Prospective study of biomarkers and risk factors for ALS incidence and progressio

https://neurodegenerationresearch.eu/survey/prospective-study-of-biomarkers-and-risk-factors-for-als-incidence-and-progressio/

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Country

USA

Title of project or programme

Prospective study of biomarkers and risk factors for ALS incidence and progressio

Source of funding information

NIH (NINDS)

Total sum awarded (Euro)

€ 1,740,388.07

Start date of award

01/04/2003

Total duration of award in years

1

The project/programme is most relevant to:

Motor neurone diseases

Keywords

Amyotrophic Lateral Sclerosis, Urate, Prospective Studies, Risk Factors, Incidence

Research Abstract

DESCRIPTION (provided by applicant): Amyotrophic lateral sclerosis (ALS) is a progressive neurodegenerative disease characterized by a loss of the neurons that control voluntary

movements. Patients lose muscle strength and in the final stages of the disease are unable to move and have difficulty swallowing and breathing. Recent advances have been made in understanding the molecular mechanisms that contribute to ALS. In contrast, little progress has been made in drug discovery – none of over 30 new drugs tested in ALS has been found to be effective, and median survival from diagnosis remains at 2-3 years. The purpose of this project, which is the continuation of an ongoing NIH supported study, is to search for clues for novel treatments by i) studying in large populations of individuals who have been followed for many years how the individuals who develop ALS are different from those who remain healthy; and ii) examining among individuals with ALS whether there are factors that predict a slower disease progression. During the past 5 years of this project, we have found that ALS risk was inversely associated with long term intakes of vitamin E and other antioxidants, and positively associated with cigarette smoking. In parallel, preliminary evidence emerged that blood levels of urate, a potent antioxidant, are inversely related to the rate of ALS progression – this is encouraging in view of urate's strong antioxidant properties, its robust inverse associations with both risk and progression of Parkinson disease, and the fact that urate concentrations can be increased by administration of inosine (a urate precursor) or other available drugs. Building on these findings, this proposal will address two key questions – whether plasma levels of urate in apparently healthy individuals contribute to predict their ALS risk, and whether plasma levels of urate among patients at an early stage of ALS contribute to predict their rate of clinical progression. Additionally, we will examine the role of other plasma antioxidants in relation to ALS risk, and we will conduct a discovery study for novel risk markers using a metabolomic approach. The proposed aims of our study stand to identify or substantiate major new contributors to ALS, with realistic prospects for mechanistic insight and therapeutic impact. Key strengths of our proposal include: 1) availability for the first time of blood samples collected before the onset of ALS; 2) use of an independently funded large randomized trial to study ALS progression; 3) interdisciplinary expertise of our research team.

Lay Summary
PUBLIC HEALTH RELEVANCE: Amyotrophic lateral sclerosis (ALS) is an incurable progressive neurodegenerative disease characterized by a loss of the neurons that control voluntary movements. One of the molecular mechanisms that seems to contribute to ALS is oxidative stress, therefore, the primary focus of the proposed project is to examine in large ongoing longitudinal studies whether plasma levels of urate and other antioxidants collected from apparently healthy individuals contribute to predict their ALS risk, and whether plasma levels of urate among patients at an early stage of ALS contribute to predict their rate of clinica progression. A further aim is the exploration of other plasma metabolites that may be related to ALS risk and progression.

Further information available at:

Types:
Investments > €500k

Member States:
United States of America

Diseases:
Motor neurone diseases

Years:

2016

Database Categories:
N/A

Database Tags:
N/A