

Comparative analysis of dentate gyrus from naive Wistar rats and human hippocampus using molecular tools.

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Abstract

In recent years, the hippocampus has been the target of several studies due to of its functional complexity, mainly because of its association with neurodegenerative diseases, such as Epilepsies and Alzheimer's. However, to understand the complex mechanisms underlying these diseases, we must understand other structures that compose the Hippocampal Formation, such as dentate gyrus (DG), subiculum and entrhinal cortex. Thus, in order to validate the Wistar rat as a suitable animal model for diseases which affects the DG, we propose to analyze such structure from naive Wistar rats and human tissues, using proteomics and transcriptomics in order to describe molecular pathways present in both species comparing them. The project was approved by CEUA protocol no. 4062-1 and CAAE 12112913.3.0000.5404.

Key words:

Hippocampus, Transcriptomics, Proteomics.

Introduction

Much of the studies related to the hippocampus are aimed to elucidate the diseases which affect this structure, such as Mesial Temporal Lobe Epilepsy (MTLE) and Alzheimer's disease (AD). However, to better understand the pathophysiology of these diseases, which are not fully elucidated, we must focus in other structures from the Hippocampal Formation, that can be involved with these mechanisms, such as the DG¹. The DG itself is also subdivided into dorsal and ventral in rodents and posterior and anterior in humans². Moreover, the neurodegenerative diseases, as others, are usually investigated using animal models, mainly rodents, due to its possibility of study the development of the diseases and not only its final stage³. However, despite its remarkable similarities with humans, it is necessary to evaluate the differences between the two species to validate the rodents as a suitable model for human pathologies. Therefore, here we present the comparative multi-OMICs analysis of the laser microdissected DG from rat and humans, intending to characterize and describe both species, validating the rat as a good animal model for human pathologies. We also present the comparative analysis of dorsal and ventral DG isolated from the rats.

Results and Discussion

These are preliminary results since the human samples are in analysis process. Also, since we have the opportunity to work with the whole hippocampus from the animals, we analyzed the dorsal and ventral DG (dDG and vDG) separately. From the proteomic analysis we have identified a total of 230 proteins in the dDG and 240 from vDG. The main enriched pathways found comparing these two regions were *glycolysis and gluconeogenesis*, *remodeling of the neurofilaments* and *synaptic vesicle fusion*. The transcriptomic analysis from dDG and vDG is also in process. When we analyzed the dDG with the vDG we found 3337 transcripts differentially expressed and 320 proteins. The main enriched pathways identified between the two regions were *glycolysis and gluconeogenesis*, *regulation of*

cytoskeleton and *oligodendrocyte differentiation and myelination*.

Conclusions

The final comparative analysis between the dentate gyrus of the naïve Wistar rat and human tissue is being generate. Here we can already highlight the importance of using OMICs technologies to analyze different cell populations in different tissues. Indeed, we had shown that there are significant differences between the dorsal and ventral DG from rats, demonstrating the importance of precise isolation of specific cell populations, especially when we are studying complex neurodegenerative diseases.

Acknowledgement

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¹ Amaral, D.G.; Lavenex, P. *Hippocampal Neuroanatomy*. In *The Hippocampus* Book. 2009, Oxford University Press. p. 2-3

² Fanselow M.S.; Dong, H.W. (2010) "Are the dorsal and ventral hippocampus functionally distinct structures?" *Neuron*. 2010 Jan 14;65(1):7-19. doi: 10.1016/j.neuron.2009.11.031. Review.

³ Guedes, F. A.; Galvis-alonso, O. Y., & Leite, J. P. (2006). "Plasticidade Neuronal Associada à Epilepsia do Lobo Temporal Mesial: Insights a partir de Estudos em Humanos e em Modelos Animais". *Journal of Neurology*.