A role of nucleus reuniens in goal-directed navigation

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Abstract

During navigation, animals require information about their current location as well as the goal destination. While the hippocampus and parahippocampal regions are thought to provide accurate information about the animal's instantaneous position, it is still largely unclear where and how the goal location is represented in the brain. A potential candidate is the medial prefrontal cortex (mPFC), as neurons in this area exhibit enhanced temporal coordination with the hippocampus during trajectory decisions [1] [2], and lesions of mPFC led to impairment in goal-directed navigation [3]. Since there is no direct projection from the mPFC to the hippocampus, the midline thalamic nucleus reuniens (RE) is considered a key node to link between mPFC and the CA1 region of the hippocampus [4]. Our previous study has shown that mPFC-RE input is essential for the next trajectory coding in CA1 place cells [2], implying a role of this input in goal-directed navigation. However, animals with lesions in RE did not show significant impairment in the Morris water maze task [5], putting the RE's role in the navigation into question. To clarify this discrepancy, we used optogenetic and chemogenetic methods to inactivate RE neurons reversibly during goal-directed navigation. Male Long-Evans rats were injected with AAVs expressing either SwiChR or hM4Di in RE, and an optical fiber was implanted together for SwiChR-injected animals. To test goal-directed navigation, we used an open field arena with evenly-distributed 25 wells on the floor to deliver water as rewards. The task is composed of repetitively-alternating two task phases, goal-directed and random-foraging phases [6]. In the random foraging phase, animals are required to explore the arena to find a randomly-chosen well that delivers water. In the goal-directed phase, the fixed home well is always rewarded, and thus rats usually took a direct path to this remembered well. When RE is inactivated by either laser application or agonist injection, animals took a longer path or spent more time particularly at the initial part of the journey to reach the home well. This is not likely due to the impairment of goal representation or memory, because the error rate of choosing incorrect wells did not increase during RE inactivation, indicating that animals were able to distinguish the home well from others. Our result together points to RE as a key structure for route planning in navigation, probably by interfacing mPFC with an internal spatial map in the hippocampus.

Keywords: *spatial navigation*

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