Neural Basis of Sensory and Motor Learning: Functional Connections

NCT05124301

Study Protocol

June 18, 2024

Research Design

Study purpose
When interacting with objects in the environment, the brain routinely adapts perceptual and movement planning processes to compensate for changes in the environment. The neural basis is poorly understood, even in the healthy brain. The purpose of this study is to assess changes in resting state connectivity that accompany multisensory perceptual learning.

Scientific background
Human perception of hand position is multisensory. The brain can estimate it visually, from an image on the retina, and proprioceptively, from receptors in the joints and muscles. The sensory inputs determining these percepts are subject to changes in environmental factors (e.g., lighting) and internal factors (e.g., movement history). Multisensory integration of visual and proprioceptive estimates gives us flexibility to cope with such changes. For example, washing dishes with the hands immersed in water creates a spatial misalignment between vision and proprioception, as water refracts light. The brain resolves this conflict by realigning visual and/or proprioceptive estimates of hand position. The neural basis of these adaptive processes is poorly understood. The purpose of this study is to find out if multisensory changes are accompanied by changes in resting state connectivity between sensory regions of the brain and other areas.

Describe the research interactions or interventions and data collection methods for the study. Include the frequency and duration of each procedure or activity.
The study takes place in the Imaging Research Facility (IRF) in the psychology building. The first session is a familiarization session for functional magnetic resonance imaging (fMRI) and the behavioral task, and is expected to last 40-60 minutes. Subjects will first fill out screening forms to confirm the answers they gave during the initial screening, and the Edinburgh handedness inventory to quantify their handedness. If subjects are still eligible, they will lie in a mock scanner and perform the functional task: Subjects will have their left index finger taped to a wooden stick, and an experimenter from the team will manipulate the finger with the stick outside of the scanner. Subjects will respond to the different movements by pressing buttons with their right hand. Subjects will also be introduced to the behavioral task, which is performed at an apparatus in the room next to the scanner: Subjects sit in front of a touchscreen and point to targets they see in a mirror. If subjects are interested in moving on to the main session at this point, the main session will be scheduled. In the Main session, subjects will first fill out the MR safety screening form. They will then perform some practice trials of the behavioral task to remind the subject of the task. This will be followed by a short DWI scan (3 minutes), the first resting state scan of the baseline condition (12 min), the 20-30 minute baseline block of the behavioral task (control, no learning), a second resting state scan (12 min), a second 20-30 minute learning block of the behavioral task (Visuo-proprioceptive realignment, perceptual learning), and a third resting state scan (12 min). Finally, the subject will do the functional task in the scanner (same as familiarization session, 12 min. total), an anatomical scan (~6 minutes), and a final DWI scan (3 minutes). The session will conclude with some questions about the subject's subjective experience of the procedures. Including transition time in and out of the scanner, the Main session is expected to take up to 2.5 hours.

Will ongoing safety review be conducted by an independent group of individuals often called a data safety monitoring board (DSMB) or committee (DSMC/DMC)?
No

Describe the plan for conducting ongoing review of study-wide data to ensure the safety of subjects. Consider the following:

- Who will review data
- What data will be reviewed, at minimum adverse event data
- How often data will be reviewed.

The PI will be responsible for data and safety monitoring. The familiarization session is intended to weed out any subjects who might find laying in the scanner uncomfortable, but it is possible subjects who find the procedures acceptable during the familiarization will change their mind during the main session and withdraw before completing the session. If so, we would report this in annual reviews. The study team will meet at least monthly to review the study data, determine whether any events need to be reported, and discuss whether the familiarization session is sufficiently familiarizing subjects, or whether any additional risks can be identified.

Research Settings

Select all of the settings where the research interactions or interventions will take place.
IU campus

Confidentiality & Privacy

Describe the procedures that will be used to ensure confidentiality of written/paper records that contain subjects' identifiable data.
Printed identifying information consists of the signed consent form and screening forms. The MR safety screening forms will be kept in locked cabinets in the IRF. The rest will be kept in the subject's folder in a locked file cabinet in our lab (PH 079), which is also locked when we're not in there.

Describe the setting where research procedures will occur and how that protects subjects' privacy. Consider recruitment, consent, and study interventions.
Directions will be given to the subject in order for them to find the IRF, where all research procedures except initial screening will take place. Initial screening will be done by e-mail or over the phone, at the subject's choosing, using a standardized list of questions. Informed Consent will be obtained upon the first visit to the IRF prior to any study procedures taking place. Once the subject arrives in the IRF, doors will be closed and only study personnel will have access to the subject.

