Running for REST: the effects of exercise in the hippocampus of aged mice

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Introduction: Exercise improves mental health and synaptic function in the brain during aging. However, the molecular mechanisms involved in this phenomenon are little understood. The modulation of the repressor element RE1-binding transcription factor (REST) and the inflammatory state by the exercise are possible mechanisms. **Objectives:** To evaluate the effect of voluntary exercise performed in running wheels (RW) in the sickness behavior and hippocampal neuroplasticity in adult and aged C57BL/6 mice. **Material and Methods:** C57BL/6 male mice of 4-6 months of age (young) and 19-21 months old (aged) (Ethics Commitee Protocol PP00760) which were divided in four groups: sedentary young (SED-young) and aged (SED-aged), and running wheel young (RW-young) and aged (RW-aged). All animals were isolated for eight weeks and the RW groups (young and aged) had free access to individual RW; while the SED groups had a locked RW. The animals daily distances races were measured by digital odometers. After 8 weeks, they were subjected to open field and tail suspension behavioral tasks, posteriorly euthanized to dissection of the hippocampus. The REST gene expression and BDNF were analyzed by RT-PCR. **Results and Discussion:** The aged animals exhibit a depressive-like and sickness behavior: less mobility in RW and in the open field, and great immobility in the tail suspension test. Gene expression showed a low profile neuroplasticity and high neuroinflammation in the hippocampus of aged animals. Exercise was anxiolytic and antidepressant, and improved motor behavior of aged animals. Exercise also boosted BDNF and REST expression, and decreased IL-1β and IL-10 expression in the hippocampus of aged animals. **Conclusions**: These data support a beneficial role of REST in the aged hippocampus, which can be further enhanced by regular exercise.

Keywords: aging; BDNF; depression; exercise; neuroinflammation; RE1-Silencing Transcription factor.

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