Molecular and Translational Study of Saturated and Unsaturated Fatty Acids, and Obesity on Early-Onset of Alzheimer Disease: The Role of GPR120 Receptor.

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Project abstract:
Obesity advances worldwide in an uncontrolled way, being considered a predisposing factor also to neurodegenerative diseases such as Alzheimer’s Disease (AD). Not only the senescence is involved in the pathogenesis of AD, but also the inflammatory process characteristic of the obesogenesis, which can anticipate its onset and even be an initial trigger. Hippocampal neuroinflammation can precipitate neurodegeneration leading to irreversible damage to memory. Diets rich in saturated fats can disrupts hippocampal homeostatic neural circuits, formed by complex circuitry among glial cells, neurons, oligodendrocytes and astrocytes. In this neuronal group, Toll-type receptors (TLR) mediate the inflammatory effects of fats, and, cytokine receptors, intensify inflammation. Consequently, inflammasomal activation, dysregulation of the endoplasmic reticulum, and autophagy failure induce apoptosis. Side-by-side inflammation, hippocampal insulin resistance can reduce the local clearance of beta-amyloid protein (βA), inducing protein tangles harmful to synapses, and hyperphosphorylates the TAU protein, which disrupts the neuronal cytoskeleton and intensifies the signs of death. Together, these phenomena imply the advancement of AD, followed by serious clinical outcomes, such as memory loss and dementia. On the other hand, omega-3 (ω3) unsaturated fatty acids are known to be potent anti-inflammatory agents, and their consumption correlates with benefits for AD patients. However, this proposal does not yet find robust mechanistic support. The ω3 is GPR120 receptor agonist, which seems to disrupt the intracellular signaling controlled by the TLR4, TNFα and IL1β receptors and by the inflammasome. However, its presence and function has not been demonstrated in
the hippocampus. Synthetic GPR120 agonists have been developed due to wide therapeutic possibilities, already under investigation on clinical trials. If plausible, this mechanism opens a new pharmacological possibilities for postponement of AD, however, the $\omega 3$ is found in food and it would also become feasible and, mainly, of access to the entire population.

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Data Collection

Gene expression; Protein content; Blood biochemical parameters; Anthropometrics; Fatty acids profile; Physiological mice parameters

The data will be generated from experimental tests on cells, animals and humans. The variables obtained in specific equipment will be plotted in software such as Excel (Microsoft).

Documentation and Metadata

Will be samples (blood and tissues [hippocampus]), animal and human body measurements, videos (mice behaviour test), graphs and spreadsheet.

Ethics and Legal Compliance

Experiments with rodents - all procedures will be approved by local ethical committee.
Human tests - Firstly, all the participants will provided written informed consent. All researchers involved in the human analysis will sign a term in order to ensure the anonimate from patients.
The generated data from these experiments will be available, at least the not protected by industrial secret.
The collected biological material will be named and organized in order to maintain the anonimate from patients.

If an intellectual product is generated, the authors involved in the creation will be invited to join the authorship.

Storage and Backup

The data will be stored in real time, in the cloud (One Drive - System provided and recommended by our Institution). At the end of the collection, the data will also be stored on 3 hard drives, kept in different locations and far from each other.

After processed, analyzed and plotted in graphs, the data already used will be available in the repository created exclusively for this project, located at: www.labgen.com.br/repositorio The address will be accessed only with a password or after registering the interested parties on
the site itself. In order to obtain access to individual data, the interested researcher will contact the LabGeN coordinator directly. By signing this Term, the researcher undertakes to use the data exclusively for the research described there, protect the information and ensure that the data will not be publicly disclosed or disclosed to third parties. Initially, individual-level information will be stored for a period of 10 years on three physically separate servers in order to maintain redundancy.

**Selection and Preservation**

The data generated from rodents: The data will be stored for, at least, 10 years in our servers. It also will be available to scientific journals repository. The data generated from humans: After the publications, these data can be used by the scientific community, once signed the terms of confidentiality. After publication, data from experimental animals or cells will be free accessed.

All generated data will be stored for, at least, 10 years in our servers.

**Data Sharing**

Grouped information (i.e., not representing individual level data) collected and generated by this project will be immediately shared in: Scientific meetings, Thesis, published articles, and repository banks when required by journals.

In order to obtain access to individual data, the interested researcher will contact the LabGeN coordinator directly. By signing this Term, the researcher undertakes to use the data exclusively for the research described there, protect the information and ensure that the data will not be publicly disclosed or disclosed to third parties.

**Responsibilities and Resources**

All students and researchers involved in this project are responsible to input and maintain the correct and organized data at the system. The backup system occurs automatically and did not requires human action. The researcher responsible for the analytical part of the project, Dennys Esper Cintra, will conduct periodic audits to confirm the proper implementation of data entry. The implementation of this plan will require periodic acquisition of hard drives for expansion of storage and backup systems.

We will only require hardwares and repository data bank maintenance.