Behavioural Brain Research xxx (2009) xxx–xxx

Contents lists available at ScienceDirect

Behavioural Brain Research

journal homepage: www.elsevier.com/locate/bbr

Research report

Oral supplementation with melon superoxide dismutase extract promotes antioxidant defences in the brain and prevents stress-induced impairment of spatial memory

Sanae Nakajima[a], Ikuroh Ohsawa[a], Kazufumi Nagata[a], Shigeo Ohta[a], Makoto Ohno[b], Tetsuo Ijichi[c], Toshio Mikami[d,*]

[a] Department of Biochemistry and Cell Biology, Institute of Gerontology, Nippon Medical School, Kawasaki, Kanagawa 211-8533, Japan
[b] Department of Graduate School of Nippon Sport Science University, 7-1-1 Fukasawa, Setagaya-ku, Tokyo 158-8508, Japan
[c] Combi Corporation, 5-2-39 Nishibori, Sakura-ku, Saitama-shi, Saitama 338-0832, Japan
[d] Department of Health and Sports Science, Nippon Medical School, 2-297-2 Kosugi-cho, Nakahara-ku, Kawasaki, Kanagawa 211-0063, Japan

ARTICLE INFO

Article history:
Received 25 October 2008
Accepted 15 December 2008
Available online xxx

Keywords:
GliSODin
Hippocampus
Stress
Memory
Neurogenesis
Antioxidant

ABSTRACT

The purpose of this study was to investigate the effect of antioxidant ingestion on stress-induced impairment of cognitive memory. Male C57BL/6 mice were divided into four groups as follows: (1) control mice (C mice) fed in a normal cage without immobilization; (2) restraint-stressed (RS mice) fed in a small cage; (3) vitamin E mice (VE mice), mice were fed in a small cage with a diet supplemented with vitamin E; (4) GliSODin mice (GS mice) fed in a small cage with a diet supplemented with GliSODin. RS, VE and GS mice were exposed to 12 h of immobilization daily. Five weeks later, spatial learning was measured using the Morris Water Maze (MWM) test. After water maze testing, we performed immunohistochemical analysis using 4-hydroxy-2-noneral (4-HNE) and an anti-Ki67 antibody. 4-HNE is a marker of lipid peroxidation. RS mice showed impaired spatial learning performance and an increased number of 4-HNE-positive cells in the granule cell layer (GCL) of the hippocampal dentate gyrus when compared to C mice. Moreover, RS mice showed a decreased number of Ki67-positive cells in the subgranular zone (SGZ). GS mice showed better spatial learning memory than RS mice. The number of 4-HNE-positive cells in the GCL of GS mice was significantly less than that of RS mice. The number of Ki67-positive cells in the SGZ of GS mice was significantly greater than that of RS mice. These finding suggests that GliSODin prevents stress-induced impairment of cognitive function and maintains neurogenesis in the hippocampus through antioxidant activity.

1. Introduction

Aging leads to suppression of brain functions such as learning and memory. This effect is accelerated by chronic stress, especially psychological stress. Chronic immobilization stress significantly impaired spatial performance in the MWM, elevated plasma corticosterone levels, and attenuated hippocampal long-term potentiation (LTP) [1]. Escape latencies in the MWM were longer in rats restrained for 21 days than in control rats [2].

Stress-induced impairment of learning and memory is closely related to suppression of hippocampal neurogenesis. Chronic restraint stress resulted in impaired performance in the MWM and a decreased number of BrdU-positive cells in the dentate gyrus [3]. Stress suppresses neurogenesis of dentate gyrus granule neurons, and repeated stress causes remodeling of dendrites in the CA3 region, which is particularly important for memory processing [4].

One of the reasons why stress suppresses hippocampal neurogenesis increased oxidative stress. Fontella et al. [5] reported that repeated restraint stress induced an increase in thiobarbituric acid reactive substance (TBARS) levels and in glutathione peroxidase activity in rats. A relationship between impairment of memory and oxidative stress has been reported. In addition, it has been reported that ingestion of the antioxidant flavanol improved spatial memory retention in adult mammals [6]. However, there have been no reports of protective effects of antioxidant on stress-induced impairment of learning and memory.

In the present study, we investigated whether ingestion of an antioxidant protected against stress-induced impairment of learning and memory. We used two types of antioxidants: GliSODin and α-tocopherol. GliSODin is superoxide dismutase (SOD) extracted from melons and combined with gliadin. SOD catalyzes the dismutation of superoxide into oxygen and hydrogen peroxide and

* Corresponding author. Tel.: +81 44 733 3719; fax: +81 44 733 3719.
E-mail address: mikami@nms.ac.jp (T. Mikami).

0166-4328/$ – see front matter © 2008 Elsevier B.V. All rights reserved.
doi:10.1016/j.bbr.2008.12.038