お茶の水ニューロサイエンス
アソシエーション（ONSA）

東京医科歯科大学 Tokyo Medical and Dental University
CBIR 脳統合機能研究センター

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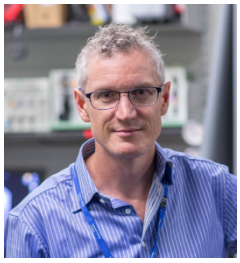
Amyloid pathology reduces dynamic range and disrupts neural coding in 5xFAD mice



演者 Prof. Simon Schultz (Imperial College London)

日時 2024 年 7 月 19 日(金) 18:00 開始

会場 ハイブリッド開催（対面＆オンライン）
会場：M&D タワー9 階 大学院講義室 4
オンライン参加者：Zoom 視聴者は事前に登録をお願いします。
https://zoom.us/meeting/register/tJwkfuuorz4rEtxTR9taZixYMZuw5_ZbIXld

講演要旨

Alzheimer's Disease (AD) is characterized by impairment in memory and cognition, and by aberrant neuronal activity notably in the vicinity of amyloid plaques. To understand how amyloidosis in AD changes circuit properties affecting memory encoding and recall, we examined the relationship between neuronal activity, distance to amyloid plaques, and spatial memory readout from hippocampal CA1 place cells in the 5xFAD mouse, a widely used model of AD. We used an air-lifted behavioural platform (Neurotar), which we have recently shown can be used to map place fields in head-fixed mice using two-photon microscopy (Go et al, Front Cell Neurosci 15:19, 2021), and imaged mice as they ran around a circular track. Studying two age groups (2-3 month old 6.5-10 month old mice) we found that during rest (non-running) periods, neuronal activity in CA1 was higher in 5xFAD mice compared to WT littermates, an effect that grew stronger with age. Moreover, neurons close to amyloid plaques (<20μm in old, <40μm in young) had elevated activity. During running, however, old 5xFAD mice showed significantly impaired dynamic range of neuronal activity in response to modulation of firing by both speed and spatial location, as well as lower spatial information rates. We then analyzed how these changes in circuit properties affect memory encoding and recall. Compared to WT mice, old 5xFAD mice required more laps around a familiar track for cells to exhibit place tuning, indicating impaired memory recall. Impaired memory encoding in a novel environment was similarly observed in 5xFAD mice in both age groups. Old 5xFAD place fields for a familiar track were less stable within a trial compared to old WT place fields. Finally, we investigated performance in a forced-alternative spatial working memory task, finding that the task sensitively captured deficits due to both aging and amyloid phenotype, as well as revealing additional feature such as the presence of "splitter cells". Our results provide new insights into the circuit mechanisms underlying the progression of memory deficits in Alzheimer's Disease.

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