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Effects of chronic trehalose supplementation on spatial learning and autophagy in aged mice

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Loss of proteostasis is regarded as one of the hallmarks of ageing, and it refers to the decrease of a cell´s ability to ensure the correct folding, stability, and eventual degradation of proteins. One of the principal mechanisms for the later, is the lysosomal degradation through autophagy. During ageing, there is a global impairment of autophagy which is particularly evident in the brain, and it has been correlated with the onset of neurodegenerative diseases. The disaccharide trehalose has been shown to have neuroprotective properties by reducing protein aggregates and, though it´s mechanism of action is still controversial, there is compelling in vitro evidence for a global regulation of autophagy by this sugar. We tested whether a chronic systemic supplementation with trehalose during ageing improves hippocampus dependent spatial memory through the upregulation of autophagy. After administration of drinking water supplemented with trehalose for four weeks, aged (18 month old) C57BL/6Jc mice were tested in the water cross maze and one week after the end of the test, autophagy was assessed by western blot by protein levels and lipidation of LC3, and protein levels of p62 in prefrontal cortex, ventral and dorsal hippocampus. Mice treated with trehalose show a decreased latency to find a hidden platform in the water cross maze that was more evident during the first day trials. However, the accuracy in finding the platform was not improved by trehalose supplementation. These behavioral changes were associated with an increase in the total protein expression levels for LC3 in the dorsal hippocampus, but without an evident change in markers of the autophagy flux. These preliminary results suggest that chronic supplementation with trehalose during ageing may rather affect initial spatial learning strategies in an autophagy independent manner without lastingly affecting spatial memory in the water cross maze.