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Research Report

Different protocols of physical exercise produce different effects on synaptic and structural proteins in motor areas of the rat brain

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ABSTRACT

The plastic brain responses generated by the training with acrobatic exercise (AE) and with treadmill exercise (TE) may be different. We evaluated the protein expression of synapsin I (SYS), synaptophysin (SYP), microtubule-associated protein 2 (MAP2) and neurofilaments (NF) by immunohistochemistry and Western blotting in the motor cortex, striatum and cerebellum of rats subjected to TE and AE. Young adult male Wistar rats were divided into 3 groups: sedentary (Sed) (n=15), TE (n=20) and AE (n=20). The rats were trained 3 days/week for 4 weeks on a treadmill at 0.6 km/h, 40 min/day (TE), or moved through a circuit of obstacles 5 times/day (AE). The rats from the TE group exhibited a significant increase of SYS and SYP in the motor cortex, of NF68, SYS and SYP in the striatum, and of MAP2, NF and SYS in the cerebellum, whereas NF was decreased in the motor cortex and the molecular layer of the cerebellar cortex. On the other hand, the rats from the AE group showed a significant increase of MAP2 and SYP in the motor cortex, of all four proteins in the striatum, and of SYS in the cerebellum. In conclusion, AE induced changes in the expression of synaptic and structural proteins mainly in the motor cortex and striatum, which may underlie part of the learning of complex motor tasks. TE, on the other hand, promoted more robust changes of structural proteins in all three regions, especially in the cerebellum, which is involved in learned and automatic tasks.

1. Introduction

Exercise induces several positive effects in the central nervous system of humans (Dustman et al., 1990; Lupinacci et al., 1993) and animals (Ferreira et al., 2010, 2011; Kleim et al., 1996, 1997; Real et al., 2010), such as improved learning, memory and plasticity (Lambert et al., 2005; van Praag et al., 1999a; Vaynman et al., 2006), increased neuronal activation (Holschneider et al., 2007; Lewis et al., 2007) and enhanced neurogenesis (Ferreira et al., 2011; van Praag et al., 1999a; van Praag et al., 1999b). Changes of neurotransmitters and their receptors (Del Arco et al., 2007b; Real et al., 2010) and of the expression of genes related to synaptic plasticity (Ferreira et al., 2010; Molteni et al., 2002), which are responsible for changing the number, structure and

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function of neurons (Ang et al., 2006; van Praag et al., 1999a), have also been observed.

Voluntary, treadmill and acrobatic exercise (VE, TE and AE, respectively) induce distinct plastic responses in different brain regions (Kleim et al., 2002; Klintsova et al., 2004; Vaynman et al., 2006). Studies using electron microscopy have shown that animals submitted to all three of these modalities presented plastic changes in the cerebellum and motor cortex. In the cerebellum, for example, there was an increase of the number of synapses of parallel fibers and Purkinje cells and an increased number of synapses per Purkinje cell, higher in the AE than the VE. This increase persisted with time (Black et al., 1990; Kleim et al., 1997, 1998b). Furthermore, it was observed that the AE group completed the designated tasks in less time, indicating a substantial gain of motor abilities (Kleim et al., 1996, 2002).

A series of studies have focused on the participation of synaptic (Ferreira et al., 2010; Lambert et al., 2005; Vaynman et al., 2004) and structural proteins (Derksen et al., 2007; Ferreira et al., 2010, 2011) in exercise-induced plastic changes. Microtubule-associated protein 2 (MAP2) and synaptophysin (SYP) have been studied after short-term AE and increases of SYP have been observed in the motor cortex, possibly related to the first 5 days of learning a motor skill. MAP2 changes, on the other hand, did not seem to increase according to the duration or difficulty of the acrobatic training (Derksen et al., 2007). Other authors have also reported increases of NF68, SYS and SYP in the striatum after short-term TE, which was accompanied by increases of SYS and NF68 in the cerebellum and a decrease, followed by increase, of NFs in the motor cortex (Ferreira et al., 2010). AE also induces increase of neurotrophins, such as BDNF, in the motor cortex and cerebellum (Klintsova et al., 2004), whereas TE increases BDNF in the striatum (Tajiri et al., 2010) and cortex (Rasmussem et al., 2009). A close relation between BDNF and the synaptic vesicle proteins SYS and SYP was observed by Vaynman et al. (2006), which demonstrated that the blockade of BDNF actions inhibited the VE-induced increase of these synaptic proteins. Learning a new motor skill (AE) can induce dendritic reorganization, synaptogenesis and changes of synaptic morphology, all of which require protein synthesis (Derksen et al., 2007). Training rats on a novel motor task can be an effective option to study the brain motor circuits in response to learning. A distinction has been made between tasks that require a high amount of attentional guidance (skilled training, internally guided) and those that do not (overlearned, automatic, and externally guided), and each has been linked with different patterns of functional brain activation and recruitment of different motor circuits (Adkins et al., 2006; Holschneider et al., 2007). In addition, it is becoming increasingly recognized that no single exercise paradigm is likely to fulfill all therapeutic needs (Cotman and Berchtold, 2007).

