

Clocks in the human brain

*Douglas researchers observe disruptions of daily rhythms
in Alzheimer's patients brains*

Montréal 27 April, 2011 – Twenty-four hour cycles, known as circadian rhythms, are important for proper body functions, including for normal brain function and mental health. Disruptions of circadian rhythms and sleep-wake cycles have been observed in patients with Alzheimer's disease. A new study by Douglas Institute researchers unravels a possible basis for these perturbations.

First study to show function of clock genes in multiple areas of the human brain

Until now, the genes contributing to this timing, known as clock genes, have only been found to be active in areas outside the brain, such as the skin and blood cells. Recent findings from the Douglas Mental Health University Institute are the first to show that these genes function in multiple areas of the human brain as well, as was shown previously in animals. These findings, published in this month's issue of the *Journal of Biological Rhythms*, have implications for the numerous individuals with sleep disturbances including those with Alzheimer's disease.

"To our knowledge, this is the first demonstration of circadian clock genes rhythmic expression in the human forebrain, or the front part of the brain," says senior author Nicolas Cermakian, a Douglas researcher and Director of the Laboratory of Molecular Chronobiology. "In addition, we showed that these rhythms are disrupted in the brains of Alzheimer's patients."

Shape of certain rhythms and the synchronization between brain areas were altered in Alzheimer's patients

Dr. Cermakian and his colleagues looked for the presence of the circadian clock genes, *PER1*, *PER2*, and *BMAL1* in the brain tissue of 58 donors; 27 were Alzheimer patients and 31 were controls. (Brain tissue was obtained from the Brain Bank of the Douglas.) All these clock genes were detected in three brain areas in both control and Alzheimer patients. In addition, there was a significant diurnal (day/night) expression of these genes in all three structures of control samples. In samples from Alzheimer's patients, the shape of these rhythms and the synchronization between brain areas were altered.

"The abnormal clock gene coordination that we observed in the tissues of Alzheimer's patients, might explain the sleep-wake deficits that are observed in this population," says Douglas Centre for Study and Treatment of Circadian Rhythms Director, Diane B. Boivin. "The altered sleep pattern worsens with disease progression and is the most frequent reason for institutionalization. Improved understanding of the process that underlies sleep-wake disruption may lead to better treatments or therapies. "Our ultimate goal is to improve the physical and mental health of individuals by providing scientifically grounded information."

Partners in research:

The Douglas Institute Foundation is proud to support Nicolas Cermakian, PhD and Diane B. Boivin, MD, PhD, and their research in mental health. The Foundation thanks its donors and volunteers for their generosity and thoughtfulness. Together, we invest in healthy minds.

This study was funded by the Canadian Institutes of Health Research and the Fonds de la recherche en santé du Québec.

About the study:

The article, "Circadian clock gene expression in brain regions of Alzheimer's disease patients and control subjects", was authored by Nicolas Cermakian, Elaine Waddington-Lamont, Philippe Boudreau and Diane B. Boivin of the Douglas Mental Health University Institute and McGill University.

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On the Web:

- Cited *Journal of Biological Rhythms* study: <http://jbr.sagepub.com>
- Centre for Study and Treatment of Circadian Rhythms:
http://www.douglas.qc.ca/pages/view?section_id=220
- Douglas Mental Health University Institute Brain Bank:
<http://www.douglas.qc.ca/page/brain-bank>

PLEASE NOTE: Nicolas Cermakian is hosting a symposium on the latest research in Canada about circadian rhythms on Thursday, June 2 and Friday, June 3 2011.

Symposium of circadian rhythms research in Canada

Douglas Institute, Montreal, June 2-3, 2011

Two general public lectures (in French) on Thursday June 2, 2011

20:00 *Renforcer les horloges biologiques pour combattre le cancer*

Francis Lévi, Ph.D.

INSERM, Hôpital Paul Brousse, Villejuif, France

20:30 *À quelle heure le marchand de sable passe-t-il?*

Diane B. Boivin, Ph.D.

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About the Douglas—www.douglas.qc.ca

The Douglas is a world-class institute, affiliated with McGill University and the World Health Organization, which treats people suffering from mental illness, and offers them hope and cures. Its teams of specialists and researchers continually advance scientific knowledge, integrate it into patient care, and share it with the community to increase awareness and eliminate stigma around mental illness.