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-214]Machine learning for detecting disturbance of neuronal networks in a mouse model of tauopathy

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Background: Evaluation of neuronal network dysfunction on a single-cell basis in vivo in tauopathy model mice is essential for understanding pathomechanisms of tauopathies. However, methods for assessing neuronal network dysfunction remain insufficient, resulting in debates about neuronal activities in rTg4510 mice, a well characterized model animal which consistently develops progressive tau pathology in the forebrain around 4-5 months of age.
Objective: We aimed to develop a method to evaluate neuronal activities and neuronal networks in living tauopathy mice using two-photon microscopy and machine learning.
Methods: rTg4510 transgenic mice expressing P301L mutated tau and non-transgenic (non-Tg) mice were utilized in this study. GCaMP6s were expressed in the barrel cortex, and calcium responses of individual neurons were measured by a two-photon fluorescence microscope. First, the frequency of spontaneous neuronal firings and the amplitude of neuronal response to sensory stimulation of each neuron were measured. Next, we utilized machine learning for evaluating function in the neuronal networks in both awake resting and behaving conditions. In the resting condition, the connectivity of the neuronal network was evaluated by the spontaneous firing pattern of neurons. In the behaving condition, reproducibility of the neuronal responses to differently oriented whisker stimulation was evaluated.
Results: The frequency of spontaneous neuronal firings and the amplitude of neuronal response of each neuron did not show significant differences between rTg4510 mice and non-Tg mice. In contrast, utilizing the machine learning method, the connectivity of the neuronal network in 3-month-old rTg4510 mice was weaker than that in age-matched non-tg mice, which was further decreased at 6 months of age. Moreover, the reproducibility of neuronal responses to two differently oriented stimulations for rTg4510 mice was significantly lower than for non-Tg mice at 3 and 6 months of age, suggesting that the ability to process information for sensory stimulation is impaired in rTg4510 mice.
Conclusion: We demonstrated that machine learning was a powerful method to determine the functional integrity of cortical neurons in vivo, which was not feasible by the conventional single neuron based calcium imaging. This strategy was also valuable to assess the dysfunction of neuronal network in rTg4510 tauopathy mice brains.