Various exercise protocols have been used to study its beneficial effects, such as acrobatic exercise, wheel running, and treadmill exercise of low to high intensity, continuous or intermittent, and of short and long duration (Ferreira et al., 2010; Kleim et al., 1997; Real et al., 2010). However, depending on the intensity of training, exercise could be, instead of beneficial, deleterious to the brain, by causing increased free radicals, cytokine production and excitotoxicity (Arida et al., 2011). Enriched environments have also been used, and all these modalities have the purpose of investigating specific exercise-induced plastic changes that occur in different brain regions (Del Arco et al., 2007a; Mora et al., 2007). We evaluated here if TE and AE could change structural and synaptic proteins in the same way in different motor areas of the rat brain. This could be used to help understand how different regions of the brain contribute to the motor learning process triggered by

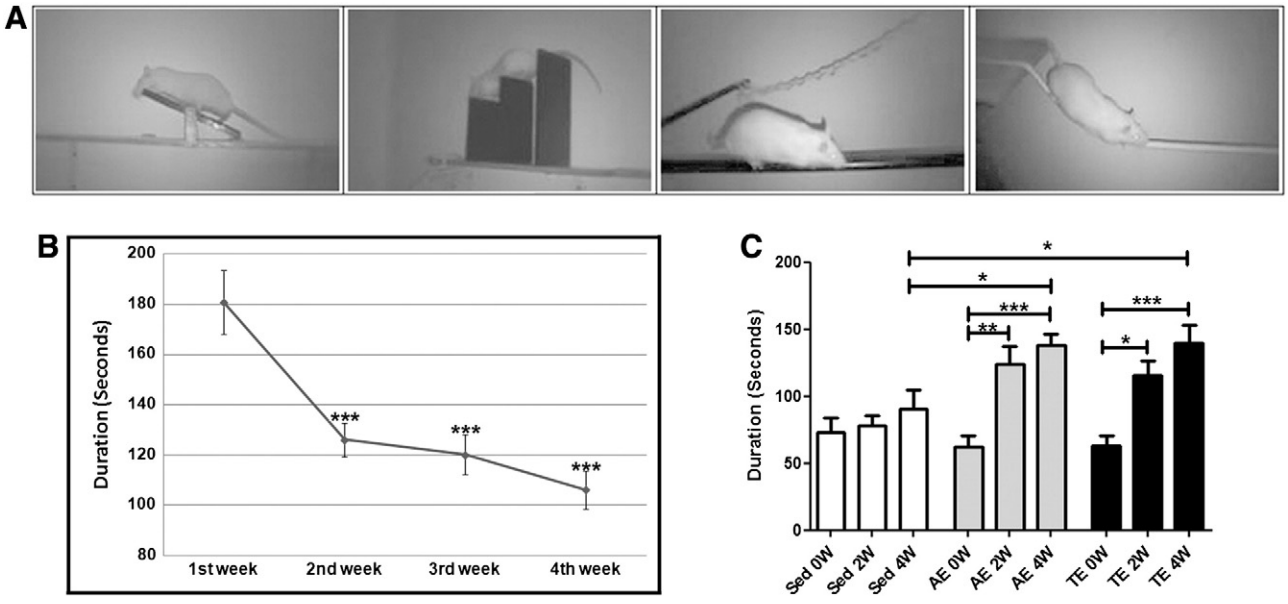

Fig. 1 – Behavioral evaluation. (A) See-saw, balance beams rope ladder and thin dowels as examples of the obstacles of the acrobatic circuit. (B) Evaluation of the acrobatic performance considering the recorded time to complete the acrobatic circuit each week. (C) Balance and coordination evaluation using the Rotarod considering the time spent on the equipment on the first day (0 W), on the second week (2 W) and on the fourth week (4 W) of the protocols.