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Research Report

Effects of moderate and chronic exercise on the nitrergic system and behavioral parameters in rats☆

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ABSTRACT

Several reports suggest that nitric oxide (NO) could play a critical role on synaptic plasticity related to physical activity improving learning and memory; thus, physical exercise would have important effects on cerebral health. In order to analyze the long-term effects of chronic moderate physical training on the morphology and activity of nitrergic neurons belonging to the cerebral cortex, hippocampus and striatum, and their relationship with behavioral parameters. Wistar rats were aerobically trained (AT) up to the age of 18 months and compared to sedentary controls (SC). At the end of the training protocol behavioral parameters were analyzed in an eight-arms radial maze. Rats were sacrificed by perfusion fixation with 4% paraformaldehyde. Brains were dissected out and coronal sections containing the three mentioned areas were obtained. The neurons expressing nitric oxide synthase (NOS) were stained using the technique of NADPH-diaphorase (NADPH-d) and their morphological and densitometric parameters were quantified by image analysis. Afterwards, the isoforms of NOS were determined by immunofluorescence. Results revealed AT rats learned faster, performed less mistakes and were more successful than SC rats in the maze. The nitrergic neurons of the cerebral cortex were larger and they had an increased number of dendrites. The NADPH-d reactivity in the cortex and striatum was upregulated. Colocalization was significant for the neuronal nitric oxide synthase (nNOS), in both groups. In conclusion, moderate and chronic exercise had a positive effect on cognitive performance and anxiety related behavior. An upregulation of the nitrergic system was detected in AT rats and this fact could be involved in this beneficial action on the aged subjects.

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Abbreviations: AT, aerobic training; eNOS, endothelial nitric oxide synthase; FP, fecal pellets; G, grooming; IF, immunofluorescence; iNOS, inducible nitric oxide synthase; IOD, integrated optical density; LM, light microscopy; max. VO_2, maximal oxygen consumption; NA, number of arms visited; NADPH-d, NADPH-diaphorase; NO, nitric oxide; NOS, NO synthase; nNOS, neuronal NOS; ROD, relative optical density; SA, somatic area; SC, sedentary control; SME, spatial memory errors; WME, working memory errors; TT, total time

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1. Introduction

Regular moderate exercise has beneficial effects on health (Goto et al., 2004; Navarro and Boveris, 2008; Sarbadhikari and Saha, 2006), particularly enhances brain function and is a non-pharmacological intervention recommended to prevent and/or mitigate the effects of aging on CNS and the loss of cognitive function (Cotman and Berchtold, 2002; Cotman and Engesser-Cesar, 2002).

Physical activity in rats and humans showed a positive effect on depression, anxiety disorders and mental activity in the elderly (Dik et al., 2003; Kramer et al., 2006; Lytle et al., 2004). Many researchers reported that exercise increases gene expression of neurotrophic factors (Chen et al., 2006) involved in development, growth and survival of certain neuronal types (Anderson et al., 2000; Bimonte et al., 2003; Chen and Russo-Neustadt, 2007; Estévez et al., 2006) in rodents.

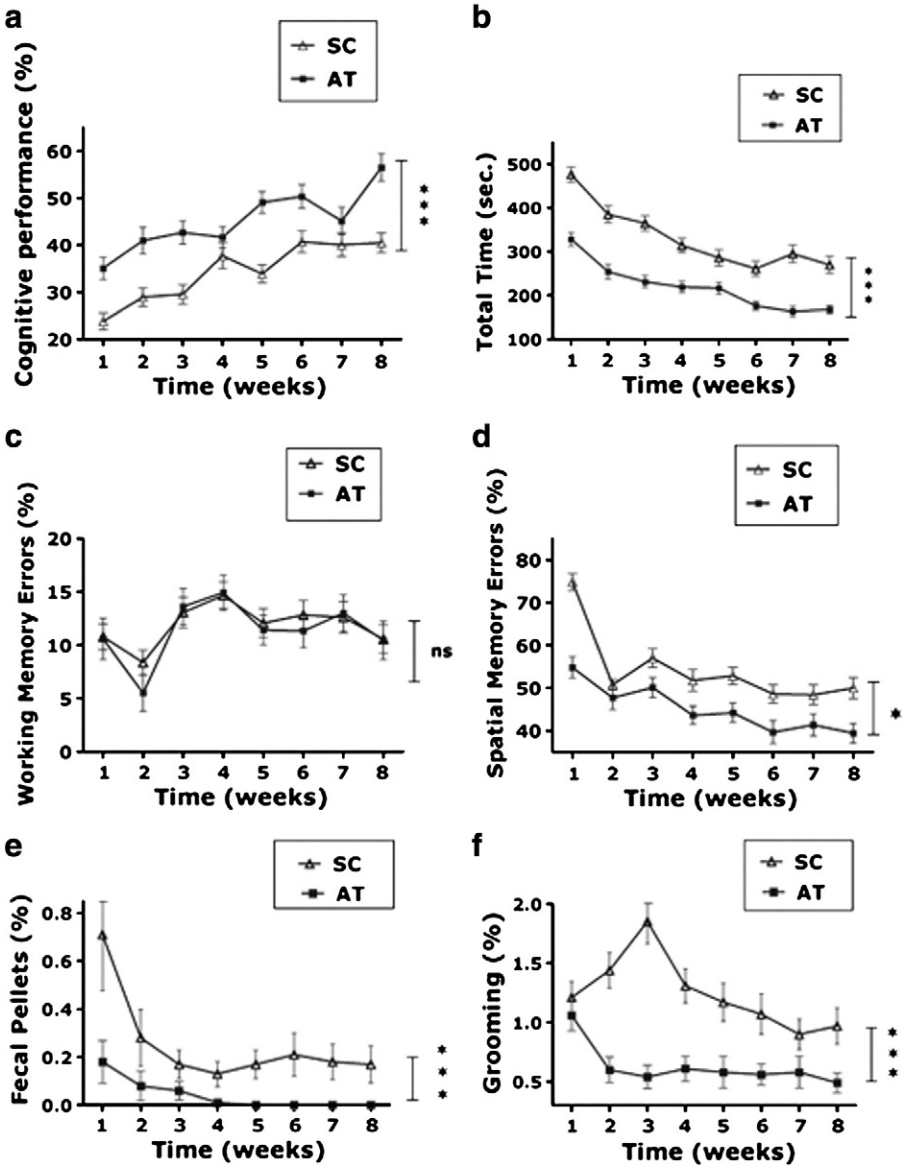

Fig. 1 – Eight-arm radial maze. Graphs represent behavioral parameters used to asses eight-arm radial maze performance of the AT (trained, N = 12) and SC (non-trained, N = 12) animals during 8 weeks at 18 months of age after the treadmill-running protocol. A two-way RM ANOVA (group × session/block) revealed that (a) AT rats had a better cognitive performance; (b) they searched faster the right arms of the maze compared with their controls; (c) no significant differences were detected in the working memory errors; (d) AT animals made significant less reference memory errors than SC. Note that the AT emotional reactivity was significantly lower as compared to controls, indicating an anxiolytic effect of exercise according with (e) the percentage of defecation pellets and (f) percentage of grooming. Points represent the means ± S.E.M. and asterisks indicate highly significant $^{***}p < 0.001$ and significant differences $^{*}p < 0.05$ between SC and AT animals (group effect). The results of the RM ANOVAS for each behavioral parameter represented in graphs a–e are summarized in Table 1.