic memory during active information seeking

Investigator and Department: Dr. Vishnu P. Murty, Department of Psychology

Who can I talk to about this research?

If you have questions, concerns, or complaints, or think the research has hurt you, contact the research team at:

vishnu.murty@temple.edu
(215) 204-4662
865 Weiss Hall
1701 North 13th Street
Philadelphia, Pennsylvania 19122

This research has been reviewed and approved by an Institutional Review Board. You may talk to them at (215) 707-3390 or e-mail them at irb@temple.edu for any of the following:

- Your questions, concerns, or complaints are not being answered by the research team.
- You cannot reach the research team.
- You want to talk to someone besides the research team.
- You have questions about your rights as a research subject.
- You want to get information or provide input about this research.

Research Consent Summary

You are being asked for your consent to take part in a research study. This document provides a concise summary of this research. It describes the key information that we believe most people need to decide whether to take part in this research. Later sections of this document will provide all relevant details.

What should I know about this research?

- Someone will explain this research to you.
- Whether or not you take part is up to you.
- You can choose not to take part.
- You can agree to take part and later change your mind.
- Your decision will not be held against you.
- You can ask all the questions you want before you decide.

Why am I being invited to take part in this research?

We invite you to take part in a research study because you are a healthy adult enrolled in our subject pool.

Why is this research being done?

The purpose of this study is to understand how exploring and seeking information influences how individuals recall their memories of the past, and what neural systems underlie these processes.

How long will I be in this research?

Your participation in this research study will take place at up to two time points. This includes the first session and a possible follow-up occurring 24-48 hours afterwards. Each session will last from 1-3 hours.

What happens if I agree to be in this research?

If you decide to take part in this research study, the general procedures include behavioral tasks on a computer, surveys/questionnaires about your everyday life, and having your brain scanned while completing tasks in an MRI scanner.

Is there any way being in this research could be bad for me?

There is minimal risk involved with this research. The most important risks or discomforts that you may expect from taking part in this research include metal projectile risks, burn risks and/or discomfort in the scanner due to noise or claustrophobia. Extensive screening and safety precautions are taken to minimize these risks. Additionally, you may feel discomfort answering questions on the surveys which pertain to your personal life. There is also a risk of breaching confidentiality during the study; however, data de-identification will be performed to decrease this risk.

Will being in this research benefit me?

It is not expected you will personally benefit from this research. You will however be paid at a rate of $15 an hour for behavioral sessions and $30 an hour for scanning sessions.

Detailed Research Consent

You are being invited to take part in a research study. A person who takes part in a research study is called a research subject, or research participant. In this consent form "you" generally refers to the research subject. If you are being asked as the legally authorized representative, parent, or guardian to permit the subject to take part in the research, "you" in the rest of this form generally means the research subject.

Why is this research being done?

The purpose of this study is to understand how exploring and seeking information influences how individuals recall their memories of the past, and what neural systems underlie these processes.

How long will I be in this research?

Your participation in this research study will take place at up to two time points. This includes the first session and a possible follow-up occurring 24-48 hours afterwards. The aim of the follow-up session is to assess judgments about experiences from the earlier session. Each session will last from 1-3 hours.

What happens if I agree to be in this research?

After you consent to participate, we will first generate a unique study ID for you. Data collected in this study will only be linked to your study ID. We will ask that you complete the following:

1. ***Behavioral Tasks:*** You will use a computer to view a series of abstract shapes/images, photographs, videos, auditory stimuli, or self-generated list of words and have to make judgements on these stimuli using keyboard responses. The judgements will mainly consist of deciding between items which you believe will provide the best outcome in the task, subjective judgements, or general descriptions. During these tasks, you may or may not be in control of which responses you choose.
2. ***Surveys*****:** You may be asked to fill out surveys or questionnaires asking about everyday life and your personality.
3. ***fMRI:*** You may be asked to complete fMRI tasks. This involves recording your brain activity while you are lying down. You must keep very still while you are in the scanner. It is noisy but completely painless. For these tasks, you may be asked to watch videos or make decisions about images we show on a computer screen.

Is there any way being in this research could be bad for me?

There is minimal risk in your participation in this research. You will be told if any new information is learned which may affect your condition, or influence your willingness to continue participation in this study.

There is a chance you may experience some minor discomfort during your participation. Below is a description of potential discomforts for all the activities you may participate in, and the methods used to decrease the likelihood of potential discomfort:

1. ***Behavioral Tasks:*** Performing this task poses low to no risk.
2. ***Surveys*****:** Questions will relate to your personal experiences.
3. ***fMRI:*** During an fMRI, you may feel a little scared about the tight space in the scanner. To decrease this potential discomfort, you may complete a practice fMRI scan prior to your real scan. During the real fMRI, you will have a device in your hand that will allow you to tell us if you need

attention immediately. You will be able to communicate with us and may stop the scan anytime you want by squeezing the device. The MRI itself produces loud noises that some people find uncomfortable or annoying. We will give you earplugs and/or earphones to wear, which will help block out some of the noise.

