## Japan-U.S. Brain Research Cooperation Program Researchers Dispatched to the U.S. Program FY2020: Report

Field:\_4\_\_\_\_

 Researcher Name: Toru Ishii Title: Visiting research fellow Affiliation: Human Brain Research Center, Kyoto University Graduate School of Medicine

## 2. Research Title:

Neural correlates of bidirectional relationship between sleep disruption and Aß deposition in Alzheimer's disease

 U.S. Joint Researchers/Institutes
Name: Ruth O'Hara
Title: Professor
Affiliation: Department of Psychiatry and Behavioral Sciences Stanford University School of Medicine

4. Research Period, from/to (yyyy/mm/dd): From 2021/10/24 to 2022/03/15

5. Abstract, Results, and Research Significance (300 Words):

Sleep spindles play a crucial role in active systems consolidation of memory. There is growing evidence that points to the importance of spindle/slow oscillation (SO) coupling as a mechanism for the efficient transfer of information from the hippocampus to the neocortex. The synchronization of spindles to the SO up-state appears to be central to the induction of synaptic plasticity underlying the formation of longer-term representations. However, it is still unknown whether all the contribution of the spindle to memory is under the effect of SO or not. Specifically, the mechanism of memory consolidation in older adults whose frequency of SO decrease with aging has not been elucidated. This study aimed to examine the relationships between overnight memory retention and spindles/SO coupling in the elderly.

Participants were 135 community-dwelling elderly people (60 females, age:  $71.7 \pm 8.0$  years). All participants took ambulatory overnight polysomnography (PSG) for sleep assessment. List-learning tests were performed before and after PSG night to assess the memory function.

The three main findings of this study are 1) Spindle activity and SO significantly positively correlated with overnight memory retention (OMR) independently. 2) Measures of spindle/SO coupling showed a significant positive correlation with OMR. 3) Activity of the fast spindle positively correlated with OMR in the individuals whose spindle/SO coupling was not significant.

These results suggest that although spindle/SO coupling plays a key role in memory consolidation, the spindle may have another pathway that contributes to overnight memory retention. This pathway may be crucial for memory maintenance in the elderly whose SO has decreased with aging.

The significance of the result is that it provides novel evidence for the mechanism of memory consolidation in the elderly. The findings may pave the way for ideal intervention to maintain the memory function of the elderly and individuals with dementia.

6. Other (Research-related concerns, particular points to note):

The research period was postponed one and a half years from the initial plan due to the Pandemic. In addition, the laboratory works were suspended temporarily just during my dispatch period because of the surge of a new variant of the virus in the US. Due to such reasons, we had to modify our initial research plan, which I submitted when I applied for this program in 2019. I appreciate your understanding regarding this point.

\*Please attach any reference materials as necessary.