Beta-cell Function and Cognition in the Restoring Insulin Secretion (RISE) Study

https://www.neurodegenerationresearch.eu/survey/beta-cell-function-and-cognition-in-the-restoring-insulin-secretion-rise-study/

Principal Investigators

CRAFT, SUZANNE

Institution

WAKE FOREST UNIVERSITY HEALTH SCIENCES

Contact information of lead PI
Country

USA

Title of project or programme

Beta-cell Function and Cognition in the Restoring Insulin Secretion (RISE) Study

Source of funding information

NIH (NIA)

Total sum awarded (Euro)

€ 1,842,514.68

Start date of award

01/09/2013

Total duration of award in years

3

The project/programme is most relevant to:

Alzheimer's disease & other dementias

Keywords

insulin secretion, Beta Cell, Metformin, liraglutide, insulin sensitivity

Research Abstract

DESCRIPTION (provided by applicant): This application is submitted in response to PAR-12-265 (Ancillary Studies to Major Ongoing Clinical Research Studies to Advance Areas of

Scientific Interest within the Mission of the NIDDK). The proposed ancillary study will examine the effects of anti-diabetic treatment on cognitive function and plasma ß-amyloid (a biomarker of cognitive decline related to Alzheimer's disease), in adults and adolescents with prediabetes or early Type 2 Diabetes Mellitus (T2DM) who are participants in the Restoring Insulin Secretion (RISE) Study. We will also examine whether therapeutic modulation of ß-cell function and insulin sensitivity predicts change in cognition and ß-amyloid. The parent adult RISE Study is a placebo-controlled, multi-center, clinical trial in 255 subjects with prediabetes and early T2DM that will address the hypothesis that intensive glucoregulatory control will restore ß-cell functio, and that restorative effects will persist after treatment cessation. Participants will be randomize into 4 treatment arms: placebo, metformin, metformin plus liraglutide, or insulin glargine followed by metformin. Intensive evaluations to assess ß-cell function, insulin sensitivity, and glucose tolerance will occur throughout a 12-month treatment period, followed by 3- and 9-month post-treatment evaluations. A parallel RISE study will be conducted with 90 adolescents who will be randomized to metformin or metformin plus liraglutide. The proposed ancillary study will assess the effects of treatment on cognition and ß-amyloid, and the relationship of endocrinologic changes to changes in cognition, by adding a battery of sensitive measures of memory and psychomotor speed (Continuous Paired Associate Learning Test, One-Card Learning Test, Detection and Identification Test, Trail-Making Test) and plasma ß-amyloid measurement to the RISE studies. We will test the hypotheses that adults in the three active treatment arms will show greater improvement in cognitive scores and lowering of plasma ß-amyloid at 12-months relative to baseline compared with placebo-assigned participants, and that adult and adolescent participants in the metformin plus liraglutide arm will show greater improvement relative to the other active treatment groups. We will also test the hypothesis that changes in insulin secretion (insulin sensitivity-adjusted ß-cell function measures derived from second phase and AIRmax responses) and sensitivity (insulin-adjusted glucose disposal rate) after 12-months of treatment will be related to cognitive and ß-amyloid changes. Finally, we will examine whether cognitive and biomarker changes are maintained after treatment cessation. The ancillary study will address the important questions of whether therapy at early stages of diabetes can improve cognition, and whether improvement is maintained after treatment ends. The study will also examine the relationship of cognitive status with metabolic mechanisms such as impaired insulin secretion and sensitivity that may underlie the increased risk of cognitive decline and neurodegenerative disease associated with prediabetes and T2DM, and thereby suggest novel approaches to treatment and prevention of cognitive decline in patients with these conditions.

Lay Summary
PUBLIC HEALTH RELEVANCE: Diabetes increases the risk of cognitive impairment and dementia, co-morbidities that greatly complicate disease management. Diabetes-induced cognitive impairment in children may also impede scholastic and occupational achievement. The proposed ancillary study will address the important questions of whether therapy at early stages of diabetes can improve cognition, whether improvement is maintained after treatment ends, and what metabolic mechanisms are associated with cognitive improvement. Findings from the study will suggest novel approaches to treatment and prevention of cognitive decline in patients with diabetes.

Further information available at:

Types:
Investments > €500k

Member States:
United States of America

Diseases:
Alzheimer's disease & other dementias

Years:
2016

Database Categories:
N/A

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