Pathophysiology of postoperative delirium and the use of biomimetic sleep as a treatment strategy in the CSICU

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Country

USA

Title of project or programme

Pathophysiology of postoperative delirium and the use of biomimetic sleep as a treatment strategy in the CSICU

Source of funding information

NIH (NIA)

Total sum awarded (Euro)

€ 3,077,687.16

Start date of award

01/09/2016

Total duration of award in years

1

The project/programme is most relevant to:

Alzheimer's disease & other dementias

Keywords

Acquired Cognitive Impairment... Aging... Alzheimer's Disease... Alzheimer's Disease including Alzheimer's Disease Related Dementias (AD/ADRD)... Behavioral and Social Science...

Bioengineering... Biotechnology... Brain Disorders... Clinical Research... Clinical Research - Extramural... Dementia... Mental Health... Neurodegenerative... Neurosciences... Sleep Research

Research Abstract
Delirium is one of the six leading causes of preventable morbidity and mortality in hospitalized elderly patients. Individuals with advanced age and Alzheimer’s disease are at greatest risk of developing delirium. A substantial proportion of patients who survive delirium are likely to experience long-term cognitive impairment similar to mild Alzheimer’s disease, and require institutional care. This suggests that delirium and Alzheimer’s disease share pathophysiological features that arise in the context of normal aging. Conditions associated with delirium are characterized by activation of the inflammatory cascade with acute release of inflammatory mediators into the bloodstream. A putative mechanism is the high interleukin-6 level that has been associated with delirium in both laboratory animals and humans. Normal aging is associated with a morphological shift of glia to an activated state. Following a systemic challenge such as critical illness, these activated glia result in an exaggerated neuroinflammatory state associated with delirium. Neuroinflammation is further exacerbated by sleep disturbances. Thus, sleep deprivation may be a modifiable risk factor for the development of delirium. However, pharmacological treatment with no current medication (benzodiazepines, antipsychotics) induces natural sleep or reliably reduces the incidence of delirium. We have found that biomimetic sleep, defined here as pharmacological induction of rapid eye movement sleep (REM) and non-REM I-III sleep states using dexmedetomidine, can now be achieved in humans. Our Specific Aims seek to: (1) investigate the benefits of preemptive biomimetic sleep for reducing the risk of developing delirium in a randomize; (2) investigate the cellular and molecular mechanisms of delirium using combined Positron Emission Tomography/Magnetic Resonance imaging and serum metabolic profiling; and (3) investigate predictors of delirium from perioperative electroencephalogram recordings. At the conclusion of these studies, we will have expanded our knowledge of the pathophysiology of delirium, evaluated a new preemptive therapeutic strategy for delirium, suggest neurophysiologically based monitoring strategies to reduce significantly the amount of anesthetic administered to elderly patients – and possibly delirium – while being certain the patient is sufficiently unconscious for surgery (individualized anesthesia care), and enable continued investigation into the pathophysiology of this clinically important disorder.

Lay Summary
Elderly patients are more likely to develop cognitive dysfunction (delirium) after surgical procedures. Sleep disturbances amongst have been associated with the development of delirium. This project will study a new method to induce sleep in humans with the rationale that it would help reduce the risk of delirium.

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

Database Tags:
N/A