

The impact of lipid signaling modulation in cognition

ABSTRACT:

Over the past years increasing amount of attention has been given to signaling lipids as well as to its modulating enzymes, such as phospholipases. Specifically, phospholipase D (PLD), that converts phosphatidylcholine to phosphatidic acid (PA), has been shown to exhibit a role in neurological development and physiology. Several studies have been associating PLD1 and PLD2, the two main mammalian PLD isozymes, to neurological processes, including neurotransmitter release, dendritic branching, cognition, and brain development. Also, the hippocampus has been suggested as one of the brain regions showing the highest PLD activity and neurodegenerative conditions such as Alzheimer's disease associated pathways have been shown to be modulated by PLD signaling. Thus, the aim of this project was to better understand the potential role of PLD in hippocampal function in adult mice upon *Pld1* or *Pld2* genetic ablation.

We performed a hippocampal related behavioral characterization of these animals, a structural analysis regarding dendritic morphology, electrophysiology neuronal plasticity evaluation and protein and lipidomic biochemical detailed analysis.

Our behavioral data, specifically considering motor and exploratory activity, anxiety and memory, showed that PLD2 knockout mice behavior is not altered when compared to their wild type littermates. Although most of this was also observed in the animals lacking PLD1, the results indicate an object recognition-dependent short-term memory deficit. Regarding hippocampal dendritic arborization, the ablation of either PLD1 or PLD2 led to significant alterations in dendritic morphology, although with a different impact of each isozyme in the dorsal and ventral hippocampus. Concerning the electrophysiological plasticity analysis we observed a deficit in long-term depression in the dorsal hippocampus of PLD1 knock-out mice.

Finally our biochemical analysis revealed a significant decrease in SNAP-25 protein levels and total levels of PA levels in PLD1 knock-out mice while no major changes were observed upon PLD2 genetic ablation.

Our results suggest that the separate ablation of PLD1 and PLD2 leads to different effects in the dorsal and ventral hippocampus, with a more significant effect upon PLD1 ablation.

Keywords

Cognition, Lipids, Memory, Learning, Hippocampus, Phospholipase D.

Published Work:

Miranda, A. M., Bravo, F. V., Chan, R. B., Sousa, N., Di Paolo, G., & Oliveira, T. G. (2019). Differential lipid composition and regulation along the hippocampal longitudinal axis. *Translational Psychiatry*, 9: 144. doi: 10.1038/s41398-019-0478-6

Os textos são da exclusiva responsabilidade dos autores
All texts are of the exclusive responsibility of the authors

Researcher's Contacts:

Tiago Gil Oliveira

Email: tiago@med.uminho.pt

Phone: +351253604923