

審査の結果の要旨

氏名 アルヴァロ キャリア ルイス

The hippocampal dentate gyrus is known to be important for the formation, recall and extinction of episodic memories. The applicant studied the activity of mature and adult-born granule cells (GCs) using  $\text{Ca}^{2+}$  imaging in freely moving mice during cue-dependent retrieval and extinction of fear memory, and related the neuronal activities with the changes in behavior of mice. The following results were found:

- 1– The number of active mature GCs was increased during cued fear retrieval-extinction in conditioned mice but not in unconditioned mice.
- 2– The activity-dependent induction of Fos immediate early gene by cued fear retrieval-extinction was higher in conditioned mice than in unconditioned controls.
- 3– Mature GCs in unconditioned mice showed a decay in the  $\text{Ca}^{2+}$  event rate through the retrieval-extinction sessions, while those in conditioned mice exhibited a transient increase in the event rate, fired more selectively to the tone, and showed a change in the active population of mature GCs along with extinction.
- 4– In conditioned mice, there was a decrease in the number of active adult-born GCs after fear conditioning that persisted through the retrieval-extinction sessions.
- 5– A part of adult-born GC population showed  $\text{Ca}^{2+}$  events more frequently and periodically. Those active and periodic adult-born GCs in conditioned mice showed similar activity to those in unconditioned mice. In contrast, adult-born GCs with low  $\text{Ca}^{2+}$  event frequency showed a switch of active population during the memory extinction session.
- 6– There were no clear tone-related effects in the  $\text{Ca}^{2+}$  event rate and cue selectivity of adult-born GCs.
- 7– Chemogenetic inhibition of mature GCs not only impaired the cue-dependent retrieval of fear memory but also compromised the effectiveness of the extinction process, whereas generalized ablation of GCs increased cue-dependent freezing and disrupted cued extinction.

To summarize, these results suggest that GCs are necessary for the retrieval and extinction of a cued fear memory and that mGCs and abGCs utilize distinct mechanisms for the processing of episodic memories. Moreover, the thesis is acceptable in the present form for the award of the Ph.D. degree.