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P34. CHEMOGENETIC MANIPULATION OF BRAIN NEURONAL PATHWAYS RESCUES SEX-DIFFERENCES IN MEMORY CAPACITY

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Memory capacity (MC) is the number of information that can be retained in memory for a short (working memory capacity – WMC) or a long (long-term memory capacity – LTMC) time interval. Its decline has been observed in many psychiatric and neurodegenerative diseases, and in physiological ageing. Although gender differences in MC are reported, less is known about the biological mechanisms at the basis. Using the Different/Identical Object Recognition Task (DOT/IOT), we found that adult male mice have a WMC of about six objects, like humans, and that only in high memory load conditions the hippocampus (HP) is recruited to solve the task. Female subjects have the same WMC as males, but they are impaired in consolidating information when challenged with high memory load conditions. This impairment in memory consolidation correlates with recruitment of different brain circuitries in the two sexes, with the HP hypoactivated in female compared to male mice. Using a chemogenetic approach, we demonstrated that reverting HP hypoactivation rescues the memory consolidation impairment in females. In parallel, we characterized MC decline during ageing in males and females at 6 and 12 months. We found that female mice have a load- and delay-dependent earlier decay of MC compared to males. These findings might be relevant in understanding the higher impact of dementia in women population compared to men, and we propose the different circuitry recruitment as a mechanism responsible for female's higher vulnerability to age-dependent memory decay.