SRTP - Project Description Form #239

PART I:

Name of Schulich faculty member who will supervise the project	David Seminowicz
Supervisor's Schulich, Western, Hospital or Lawson Email	dseminow@uwo.ca
Schulich Department	Medical Biophysics

PART II - Project Description

Title of Project	Spatiotemporal cortical control by claustrum

Background

This project aims to determine the relationship between the claustrum and pain and cognitive control using high field fMRI and data modelling. The claustrum is a thin, elongated sub-cortical nucleus containing bidirectional connections with many areas of the cerebral cortex, and has many characteristics consistent with a network hub. It interacts considerably with cognitive control regions and shares its densest structural connectivity with frontal cortices, which anchor cognitive control networks. Furthermore, the claustrum receives strong input from the anterior cingulate cortex (ACC), a key node in the cingulo-opercular network, which has been placed within a "core system" for cognitive control. Thus, the claustrum is situated to receive such cognitive control signals and may serve as a hub through which prefrontal cortical regions direct dynamic interplay of cortical networks to optimize cognitive control.

The claustrum has the highest connectivity per unit volume in the brain, and removing (via modelling) connections to and from the claustrum has the effect of cutting communication between brain networks. Damage to hub regions leads to more severe brain disorders compared with damage to non-hub areas. Accordingly, claustrum abnormalities are associated with a variety of neuropsychiatric symptoms, including difficulties in cognitive control. These data support claustrum as a hub area, able to support coordinated activity across long-distance brain regions. Recently, a new model named Network Instantiation in Cognitive Control (NICC) has been proposed to explain the functional importance of the claustrum in the coordination of brain networks that are involved in various cognitive activities. This study explores the various hypotheses that are implicated in this model.

Hypothesis

The NICC model predicts that the claustrum: 1) receives a signal from ACC to prompt emergence of a specific network (a network initiation signal); 2) transforms and amplifies this signal and; 3) broadcasts the transformed signal through return projections to frontal cortices and projections to posterior sensory and association cortices to disrupt prior processing and bring targeted cortical network nodes into phase. This allows other inputs (such as from thalamus) to set oscillatory frequency and continue maintenance of synchronization. We hypothesized that successful performance of tasks that require cognitive control requires this transformation of signals through the claustrum.

Proposed Methodology

We will focus on the role of the claustrum in cognitive control during thermal nociception. To achieve that, we will use 7T functional MRI to evaluate claustrum activities during thermal stimulation and various cognitive tasks using a "deep phenotyping" approach, whereby a small number of participants are tested for long durations and in various conditions. Participants will perform cognitive tasks with painful or non-painful stimuli in the MR scanner for up to 7.5 hours over 5 sessions.

A recent advance in neuroimaging techniques, known as small region confound correction, allows isolating signals from

the claustrum without the contamination from neighbouring areas. This method revealed that the claustrum is connected at rest to widespread brain networks largely thought to be involved in cognition, and that during a cognitive task, the claustrum is transiently activated at task onset. Functional and effective connectivity between the claustrum and the rest of the brain will be computed to validate the proposed temporal dynamics of brain signals. Based on these findings, this proposed study will evaluate the hypotheses delineated in the NICC model.

Expected Outcomes
It is expected that the claustrum will be activated transiently at task onsets according to the NICC model, and possibly at task offsets to interrupt the extrinsic-mode network and bring the default-mode network back into working. It is also predicted that the claustrum exhibits functional and effective connectivity between the ACC, frontal cortices and posterior sensory and association cortices.

Research Environment – Description of the number of research personnel, primary location of research, size of lab, etc
The core of our lab is located in Robarts Research Institute, right next to the Center for Functional and Metabolic Mapping, where the 7T MR scanner is located. Currently, there are 1 postdoc, 1 PhD student, 2 Masters students and an expanding number of undergraduate students. Workstations are available for student interns to work in the lab. Students will be able to work on experimental design and stimuli, conduct fMRI experiments and perform data analysis. There is also an extensive network of collaborators and trainees at Parkwood institute, University of Maryland, Baltimore and Neuroscience Research Australia to whom the student will have opportunities to connect.

Names and titles of other individuals who will be involved with the research project?
Sahejpreet Mundh (dental student)
Celine Huang (undergraduate student)
Chloe Cheung (Masters student)
Yuan Yao (Masters student)
Somayeh Mashatan (Phd student)
Chun Yin Liu (Postdoc)

Can this project be done remotely?	No
Duration of Project	Two Summers

Expected Objectives/Accomplishments for Student for Year 1?
Training on fMRI analysis. Address main research question described above.

Expected Objectives/Accomplishments for Student for Year 2?
Develop independent project and analysis plan.

PART III - Certifications

If the project will require any certification approvals from one or more of the following offices, please check the appropriate box below.	- Human Ethics
Human Ethics: If you have the protocol information, please enter it below (or enter the status of the approval).	REB already approved

Note: certification approval should be obtained prior to the start of the summer. Projects without this approval will not be a priority for funding.