Eligibility and Recruitment

List the criteria that would make people eligible to be included in this study.
Potential subjects must be between the ages of 18-45 years old and right-handed. Aging has been shown to affect the morphology of sensory and motor nerves, conduction velocities of nerves, and number of motor neurons in the spinal cord; to avoid these confounding factors we will only examine younger-to middle-aged adults. There are differences in cortical function and corticospinal projections such that testing the right arm of a right-handed individual is not

necessarily equivalent to testing the left arm of a left-handed individual. To eliminate this confound, we will only test right-handed individuals. Covid has been found to have neurological effects in some people, but mostly the effects on sensorimotor control and neurophysiology are unknown. So we want to reduce the chances of inadvertently testing subjects who have covid. We will therefore only include individuals who report being free of Covid symptoms in week preceding testing.

List the criteria that would exclude people from this study.
Participants will fill out two screening forms: (1) At the familiarization session, they will fill out the in-person screening form to confirm the information they gave by e-mail or phone. The experimenter will make a preliminary eligibility determination based on this information. (2) At the main session, the subject will fill out the IRF's standard MR safety screening form, and a level 2 MR personnel will make the final eligibility determination. Both forms are included with this submission. The IRF technician will exclude subjects who have metallic, mechanical, or magnetic implants; are claustrophobic, or are unable to remain still for long periods of time; or use an intra-uterine device (IUD) whos MR compatibility has not been established. Women who are pregnant or think they might be pregnant will also be excluded, as effects of fMRI on the unborn are not known. People who have a BMI over 30 will be excluded as it may be uncomfortable or impossible to lay in the MRI scanner and reach the button box. Potential subjects will be excluded if they have any neurological disorders, or orthopedic or pain conditions in the upper limbs. We will also exclude subjects who do not have normal vision, or corrected-to-normal vision with contacts, or the imaging center does not have a pair of MRI compatible glasses that fits their prescription. In addition, we will invite subjects to reschedule if they have any of the common Covid symptoms within the last week. If they don't believe they can meet these criteria on another date, they will be excluded. After giving their consent, participants may be excluded during the study if they are unable to perform the tasks or follow instructions.

Will subjects be offered any of the following for their participation in the study? All of these are forms of payment. Select all that apply.
Cash, gift card, or check

Explain why the amount offered is reasonable in relation to the subjects' involvement in the study.
Subjects will receive a gift card after completing the main experimental session. The value will depend on the time spent: $10/hour for the familiarization session, $25/hour for the main session. Subjects who came to at least the familiarization session but were then excluded for one of the reasons above will receive partial payment. This is consistent with rate of pay for similar studies at IU.

Describe your recruitment process, including how subjects will be identified and contacted.
Main experiment: Potential subjects will initiate contact with the research staff in response to the recruitment flyers that will be electronically distributed in IU e-mail lists or electronically posted on the IU Classifieds site, or posted in appropriate physical locations around campus. The flyers invite potential participants to either visit a Qualtrics survey to receive information about the study and answer the eligibility questions, or else to e-mail the lab. If the inquiry is made by e-mail, the investigator will respond with the "Initial E-mail and Screening" message, which is included in this submission. It provides the same information and directs the person to the Qualtrics survey to determine eligibility. If they are interested in participating and meet the inclusion/exclusion criteria,

then the experimenter will send the "Follow-up to eligible subjects" message to schedule the familiarization session and remind them of the elements that may affect their choice of when to schedule.

Will any information be kept about individuals who decline participation or are found to be ineligible?
No

If a subject participates in this study, would it stop or prevent them from participating in another study?
No

Consent/Assent/Authorization

Will all or some subjects consent to participate in the research?
All subjects will consent to participate in the research.

Does your study require any research procedures to occur prior to discussing study participation with subjects?
No

Describe your typical consent process for this study.
After a subject has contacted us, had the study explained, and answered the screening questions, but prior to doing anything else related to the study, a time will be arranged for the familiarization session. The principal investigator or other key personnel will explain the study again in person and the subject will complete in-person screening form ("first visit" version) to ensure the information obtained during the initial screening has not changed. Then the consent process will begin. No one will be in the room with the subject except the investigator(s). The experimenter will review each section of the ICS with the subject in person, in the IRF, at the beginning of the first session. The subject will then have time to read the informed consent to themselves. The investigator will wait till the subject finishes reading, and then ask if they have any questions before inviting them to sign the ICS. This process will last about 15 minutes and will take place in the IRF with the doors closed.

