The Effect of Nigella Sativa on Learning and Memory in Male Diabetic Rats

Mohammad Reza Jalali [1,*], Mehrdad Roghani

1. Department of Pathology, School of Medicine, Shahed University,Tehran, Iran

Article info:
Received: 27 July 2009
First Revision:13 August 2009
Accepted: 20 September 2009

Key Words:
Nigella sativum,
Learning,
Memory,
Diabetes Mellitus

ABSTRACT

Introduction: Diabetes mellitus accompanies with disturbances in learning, memory, and cognitive skills in the human society and experimental animals. Considering the beneficial antidiabetic potential of Nigella sativum (NS), this research study was conducted to evaluate the effect of chronic consumption of NS on learning and memory in diabetic rats using passive avoidance and Y-maze tests.

Methods: Male Wistar rats were randomly divided into control, NS-treated control, diabetic, and NS-treated diabetic groups. NS treatment continued for 1 month. For induction of diabetes, streptozotocin was injected i.p. at a single dose of 60 mg/kg. For evaluation of learning and memory, initial latency (IL) and step-through latency (STL) were determined at the end of study using passive avoidance test. Meanwhile, alternation behavior percentage was determined using Y maze.

Results: There was a significant increase ($p<0.05$) in IL in diabetic and NS-treated diabetic groups after 4 weeks as compared to control group. In this respect, there was no significant difference between diabetic and NS-treated diabetic groups. On the other hand, STL significantly decreased ($p<0.05$) in diabetic group and significantly increased ($p<0.01$) in NS-treated diabetic group as compared to control group at the end of study. In addition, results of Y-maze test showed that there is a significant difference between diabetic and NS-treated diabetic groups ($p<0.05$) regarding alternation behavior.

Discussion: In summary, chronic oral administration of NS could enhance the consolidation and recall capability of stored information and spatial memory in diabetic animals.

1. Introduction

Diabetes mellitus is a chronic metabolic disorder, characterised by disturbed glucose metabolism due to an absolute or relative insulin deficiency. In the long term diabetes leads to complications in a number of organ systems. As these complications can be only partially prevented by maintaining strict glycaemic control, additional therapeutic interventions are in demand. It is increasingly recognised that the brain is another site of diabetic end-organ damage (1). Diabetic patients may express cognitive deficits, which are generally modest in young adults and, but can be quite marked in the elderly (2).

Cognitive deficits are also reported in animal models of diabetes. Streptozotocin (STZ)-diabetic rats develop learning deficits which can be prevented, but not fully reversed, with insulin treatment. Moreover, STZ-diabetes affects long-term potentiation (LTP) in the hippocampus. LTP is a form of activity-dependent synaptic plasticity, which is widely accepted as a model for the neuronal substrate of learning and memory. Like in dia-

**** Corresponding Author:***
Dr. Mohammad Reza Jalali Nadoushan
Department of Pathology, Shahed Univ., Tehran, Iran.

betic patients, cognitive deficits in STZ-diabetic rats develop in association with other functional and structural deficits in the brain, among which increased auditory and visual evoked potential latencies (3-4).

Considering the beneficial antidiabetic potential of Nigella sativum (NS), this research study was conducted to evaluate the effect of NS feeding on learning and memory in diabetic rats using passive avoidance and Y-maze tests.

2. Methods

Adult male Wistar rats (Pasteur's Institute, Tehran), weighing 210-250 g at the start of the experiment were housed three to four per cage. Animals were given free access to water and food.

Rats (n = 28) were randomly divided into control, NS-treated control, diabetic, and NS-treated diabetic groups. NS treatment continued for 1 month. For induction of diabetes, streptozotocin was injected i.p. at a single dose of 60 mg/kg. For evaluation of learning and memory, initial latency (IL) and step-through latency (STL) were determined at the end of study using passive avoidance test. Meanwhile, alternation behavior percentage was determined using Y maze.

