CIA Pilot Scan Request (example)

Prior to scheduling MRI scans, please complete the following sections of the CIA User application and submit to: cia@ini.usc.edu Once approved, you will be authorized to request scans online through The Scheduler.

Study Title

A cross-modality neuroimaging and neurohistological study of hippocampal dysfunction in Alzheimer's disease

Brief background to study

The hippocampus, a brain region critical for learning and memory, is believed to be one of the earliest sites affected in Alzheimer's disease. Human functional MRI studies have identified early neural alterations in the CA3/dentate gyrus (DG) region of the hippocampus, wherein the brain signal becomes aberrantly hyperactive in patients with mild cognitive impairment, and subsequently hypoactive when patients progress to dementia. Data from animal models suggest that this hyperactivity may be due to an over-excitation of glutamatergic neuronal activity due to loss of inhibitory function, or parvalbumin (PV) interneurons that support synaptic integration and long-range synchrony of neural circuits. However, the link between aberrant brain function and interneuron dysfunction in humans has not been established.

Rationale and clear statement of hypotheses to be tested

The goal of this pilot proposal is to explore hippocampal fMRI brain signal alterations and the their relationship to excitatory-inhibitory neuronal expression in Alzheimer's disease patients. To do this, we will assess the brain signal during the hippocampal-dependent fMRI memory paradigm in patients with mild cognitive impairment relative to healthy controls. We hypothesize that there will be an impaired hippocampal signal during pattern separation in CA3/DG in the AD patients compared to the healthy controls. We will then compare brain signal with blood-serum markers of inhibitory and excitatory neuronal expression from collected blood samples. If successful, this line of research could identify a sensitive biomarker for target engagement in clinical trials.

Description of subjects to be tested

We will recruit 10 older adults between 60-95 years of age, with either normal cognition (controls) or mild cognitive impairment without dementia, as determined by clinical evaluation. Participants will have competent English skills, and ability to complete the fMRI scan.

Specifications of protocol to be employed

We will use an fMRI paradigm that capitalizes on the role of the hippocampus for pattern separation and pattern completion. The participants will view a series of objects presented on a computer and be instructed to remember the objects. Following the encoding period, they will begin their fMRI scan and be asked to indicate if they recognize the objects on the screen, which will be *targets* (objects previously seen), *lures* (objects similar to those previously seen) or *novel (*unrelated objects). This hippocampal-dependent paradigm has been validated in healthy younger adults, healthy older adults and in individuals with mild cognitive impairment.

Stimulus presentation requirements (audio, visual, other)

Visual

Analyses to be performed

Multiple regression analyses of the fMRI timeseries will be modeled with separate regressors for each stage of the trial and convolved with a canonical Gaussian hemodynamic response function. We will conduct a priori analysis for regions of interest (ROI) analyses in the hippocampus using functional and anatomical constraints using the WFU Pickatlas. Data will be controlled for multiple tests and a minimum cluster size of 24 voxels will be accepted for $p < 0.05$ for each ROI.

Source of proposed grant application after piloting

Pilot data acquired through this proposal will be used to demonstrate feasibility and proof of concept for a comprehensive NIH project with larger sample sizes.

Names and degrees of all personnel involved in the study's MRI component

Judy Pa, Ph.D. (PI); Zachary Hobel, B.A. (RA)

Qualifications of the team for running the study

Dr. Pa is a tenure-track Assistant Professor at USC in the Department of Neurology and part of the Institute for Neuroimaging and Informatics. Dr. Pa is a clinical neuroscientist and early stage investigator, who trained in neurodegenerative disease during her postdoctoral fellowship at the UC San Francisco Memory and Aging Center and during her subsequent 5 years on the UCSF Neurology faculty. She received an NIA K01 Career Development Award for functional neuroimaging investigations in brain changes in MCI and followed a cohort of 60 MCI patients and healthy older participants for both observational and interventional longitudinal studies. She has published 16 studies in MCI for functional brain imaging. Dr. Pa received comprehensive training in state-of-the-art functional neuroimaging methodology, including toolbox programs such as Statistical Parametric Mapping (SPM) used for fMRI and PET analysis. She has superior knowledge of neuroimaging analysis obtained during her graduate and K01 award training and will not have any difficulties with conducting the proposed work. The proposed project is a natural extension of Dr. Pa's interests in advancing knowledge of brain mechanisms associated with treatments for older adults at risk for AD.

Zachary Hobel has a B.A. in Neuroscience and has conducted clinical research in at-risk populations for more than 3 years. Under Dr. Pa's supervision, Mr. Hobel is actively acquiring skills in neuroimaging analysis and will be involved in all aspects of this pilot study.

Number of scans and time / scan requested (maximum = 10)

10 subjects @ 1 hour/subject over 1 year

Projected start and completion dates

Anticipated start date: Nov 1st, 2016

Anticipated completion date: Oct 31th, 2017

IRB approval and number (if pending, state so)

IRB approval has already been granted.

IRB No.: HS-14-00609

Have you completed the user training and safety training sessions listed on the CIA website and provided documentation to CIA admin?

Yes, I completed the user training on 5-30-15 with Dr. Kristi Clark and the video safety training on 6-1-15.

Do you have an existing account for The Scheduler?

Yes, jpa@ini.usc.edu

Have you or the listed PI been allocated pilot scans within the last 12 months? If not, when was the last time you or the listed PI was allocated pilot scans?

No, this is my first request for pilot scans.