Environmental Enrichment and Rat Brain Plasticity: A Study on CNPase and Connectivity

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Introduction: Interest in the retrosplenial cortex (RSCx) has grown due to its association with spatial navigation and its integration into the default mode network. Several studies have revealed the importance of this brain region, particularly in proficient navigators who exhibit increased activity in the retrosplenial cortex during the processing and consolidation of landmarks (Auger et al, 2017). Additionally, the anterior cingulate cortex has been implicated in navigation, particularly in path planning, further highlighting the involvement of these regions in spatial cognition and memory (Patai and Spiers, 2021). Environmental enrichment (EE) has been demonstrated to have diverse cognitive, behavioral, and physiological effects, including alterations in myelination and functional brain connectivity. CNPase is an enzyme that plays a crucial role in myelination. It is primarily expressed in oligodendrocytes and is responsible for producing myelin sheaths around axons. Rats living in an enriched environment have been found to have an increased total number of CNPase cells (Zhao et al, 2011). Notably, research by Hakon et al. (2017) revealed that housing rats in an enriched environment post-stroke led to enhanced regional resting-state functional connectivity compared to those in standard housing, suggesting potential therapeutic implications of environmental stimulation. Looking at the connection between myelination and connectivity Hermunstad et al. (2013) discovered that more connections generally lead to stronger functional connectivity, regardless of their location. However, the influence of connection length on strong functional connectivity varies between inter- and intrahemispheric connections, depending on the specific brain regions involved. Taking these findings we were interested in the effects different environments have on myelination and on functional connectivity and how they might be connected.

Methods: In our study, we investigated the impact of different environmental conditions on the brain functional connectivity between the anterior cingulate cortex and the retrosplenial cortex in a longitudinal study involving healthy Wistar rats using MRI. At the end of the study we measured the CNPase expression using an immunohistochemistry analysis, and the behavior related with the activities of these regions through water maze task (learning and memory functions).

Results: Our findings revealed a natural increase in functional connectivity between these regions as the rats aged ($F(2,65) = 0.335$, $p = .001$). Surprisingly, we did not observe significant effects of housing conditions on this connectivity ($F(2,65) = 7.490$, $p = .716$). Regarding CNPase expression, we found an increase in RSCx for the enriched environment group, compared to the control group ($p=0.029$). The behavioral outcomes associated with the functions of the RSCx region include spatial learning capacity. In the context of the water

maze task, the results indicate that the Enriched Environment (EE) group exhibited superior performance during the learning sessions (significant day effect with p= .001). During the subsequent test session, there was a trend in the EE group towards spending more time in the platform zone; however, this difference did not reach statistical significance when compared to the control group (p= .588).

Conclusion: These results contribute to our understanding of how environmental factors may shape the development and changes in functional connectivity within the brain. While age-related changes in connectivity were evident, the specific housing conditions we examined did not appear to exert a substantial influence.