Proteomic analysis of dorsal and ventral subiculum isolated from the pilocarpine model of Mesial Temporal Lobe Epilepsy

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Abstract
Mesial temporal lobe epilepsy (MTLE) is the most frequent type of epilepsy in adults and it is usually refractory to clinical treatments. In most patients with MTLE a characteristic histopathological lesion is observed, including hippocampal sclerosis (HS). The subiculum is an important area which connects the hippocampus with the enthorinal cortex. In the present work we aim to use laser-capture microdissection (LCM) to isolate dorsal and ventral subiculum from epileptic rats induced by the classic pilocarpine protocol. With this material we will perform proteomics analysis to identify molecular and biochemical changes that could be involved in the context of MTLE.

Key words: Epilepsy, Subiculum, Proteomics

Introduction
Epilepsy is a neurological disorder characterized predominantly by spontaneous and recurrent seizures. In the histopathological aspect the most frequent feature is hippocampal sclerosis (HS), which basically is characterized by the loss of pyramidal neurons in CA1 and CA3 regions [1]. The hippocampus is a structure localized in the mesial temporal lobe and its function is related with memory formation and emotional control. The hippocampus is divided into dorsal and ventral regions. Electrophysiological analysis in rodent shows that the dorsal region is related to spatial learning, and the ventral region to emotional responses. The subiculum forms the transition that connects the hippocampus with the enthorinal cortex, which allows for high amplification and modulation of the neuronal response, and it is involved in the recovered short-term memory and spatial memory codification. In this study, we aim to isolate dorsal and ventral subiculum from an epilepsy animal model induced with pilocarpine. Isolation of the subiculum regions will be achieved by LCM and used to perform proteomic analysis.

Methodology

Results and Discussion

Table 1. Number of proteins identified, total and differentially expressed, from the ventral subiculum of Sham controls and induced animals, number of enriched pathways and their respective proteins. Data by MaxQuant/Perseus and Metacore softwares

<table>
<thead>
<tr>
<th>Total proteins</th>
<th>Differentially expressed protein</th>
<th>Enriched pathways</th>
<th>Altered proteins in enriched pathways</th>
</tr>
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<tbody>
<tr>
<td>186</td>
<td></td>
<td>9</td>
<td>24</td>
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Fig 1. A Hippocampus from control Sham. Green coloring indicates sub region CA1, red coloring indicates sub region CA2, blue coloring indicates sub region CA3, orange coloring indicates the granular layer of the dentate gyrus and purple indicates the molecular layer of the dentate gyrus. Circulated areas in black indicates the dorsal subiculum region. B Control sham hippocampus marked to the same colors, and circulated in black is the ventral subiculum region.

Table 2. Main enriched pathways identified in the ventral subiculum and their respective altered proteins.

Conclusions
We have identified some altered proteins in ventral subiculum that are related with important biological pathways. As the dorsal subiculum is still under evalution we expect that it will present different altered biological pathways as previously described in literature. Therefore we presented new biological pathways of the ventral subiculum that can be involved with the epileptogenic process of the pilocarpine model of MTLE.

Acknowledgement

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1. Fisher, R. S. et al. Epileptic seizures and epilepsy: definitions proposed by the international League Against Epilepsy (ILAE) and the International Bureau for Epilepsy (IBE). Epilepsia, 2005.