Poster | Disorders of Nervous Systems and Treatment

[3P]Alzheimer's Disease and Dementia

Fri. Jul 31, 2020 1:30 PM - 3:30 PM Poster Session

*Videos are available throughout the meeting period.

[3P-209]Cilostazol, a phosphodiesterase 3 inhibitor, ameliorates spatial memory in APP knock-in mouse model of Alzheimer's disease.

*Syuichi Yanai[1], Tomoko Arasaki[1], Takashi Saito[2,3], Takaomi Saido[2], Shogo Endo[1] (1.Aging Neuroscience Research Team, Tokyo Metropolitan Institute of Gerontology, 2.Laboratory for Proteolytic Neuroscience, RIKEN Center for Brain Science, 3.Department of Neurocognitive Science, Institute of Brain Science, Nagoya City University)

As cAMP plays an essential role on learning and memory in many species, recent studies have focused on the cAMP-PKA-CREB pathway as potential therapeutics for age-related cognitive impairment. Intracellular concentration of cAMP is regulated by the balance between its synthesis by adenylate cyclase and hydrolysis by phosphodiesterases (PDEs). Therefore, inhibitors of PDE, which elevate intracellular cAMP concentration, are promising targets for the development of cognitive enhancement drugs. Recently, we reported that long-term administration of cilostazol, a selective PDE3 inhibitor, prevented the impairment of hippocampus-dependent memory associated with normal aging in C57BL/6J mice. To begin investigating the effect of cilostazol on memory impairment in Alzheimer's disease, we used the APP $^{NL-G-F}$ mice that harbors three humanized mutations within the murine Aβ sequence. These mice exhibit spontaneous Aβ deposition in subcortical / cortical regions and cognitive impairment. In the present study, we evaluated the effect of long-term cilostazol administration on hippocampus-dependent memory task in APP^{NL-G-F} mice.

The original line of APP^{NL-G-F} mice were obtained from Dr. Saido of RIKEN center for Brain Science. The APP^{NL-G-F} and APP^{WT} mice were generated by *in vitro* fertilization and were fed the feed containing cilostazol (0 or 1.5%) *ad libitum* starting from 6 months of age. When they reached 12 months of age, they were subjected to the behavioral test battery. In the Morris water maze probe test, 0% cilostazol-APP^{NL-G-F} mice performed poorly compared to 0% cilostazol-APPWT mice, suggesting that spatial memory was impaired in 12-month-old APP^{NL-G-F} mice. However, 1.5% cilostazol-APP^{NL-G-F} mice performed significantly better than 0% cilostazol-APP^{NL-G-F} mice, allowing them to achieve a similar level of 0% cilostazol-APP^{WT} mice. In the open field test, three groups of mice showed similar performance on immobile time and distance traveled. These results suggest that long-term administration of cilostazol ameliorate spatial memory impairment in a mouse model of Alzheimer's disease without no significant behavioral side effect. Further basic study of cilostazol in APP^{NL-G-F} mice will elevate cilostazol as a new therapeutic candidate for treating cognitive impairment due to Alzheimer's disease.