Alteration of Metabolism in Amyotrophic Lateral Sclerosis

https://neurodegenerationresearch.eu/survey/alteration-of-metabolism-in-amyotrophic-lateral-sclerosis/

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Country

Sweden

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Alteration of Metabolism in Amyotrophic Lateral Sclerosis

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Swedish Research Council

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4

The project/programme is most relevant to:

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Keywords
Research Abstract

Amyotrophic lateral sclerosis (ALS) is a devastating adult-onset neurodegenerative disorder that leads to death 2-3 years after diagnosis on average. The etiology of ALS, especially sporadic ALS, is largely unknown. Defects of energy metabolism are clinically distinctive among ALS patients and have great potential as therapeutic candidate targets. Little is however known regarding whether metabolism defects are a cause, prodromal symptom, or consequence of

motor neuron degeneration in ALS. In the present proposal, we aim to systemically investigate the link of metabolism with ALS and to identify potential underlying mechanisms for such link. We will first take advantage of a unique and large longitudinal study with rich information on metabolism biomarkers to assess the temporal relationship between metabolism profiles and ALS. Such new findings will be the first human evidence to demonstrate whether energy metabolism defects are preceding or succeeding events of motor neuron degeneration. As a novel attempt, we will also test the diagnostic utility of metabolic biomarkers for early detection of ALS. We aim to conduct statistical analysis and write up two manuscripts based on this research aim, during 2016-2017. The existing literature focuses on mitochondria dysfunction as the explanation for metabolism defects in ALS. We will conduct a new population-based case-control study of ALS in Stockholm, aiming to examine the roles of other contributors to metabolism homeostasis, namely gut microbiome and immune response, on ALS. The potential synergistic effect of metabolism and immune modulation will also be examined. Previous studies have focused on glucose and lipid metabolism, and as a result proposed muscles as the responsible organ for metabolism defects in ALS. We will in the present proposal instead study the broader spectrum of metabolism, including bone, human gut microbiome and immune modulation. We have prepared the study protocol and obtained ethical approval for the case-control study. The official enrolment of case-control study will start from autumn 2015. Lab analyses for different samples will be carried out throughout the years and during 2018-2019, we aim to analyze data and produce 3-4 manuscripts. There is no cure for ALS to date. The only drug approved by the US FDA is Riluzole, and prolongs on average the survival of ALS patients by a few months. All clinical trials based on promising findings from ALS animal models have been proven as unsuccessful. More research in identifying potential therapeutic candidates for ALS is clearly needed. Metabolism profiles and gut microbiome are largely modifiable, through for example diet, drugs, or physical exercise. If proven to be of primary and causative roles for ALS, modulation of metabolism or microbiome may be advisable for both primary (high risk individuals) and secondary (clinical patients) preventions. Our proposal will further evaluate the role of immune modulating leucocytes, including the so-called regulatory T cells, as well as the interaction between these cells and human microbiome, on ALS. This new set of knowledge may facilitate the establishment of protocols where immune modulating cells may be used to treat ALS patients. My research team includes two senior ALS specialists (former and current heads of ALS unit in the Neurology Clinic, Karolinska University Hospital), two professors on metabolism and metabolic diseases, one molecular epidemiologist and professor on human microbiome and upper gastrointestinal diseases, one immunologist on immune suppression especially Treg cells, and one senior bioinformatician. We will employ one full time PhD student, two part time postdocs, and a 50% research nurse for all the proposed studies. The team will also have support on data management, biostatistics, and research administration from the host institution. I will serve as the principal investigator, coordinate the research team and supervise the PhD student as well as the postdocs.

Lay Summary
Further information available at:

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