There are several short-term risks. These can be easily managed and minimized:

a) External Projectile Risks: The size and strength of MRI magnets is such that they can attract very large, very heavy iron containing objects, such as oxygen tanks, and 'suck' them to the MRI. This can cause serious injury and even death. Even smaller objects, bobby pins and nail clippers, can cause serious injury to patients in the scanner. Death due to such incidents is very rare. To protect against external projectile accidents, patients are required to remove all metal objects, including underwire bras, sometimes changing into scrubs. Other personnel are restricted from the areas near the magnet to help assure that no iron-containing materials are inadvertently brought into the MRI. Last, the scanner is operated by trained MRI technicians who are well versed in MRI safety issues.

b) Internal Projectile Risk: Metal that is embedded in bodily tissue, such as a metal plate or implanted medical device, can move or rotate, or even worse, be rapidly extruded from the body if proximal to a strong magnetic field. Swelling and irritation of skin due to motion of iron oxides in tattoo pigments is also possible. Subjects with embedded metal or tattoos on the neck and/or face will be excluded from participation.

c) Burn Risk: There is a risk of burns from medicinal patches during MRI. All subjects will be asked to remove any patches prior to the scan session. Burn risks are also associated with ECG leads, presence of piercings, or any metal cabling. Subjects will be required to remove all metal objects prior to scanning.

d) Acoustic Risk: The sound level of a typical scanner during echoplanar imaging is around 95 dB. Earplugs reduce this value by 18-29 dB. This is within the OSHA guidelines for daily exposure.

e) Gradient Field Change: This causes peripheral nerve stimulation effects that range from distracting to painful. Risk will be minimized by making sure subjects do not cross arms or legs.

f) Onset of Claustrophobia: It will be ameliorated by talking to subjects throughout the scan session and by having a panic button in the scanner.

g) Pregnancy: Although there is no known risk of MRI to pregnant women or fetuses, there is a possibility that there is some unknown risk. Therefore, women who think they may be pregnant or plan to become pregnant during the course of the study are not eligible to participate in the MRI portion of this study.

Some other potential risks include getting tired or uncomfortable from completing any of the activities. You will be encouraged to take short breaks between sessions, express any concerns and ask questions throughout the session to decrease this risk. There is also a risk of breaching confidentiality during the study; however, data de-identification will be performed to decrease this risk. If you have any questions, concerns or discomforts arising from these procedures, you are encouraged to contact Dr. Murty at (215) 204-4662.

What happens to the information collected for this research?

All of the information collected as part of the study will be de-identified. We will be collecting your full name in order to provide compensation, but your personal identification will never be connected to the study information.

Data Sharing. The data and samples from this study might be used for other, future research projects in addition to the study you are currently participating in. Those future projects can focus on any topic that might be unrelated to the goals of this study. We may give access to the data we are collecting to the general public via the Internet and a fully open database. The data we release to the general public will not contain information that can identify you. The data will not have your name on it, only a code number, so people will not know your name or which data are yours.

If you change your mind and withdraw your consent to participate in this study (you can call Dr. Murty at 215-204-4662 to do this), we will not collect any additional data about you. We will delete your data if you withdraw before it was deposited in the database. **However, any data and research results already shared with other investigators or the general public cannot be destroyed, withdrawn or recalled.**

By agreeing to participate, you will be helping the researchers and the science community. It is possible that some of the research conducted using your information eventually could lead to the development of new methods for studying brain, new diagnostic tests, new drugs or other commercial products. Should this occur, there is no plan to provide you with any part of the profits generated from such products and you will not have any ownership rights in the products.
Letting us use and share your data is voluntary. However, you must be willing to share your data in this way in order to participate in this study. If you are not willing, you cannot participate in this study.

By signing below, you agree to provide your data for future research. You agree that these may be shared with other investigators at other institutions from around the world. Any data shared with other investigators will not contain information that can identify you. The details, results, and implications of these studies are unknown. Additionally, Temple University, Temple University IRB, and the National Institute on Drug Abuse can inspect study information.

Certificate of Confidentiality. This research is covered by a Certificate of Confidentiality from the National Institutes of Health. A Certificate of Confidentiality helps protect your identifiable information and biological samples. The researchers with this Certificate may not disclose or use information, documents, or biospecimens that may identify you in any federal, state, or local civil, criminal, administrative, legislative, or other action, suit, or proceeding, or be used as evidence, for example, if there is a court subpoena, unless you have consented for this use. Information, documents, or biospecimens protected by this Certificate cannot be disclosed to anyone else who is not connected with the research except, if there is a federal, state, or local law that requires disclosure (such as to report child abuse or communicable diseases but not for federal, state, or local civil, criminal, administrative, legislative, or other proceedings, see below); if you have consented to the disclosure, including for your medical treatment; or if it is used for other scientific research, as allowed by federal regulations protecting research subjects.

What if this research has additional findings about me that were not related to the research questions?

The MRI portion of the study is done for research purposes rather than diagnosis. The brain images collected will not be routinely examined by health professionals for potential structural and functional

clinical abnormalities. However, in the event an abnormality is detected by the investigator or the MRI technician, you will be informed, and if you so desire, referred to a qualified radiologist for further examination.

What will I be paid for taking part in this research?

If you agree to take part in this research, you will be compensated $15 an hour for any behavioral sessions and $30 an hour for MRI sessions in the form of a gift card. If you decide to leave the study, you will be paid a prorated amount for your time. Compensation will be determined by rounding up to the nearest half hour. Participants compensation will range between $30-$90, depending on the length of their session. In addition to this baseline compensation, you may have an opportunity to earn a bonus of $0-$30 gift card based on your performance in this experiment. Federal tax law requires you to report this payment as income to the Internal Revenue Service. You may be asked to tell us your social security number, full name, address, or other identifying information in order to compensate you for your participation. This is because we are required to report payments more than $599.00 to the Internal Revenue Service. In this case, you will be sent a Form 1099-MISC. Your identifying information will in no way be connected to the information collected for the study.

Do not provide consent unless you have had a chance to ask questions and have received satisfactory answers to all of your questions.

Consent

Your signature documents your permission to take part in this research.

Signature of subject

Date

Printed name of subject

Signature of person obtaining consent

Date

Printed name of person obtaining consent

Please check the box below if you consent to being contacted for future studies.

☐ I give my permission for my contact data to be stored to be contacted for future studies.