

Environmental Epidemiology of Essential Tremor

<https://www.neurodegenerationresearch.eu/survey/environmental-epidemiology-of-essential-tremor/>

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Country

USA

Title of project or programme

Environmental Epidemiology of Essential Tremor

Source of funding information

NIH (NINDS)

Total sum awarded (Euro)

€ 3,485,950.46

Start date of award

01/03/2016

Total duration of award in years

5

The project/programme is most relevant to:

Parkinson's disease & PD-related disorders

Keywords

Essential Tremor, Environmental Epidemiology, Parkinson Disease, Tremor, Intention Tremor

Research Abstract

? DESCRIPTION (provided by applicant): Our research is devoted to studying the causes of tremor, and especially essential tremor (ET), which is the most common type of tremor. Since 2000, we have been investigating whether several environmental neurotoxins are associated

with ET. A link between harmane (HA) (1- methyl-9H-pyrido[3,4-b]indole) and ET has been emerging from these studies, which show that blood and brain HA concentration ([HA]) is elevated in ET cases (esp. familial ET) vs. control subjects. HA is a neurotoxin present in the diet (esp. in meat). Administration of HA to laboratory animals produces severe action tremor resembling ET. Yet the link between HA and ET has not been convincingly established. All epidemiological studies have been case-control studies; thus, it is not clear whether high blood [HA] precedes the onset of ET. Aim 1 of this proposal will address this issue. The HA story has also become more complex and multi-dimensional. Thus, we were recently intrigued to find that blood [HA] was higher in Parkinson's disease (PD) cases than controls in New York. HA is structurally similar to MPTP, a neurotoxin closely linked with PD. ET and PD are both tremor disorders; some patients develop both disorders (ET+PD; i.e., they are comorbid for the two conditions). Whether the HA – PD link is reproducible, whether it tracks with the subtype of PD in which tremor rather than bradykinesia/rigidity is the predominant feature, and whether biomarker findings from blood also occur in the target organ of interest (i.e., the brain) in PD is not known. Aim 2 of this proposal will address this myriad of issues. Finally, whether individuals who are comorbid for both ET and PD have the highest blood [HA] is not known. Aim 3 of this proposal will address this issue. To close these gaps in knowledge, in this application, we propose a 5-year study with 3 inter-related aims that draw on several types of human tissue (blood, brain): AIM 1: To nail down the links between HA and ET by studying the association between baseline blood [HA] and the development of incident ET in a cohort study. AIM 2: To further solidify the emerging links between HA and PD by extending our observations to another country (Spain). AIM 3: To assess blood levels of HA in patients who have both ET and PD (ET+PD). This would be the only study heading in this direction – exploring the etiological role of environmental factors, and more specifically toxins, in ET. It would thus complement the many ongoing studies searching for ET genes. The study could lead to the clear identification of the first modifiable risk factor for ET (i.e., dietary HA). This would also be the only study assessing the possible etiological role and tissue concentrations of this toxin, HA, which is structurally similar to MPTP, in patients with PD.

Lay Summary

PUBLIC HEALTH RELEVANCE: Our research is devoted to studying the causes of tremor, and especially essential tremor (ET), which is the most common type of tremor. Our studies have revealed a link between harmane [HA], a dietary neurotoxin, and ET; these studies now also suggest a link between this toxin and Parkinson's disease (PD), a related tremor disorder. Yet these links are tentative rather than conclusively established; therefore, in this new patient-based proposal, which incorporates investigations spanning two continents (North America and Europe), utilizes several complementary study designs (prospective cohort, case control), and draws on several types of tissue (blood, brain), our goal is to nail down the links between HA and ET and to further solidify the emerging links between HA and PD.

Further information available at:

Types:

Investments > €500k

Member States:

United States of America

Diseases:

Parkinson's disease & PD-related disorders

Years:

2016

Database Categories:

N/A

Database Tags:

N/A