Treadmill Training Modifies KIF5B Motor Protein in the STZ-induced Diabetic Rat Spinal Cord and Sciatic Nerve

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Abstract

Background: Previous research has demonstrated diabetic-induced axonal transport deficits. However, the mechanism of axonal transport impairment induced by diabetes is poorly understood. Kinesin motor proteins have been shown to transport various cargos along highly polarized neurons. In the present study, we investigated the effect of regular treadmill exercise on KIF5B and Sunday Driver (SYD) mRNA levels in sensory and motor parts of spinal cord and KIF5B content in sciatic nerves of streptozotocin (STZ)-induced diabetic rats.

Methods: Forty male Wistar rats were divided into four groups: (1) diabetic trained (DT: n = 10); (2) Non-trained diabetic (NTD: n = 10); (3) normal control (NC: n = 10), and (4) normal trained (NT: n = 10). Two weeks after STZ injection (45 mg/kg, i.p.), the rats were subjected to treadmill exercise for 5 days a week over 6 weeks. We determined mRNA levels and protein content by Real-time PCR and ELISA.

Results: Exercise training decreased blood glucose levels in the DT rats. Diabetes increased the KIF5B and SYD mRNA in both sensory and motor parts and KIF5B content in sciatic nerves in the NTD. Moreover, exercise training modulated the KIF5B and SYD mRNA and KIF5B content to normal levels in the DT. Exercise training in NT rats increased KIF5B and SYD mRNA in sensory and motor parts and KIF5B content in sciatic nerves.

Conclusions: Our results suggest that diabetes seems to change spinal cord KIF5B and SYD mRNA and sciatic nerves KIF5B content and exercise training modifies it, which may be attributable to the training-induced decreased hyperglycemia.

Keywords: Diabetes, exercise, kinesin, sunday driver

Introduction

Among the most prevalent complication of diabetes, neuropathy develops as an irreversible complication in more than half of with diabetes type 1 or 2.1 Diabetes is associated with slowing of motor nerve conduction velocity and reduced muscle contractile properties.2,3 In contrast, on the sensory side, there is not only slowing of sensory nerve conduction velocity but also atrophy of perikarya and axons associated with down-regulation of structural protein synthesis and loss of terminal epidermal axons.4,5 Several studies have demonstrated that axonal transport deficits in many neurodegenerative diseases might be due to alterations of molecular motor proteins that carry cargos, structural and regulatory microtubules protein that serve as rail roads, adaptors and scaffold proteins that regulate cargoes attachment to motor proteins, and metabolic modification that disrupt energy supply of motor proteins.6-12 Among different regulators of axonal motor proteins, SYD as a scaffold protein can interacts with kinesin and mediates the axonal transport of at least three classes of vesicles.13,14 It was shown that SYD interacts directly with the tail domain of kinesin heavy chain and activates it for microtubule-based transport.13 Among the 45 kinesin motor proteins that are involved in axonal and intracellular transport, in neuronal cells KIF5B transport synaptic vesicle precursors, membrane organelles, and mitochondria.15,16 On the other hand, impairment of anterograde axonal transport of some neurotrophic factors and synaptic proteins is demonstrated in neuronal cells of diabetic rats.17,18 Also, indirect evidence shows that axonal transport of mitochondria may be decreased in diabetic neuropathy.18

Previous studies have shown that treadmill exercise training can improve peripheral nervous tissue regeneration in non-diabetic rats and mice after nerve injury and in diabetic rats, improves neuropathic pain and increases axonal regeneration after sciatic nerve transection.19-24 Exercise training is an interesting model with which increase activation of sensory and motor neurons, axonal transport of proteins, and synaptic remodeling.25-28 We have previously demonstrated that the amount of CGRP anterogradely transported along axons by fast transport is increased in sciatic motoneurons of exercise-trained rats.29 These studies have proved that exercise training increases the quantity of axonal proteins and axonal transport, but the effects of exercise training on motor proteins that transport these neurotrophic factors are not elucidated.

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