

## 2<sup>nd</sup> International Conference on **Alzheimer's Disease and Dementia** September 23-25, 2014 Valencia Convention Centre, Spain

### Early brain network alterations are correlated with $\beta$ -CTF in Alzheimer's transgenic mouse model

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Alzheimer's disease is defined by the presence of amyloid- $\beta$  ( $A\beta$ ) and tau protein aggregates. However, increasing data is suggesting that earlier phenomena such as brain network alterations rather than protein deposition could account for the pathogenesis of the disease. Here we found that earlier fragments of  $A\beta$  processing rather than plaque deposits are critically associated to abnormal function of brain networks. By measuring brain protein alterations in the hippocampus of Alzheimer's J20 transgenic mouse model at four weeks of age, we found significant increases in  $\beta$ -CTF, a protein precursor to  $A\beta$  peptides. In addition, the  $\beta$ -CTF increase was found to be directly correlated with hippocampal circuit malfunction at this age. By performing extracellular field recording method at the subiculum region *in vitro*, we found reduced theta-gamma cross-frequency coupling at low (25-45 Hz) and high (150-250 Hz) gamma range. Interestingly, despite these network changes, the J20 mice did not present cognitive deficit at this age. In summary, our data suggests that brain network alterations precede the canonical  $A\beta$  protein deposition. In addition, we found that circuit alterations may be caused by  $\beta$ -CTF, suggesting that early pharmacological prevention of brain circuit alterations might represent a more promising strategy towards delaying the development of Alzheimer's disease.

#### Biography

Siddhartha Mondragon Rodriguez graduated in Chemical Engineering from Michoacan University of Saint Nicolas of Hidalgo (UMICH) in 1996 - 2002. Master Degree (MsC) in Molecular Biomedicine from National School of Medicine from the National Polytechnic Institute of Mexico City. PhD from Center of Research and Advanced Studies of the National Polytechnical Institute in August 2005 - August 2009. Postdoctoral Fellow from Universite de Montreal. Faculte de Medecine, Departament de physiologie., Montreal, Qc, Canada. Postdoctoral Position in McGill University.

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