Describe how you will protect against, or minimize, each of the risks listed in the consent document(s).
The only potential risk connected to the reaching task is fatigue or boredom. Subjects will be told to go at their own pace and ask for a break if they need it. MRI 1) This MRI scan is not a medical test. It is designed to address research questions and it is not a complete scan for any clinical purpose. If there is an abnormality, the scan, the MRI technician, or the researcher may not detect it. If the technician or researcher suspects a possible abnormality, the scan will be sent without any participant identifiers to a neuroradiologist for further review. If the neuroradiologist recommends further action, the subject will be notified. 2) Because of the strong magnetic fields used for MR imagers, persons who have magnetic life-support devices (e.g., pacemakers and aneurysm clips), metal prostheses or other metallic objects (e.g. cochlear implants, steel pins implanted to help repair and strengthen broken bones, metal fragments from previous injuries) cannot participate in this research. Anyone who does not pass the MRI screening checklist will not be permitted to participate in the study. 3)The MRI environment may be confining to some individuals (claustrophobia). Anyone who wants to be removed from the MRI will be removed immediately.

4)There is potential risk of loss of confidentiality. The potential risk of loss of confidentiality will be minimized, as outlined below. 5)During MRI imaging it can be loud. Noise levels are below FDA limits and ear protection is provided to further reduce noise. 6)In extremely rare cases (about one in a million), the radiofrequency energy used in MRI has produced burns (most of them minor). It is indicated in the consent form for participants to inform staff immediately if they feel any type of burning sensation. They would be removed immediately. 7) Having to stay still during MRI scan may be uncomfortable. The magnet bed will be equipped with extensive padding. 8) Risks of MRI scans to pregnant women are not known. Pregnant or possibly pregnant women will not be permitted to participate in this study. 9) Some people may be uncomfortable filling out the MRI screening form because there are questions about tattoos, piercings, and birth control methods. Only the MRI technician goes over the MRI screening form with the subject and the forms are kept in a secure location. 10) While there is no evidence of increased risk with multiple scans, the risks associated with multiple scans are not known. The IUB imaging center is adopting an arbitrary maximum of 40 hours of scanning time per individual per year and the time involved in the present study is well below that limit. Confidentiality The risk of loss of confidentiality will be minimized by storing identifying information only in two places, both secured to the best of our ability: (1) Printed identifying information consists of the signed consent form and screening forms. The MR safety screening forms will be kept in locked cabinets in the IRF. The rest will be kept in the subject's folder in a locked file cabinet in our lab (PH 079), which is also locked when we're not in there. (2) Electronic identifying information exists in a password-protected spreadsheet of subject names and contact information, with the numerical code that will be associated with the experimental data. The spreadsheet is kept on a secure network drive on the IU Teams server, accessible only to the investigators. If subjects respond to the initial screening questions over e-mail, we will delete this e-mail after determining eligibility. The text of the initial screening e-mail tells the subject we are happy to ask the screening questions by phone, so they know they have the option of not writing personal information in an e-mail. All the information we ask in the initial screening is replicated on the in-person screening form, which subjects fill out when they come to the lab, and this form is used to officially determine eligibility, so there is no need to retain the initial e-mail. To protect the subject's confidentiality, we will only e-mail the subject from an IU e-mail account (ending in indiana.edu or iu.edu). There will be no other electronic or paper identifying information, as all experimental data we collect (through software or a paper data sheet during the experiment) will only have the numerical code assigned to the subject.

For those subjects who will consent to participate, choose whether the consent and authorization process will be documented by a signature from subjects.
All consented subjects will provide a signature as documentation of consent and, if applicable, authorization.

Will subjects participate in any study activity prior to signing a consent document?
No

Statistical analysis plan

Primary outcome variables include resting state functional connectivity between each unique pair of ROIs and weighting of vision vs. proprioception. Multiple regression will determine whether functional connectivity is related to participants' weighting. Priority ROIs are ventral premotor cortex (PMv) and primary motor cortex (M1).