Influence of neuromuscular pathology on parkinsonian communication deficits

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Contact information of lead PI
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USA

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Influence of neuromuscular pathology on parkinsonian communication deficits

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NIH (NINDS)

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01/08/2015

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4

The project/programme is most relevant to:

Parkinson's disease & PD-related disorders

Keywords

neuromuscular, Parkinsonian Disorders, Deglutition, PINK1 gene, Tongue

Research Abstract

? DESCRIPTION (provided by applicant): Individuals with Parkinson disease (PD) experience devastating communication and swallowing deficits that negatively impact quality of life. Recent

research has shown that PD pathology is widespread, including not only central nervous system regions, but also peripheral structures such as nerves and muscles involved in communication and swallowing. However, despite these recent data, very little is known about how peripheral pathologies contribute to communication and swallowing deficits and when in the disease process these deficits emerge. Furthermore, it is unknown how behavioral treatments used clinically, such as exercise-based voice and swallow therapies, affect the manifestation of these deficits. To develop more effective treatments, a clear understanding of the progression of peripheral pathologies and the manner in which these pathologies affect communication and swallowing must be obtained. These unknowns will be addressed in the proposed research by studying a progressive, novel genetic rat model of PD: homozygous knock-out (KO) of PINK1, a gene mutation known to cause PD, comparing these rats to non-affected controls (wild type; WT), and by manipulating exercise conditions. This approach provides a direct mechanistic link to PD in humans, insight into the effects of treatments in current clinical use, and knowledge of previously unexplored peripheral pathology in PD associated with vocalization and swallowing deficits. Employing tasks and behaviors analogous to those used in humans will maximize translation. Rats will be studied at ages that correspond to early, mid, and late stage PD (6, 10 and 14 months). Our central hypotheses are: (1) PINK1 KO rats will show behavioral deficits accompanied by peripheral pathologies that will progressively increase in severity by disease stage, (2) PINK1 KO rats that undergo exercise will show prevention or reversal of functional deficits and modulation of peripheral neuromuscular pathology. To address these hypotheses, this proposal has 3 specific aims: (1) To quantify pathological changes to peripheral nerves and muscles that mediate vocalization and swallowing across stages of PD; (2) To determine how neuromuscular pathology relates to deficits in vocalization, tongue strength and functional eating across stages of PD; and (3) To determine how exercise of the tongue and larynx affects neuromuscular pathology. This proposal is timely and innovative because our understanding of PD now embodies widespread pathology that includes muscles and nerves. The proposed research will provide in-depth knowledge of neuromuscular pathology that is relatively unexplored in PD and will also be the first to examine how exercise can prevent or reverse biological changes within the tongue and larynx. Our systematic and controlled studies in the PINK1 KO rat combine techniques and theory from behavioral, anatomical, and physiological sciences and provide an opportunity to learn how neuromuscular pathologies inform observed behavioral changes in vocalization and swallowing. This translational research has a high likelihood of yielding meaningful findings related to important scientific and clinical issues.

Lay Summary

PUBLIC HEALTH RELEVANCE: The proposed research examines how muscles and nerves involved in communication and swallowing may be affected by Parkinson disease. Experiments will determine how pathologies in muscles and nerves contribute to communication and swallowing deficits and when in the disease process these deficits emerge. Further, this work will examine how exercise-based voice and swallow therapies prevent or reverse muscle and nerve pathologies using a novel genetic rat model.

Further information available at:

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Investments > €500k

Member States:

United States of America

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Parkinson's disease & PD-related disorders

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