Title:	Medail septum Deactivation using DREADD
Authors:	Verma, Priyansha (/jspui/browse?type=author&value=Verma%2C+Priyansha)
Keywords:	HIPPOCAMPUS TEMPORAL MICROINJECTION MICROPROBE
Issue Date:	May-2024
Publisher:	IISER Mohali

Abstract:	Damage to the hippocampus, the key brain structure involved in spatial navigation and learning, results in deficits in memory formation, consolidation and retrieval (Lehmann et al., 2007; Froudist-Walsh et al., 2018; Watson et al., 2013). Numerous studies have shown that hippocampal theta (a 4-12 Hz global oscillation very prominent in the hippocampus and surrounding areas) plays a vital role in sequentially encoding memories formed by the hippocampal place cells by enabling the formation of stable representations of these experi- ences for later retrieval (Nuñez Buño, 2021). The neural circuitry underlying memory and navigation are closely interwoven since both are encoded with the help of hippocampus. Decoupling the environment from the events experienced in that environment is imperative to understand the role of theta in each of them distinctly. Previous studies (Barry et al., 2012; Petersen Buzsáki, 2020; Gemzik et al., 2021) have disrupted theta oscillations in the hippocampus to analyse its role in navigation by using various pharmacological, temperature and optogentic manipulations of the medial septum (MS), a brain area thought to act as a pacemaker for theta oscillations in the hippocampus (Stewart and Fox, 1990). The approach of most of these earlier studies was to inactivate MS activity; the manipulation resulted in impaired spatial memory. However, these studies have provided limited information because a side effect of MS inactivation is disruption of the place cell firing, making it unclear whether the navigational deficit was due to the inability of the hippocampus to organize information temporally or to a general disrup- tion of the spatial cognitive map of the hippocampus. The definitive proof that temporal organization of hippocampal activity is critical for spatial navigation came from a more recent study which used gabazine, a GABA-A receptor antagonist, to selectively disrupt the rhythmic activity of MS inhibitory interneurons which project directly to the hippocam- pal interneurons (Bolding et al., 2020).. Alteration of the rhythmic MS activity markedly reduced theta oscillations (presumably disrupting temporal organization of hippocampal activity), and impaired spatial navigation, while at the same time preserving normal firing in hippocampal place cells. Selectively disrupting temporal aspects of hippocampal activ- ity while preserving the spatial coherence of the representation is a critical manipulation for studying episodic memory, which encodes the occurrence of various personally experi- enced events along a timeline (Tulving Donaldson, 1972). Our experiment aimed to develop a protocol to reversibly dysregulate theta in mice us- ing a novel chemogenetic technique- DREADDs to target the GABAergic interneurons of MS. We injected Gi-DREADD, which can be employed to obtain an effect similar to gabazine, into the medial septum and recorded the hippocampal activity using silicon probes. Our results showed that alteration of MS activity via deschloroclozapine (DCZ), an activator drug, caused changes in the theta without significantly impacting the firing rates of the cells in the hippocampus. However, more repeats are essential to conclude if spa- tial maps are preserved for an environment learned without the influence of drugs in mice. The preliminary results on the effects of this manipulation on spatial information encoded by these place cells show no significant change in the spatial score, hinting that the spatial map should be preserved. However, the effect of manipulation on the preservation of spatial maps needs to be investigated further.
Description:	Under Embargo Period
URI:	http://hdl.handle.net/123456789/5705 (http://hdl.handle.net/123456789/5705)
Appears in Collections:	MS-19 (/jspui/handle/123456789/4302)

Files in This Item:

File	Description	Size	Format	
embargo period.pdf (/jspui/bitstream/123456789/5705/1/embargo%20period.pdf)		6.04 kB	Adobe PDF	View/Open (/jspui/bitstream/123456789/5705/1/

Show full item record (/jspui/handle/123456789/5705?mode=full)

(/jspui/handle/123456789/5705/statistics)