The Role of Brain Beta-Amyloid and Tau Protein in POD and POCD

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Research Abstract

? DESCRIPTION (provided by applicant): Postoperative delirium (POD) and postoperative cognitive dysfunction (POCD) are the two most common postoperative complications in older adults, and increase perioperative morbidity, mortality, and cost of medical care. However, at the present time, both POD and POCD are clinical phenomena and their pathogenesis is largely

unknown. This gap in knowledge has impeded the progress of research to develop targeted interventions for POD and POCD. We have shown that low pre-operative Aß/Tau ratio in cerebrospinal fluid (CSF), a biomarker of Alzheimer's disease, may identify individuals at high risk of POD and POCD. However, the direct association between brain Aß, Tau, and neuroinflammation (e.g., microglia activation) levels with POD/POCD remains to be investigated. Our co-investigator Dr. Johnson has developed the innovative technology of measuring brain Tau [(F-18)T807] and Aß (Pittsburgh compound B) levels by using positron emission tomographic imaging. We have developed methods to assess POD/POCD and to measure CSF levels of Aß and Tau. Taken together, the proposed research is aimed at establishing a system/protocol that will help us for a potential larger scale study to investigate the association of brain, CSF, and plasma Aß and/or Tau levels, and brain microglia activation level, with the incidence and severity of POD and POCD. Our overall hypothesis is that high pre-operative brain Aß and Tau levels, and high postoperative neuroinflammation represent markers of brain vulnerability under perioperative stress, leading to POD and POCD. We will employ bed-side cognitive tests, bench-side enzyme-linked immunosorbent assays, and brain imaging to accomplish two Specific Aims: (1) to conduct a pilot study determining the feasibility and safety of our system/protocol in 24 participants; (2) to obtain preliminary effect size estimates of the association of brain Aß, Tau, and/or microglia activation levels with POD/POCD in the recruited 24 participants. The outcomes from the proposed studies will provide crucial information in regard to a future definitive study, including: (1) eligible:recruit ratio; (2) retetion rates; (3) safety; and (4) preliminary effect sizes for the associations of interest. The results fom our pilot study will guide us in determining whether we should apply for the R01; and if so, how many participants are needed. The proposed studies are highly innovative and significant, because the anticipated results would lead to an R01 study, which could illustrate that high brain Aß, Tau, and/or microglia activation levels are associated with POD and POCD. These findings would suggest that we should avoid or treat perioperative factors (e.g., anesthetic isoflurane, hypothermia, and severe inflammation) which may cause Aß accumulation, Tau phosphorylation, and/or neuroinflammation, leading to POD and POCD. Ultimately, the proposed R21-supported system/protocol study and the future R01-supported confirmative/ definitive research could lead to better anesthesia and surgery care for older adults.

Further information available at:

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United States of America

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