# P6

## Neuronal Activity in the Mouse Retrosplenial Cortex during Context Discrimination in Virtual Environments

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The retrosplenial cortex (RSC) densely interconnects with cortical, hippocampal and thalamic structures and plays an important role in memory and spatial navigation. Previous studies have suggested that RSC manipulations affect behavioral performance on spatial and contextual tasks; however, the neural circuit dynamics underlying the function of the RSC during acquisition and recall of contextual memories is not well understood. To address this, we established in vivo two-photon calcium imaging of neuronal activity in the RSC of head-fixed mice performing a behavioral task in virtual environments consisting of varying contexts. Mice learned to discriminate between contexts and associate a water reward with a particular context at a specific location and, after learning, showed a significant reduction of running speed proceeding the reward zone only in the rewarded context. To characterize the role of the RSC in this paradigm, we tested its involvement in the formation and retrieval of contextual memories by using a chemogenetic approach (DREADDs) to temporarily inactivate RSC neurons (virally transduced to express the inhibitory hM4Di receptor) after systemic injection of clozapine-N-oxide (CNO). Mice failed to learn the association when the RSC was silenced during training; however, when the RSC was silenced after learning (during recall), mice still demonstrated behavioral context-discrimination and context-specific reward associations. Additionally, analysis of neuronal activity revealed that RSC neurons encode information regarding context, position, and speed within the virtual environment. Furthermore, the RSC predominantly contains multitasking cells, the proportion of which increased after relearning. Thus, this multitasking encoding may assist the RSC in its role in navigation and contextual memory formation.

*Key words: Retrosplenial cortex, two-photon imaging, virtual reality, context discrimination, learning and memory, DREADDs*