Project 3: To evaluate how OSA impacts the cerebral mechanisms underlying Mild Cognitive Impairment (MCI)

CIHR Related Themes: Biomedical, Clinical

Background: Clinically relevant cognitive impairments in the elderly often refer to a diagnosis of MCI, a well-known risk factor for dementia {Gauthier, 2006 #4085}. Up to 50% of MCI individuals, particularly those with an amnestic MCI subtype, will develop Alzheimer's disease (AD) or another dementia after three years {Petersen, 2008 #4086}. OSA was recently shown to increase the risk of developing MCI and dementia in five-year longitudinal cohort studies and hypoxemia was the factor that most strongly predicted the development of MCI or dementia {Yaffe, 2011 #4087; Chang, 2013 #4088}. However, to our knowledge, no current national or international neurodegenerative database initiative includes PSG evaluation to detect OSA. We recently observed that older OSA subjects showed hypoperfusion in the parietal cortex and this pattern of hypoperfusion is among the most reliable biomarker of early AD {Baril, 2015 #4089}. The mechanisms by which OSA in MCI patients impacts the brain are not well understood. This information is crucial since OSA treatment may contribute to reducing risk factors associated with progression toward dementia and to improving cognitive functioning in the MCI population.

Objectives: To evaluate how OSA impacts cognitive and cerebral biomarkers in patients with MCI.

Hypotheses: OSA severity (sleep fragmentation and hypoxemia) in MCI patients will be significantly associated with AD biomarkers (i.e. enhanced beta-amyloid deposition, CSF tau level, brain atrophy in the entorhinal cortex and the hippocampus, and vascular brain damages). Compared to MCI patients without OSA diagnosis, MCI subjects with OSA will show a more rapid progression of AD biomarkers over time and they will be more at risk of progressing toward dementia.

Methods: To achieve this goal, the CSCN will work with the Consortium for early Identification of Alzheimer's Disease – Québec (CIMA-Q). The overarching goal of CIMA-Q is to foster and potentiate Québec's expertise on AD research in order to facilitate earlier diagnosis, develop new sensitive, valid, and clinically relevant functional and diagnostic markers, identify novel therapeutic targets, and refine preventive strategies. The initial CIMA-Q clinical registry, which started in November 2014, will consist of a cohort of 50 patients with mild AD and 300 subjects with MCI. These patients have prospective complete evaluations including health, psychological and neuropsychological assessments, blood samples, anatomical magnetic resonance imaging (MRI), diffusion MRI, resting-state functional MRI, FDG positron emission tomography (PET). The CIMA-Q database includes subjective sleep evaluation but not a polysomnographic (PSG) evaluation necessary for an OSA diagnosis. The CSCN will add a PSG evaluation to a sample of CIMA-Q patients in Montreal. The CSCN will have full access to CIMA-Q cognitive and AD biomarkers dataset for patients who will have a PSG evaluation. This access is worth $852,612 in data acquisition (see letter of support).

Project Plan: 1) Analyses of subjective sleep questionnaires and AD biomarkers; 2) PSG acquisitions in 25 MCI patients per year in the first three years (75 MCI patients); 3) PSG and AD biomarker analyses; 4) Follow-up PSG evaluations in 25 MCI patients in the last two years (50 MCI patients with follow-up); 5) Once sample size calculations are possible, a full applications to CIHR OOGP will be submitted.

Feasibility: Our preliminary data from a CIHR funded project (Gosselin, Montplaisir, Gagnon) showed that among 100 individuals aged > 55 years old, at least 35% of individuals with mild to severe OSA have a MCI.

Multidisciplinary and multi-thematic research: This initiative will integrate research in neuroimaging, neuroscience, neuropsychology (Drs. Carrier, Gosselin, Montplaisir, Gagnon, Desautels, and Lorrain) and respiratory medicine (Drs. Ayas and Series).