2.1. Y-maze Task

Working short-term memory performance was assessed by recording spontaneous alternation behavior in a single session in Y-maze. Each arm was 40 cm long, 30 cm high, and 15 cm wide. Each rat was placed at the end of one arm and allowed to move freely through the maze during an 8-min session. The series of arm entries was recorded visually. Arm entry was considered to be completed when the base of the animal's tail had been completely placed in the arm. Alternation was defined as successive entries into the three arms on overlapping triplet sets. The alternation percentage was calculated as the ratio of actual to possible alternations (defined as the total number of arm entries minus two).

2.2. Single Trial Passive Avoidance Test

The apparatus consisted of an illuminated chamber connected to dark chamber by a guillotine door. Electric shocks were delivered to the grid floor by an isolated stimulator. On the first and second days of testing, each rat was placed on the apparatus and left for 5 min to habituate to the apparatus. On the third day, an acquisition trial was performed. Rats were individually placed in the illuminated chamber. After a habituation period (2 min), the guillotine door was opened and after the rat entering the dark chamber, the door was closed and an inescapable scrambled electric shock (1 mA, 2 s once) was delivered. In this trial, the initial latency (IL) of entrance into the dark chamber was recorded and rats with ILs greater than 60 s were excluded form the study. Twenty-four hours later, each rat was placed in the illuminated chamber for retention trial. The interval between the placement in the illuminated chamber and the entry into the dark chamber was measured as step-through latency (STL up to a maximum of 600 s as cut-off).

3. Results

There was a significant increase ($p<0.05$) in IL in diabetic and NS-treated diabetic groups after 4 weeks as compared to control group. In this respect, there was no significant difference between diabetic and NS-treated diabetic groups. On the other hand, STL significantly decreased ($p<0.05$) in diabetic group and significantly increased ($p<0.01$) in NS-treated diabetic group as compared to control group at the end of study (Fig. 1).

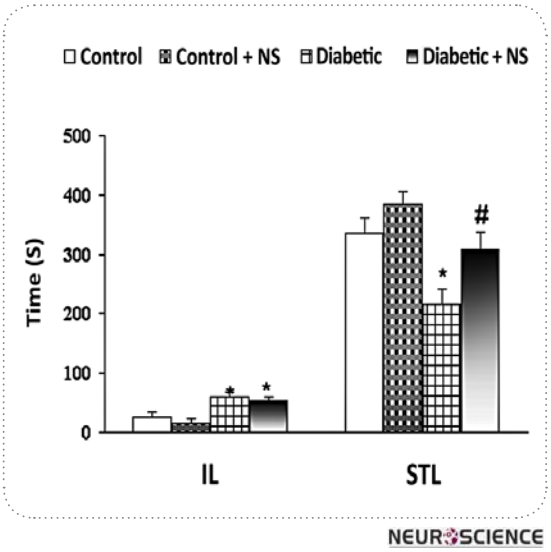

Figure 1. The effect of NS administration on passive avoidance scores in treated groups

* $p<0.05$ (Compared to control)

\# $p<0.05$ (compared to diabetic)

In addition, results of Y-maze test showed that there is a significant difference between diabetic and NS-treated diabetic groups regarding alternation behavior ($p<0.05$) (Fig. 2).

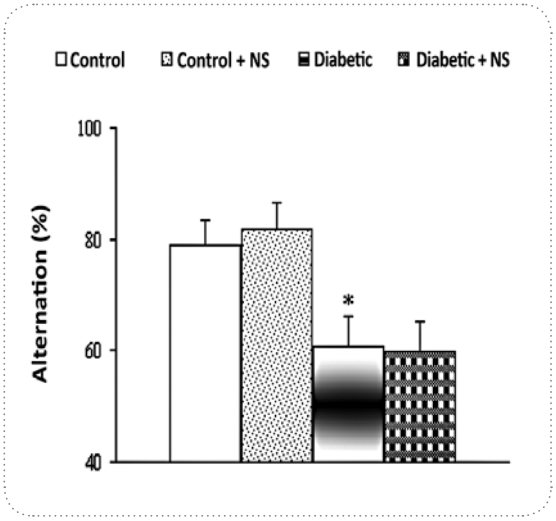

Figure 2. The effect of NS administration on Y maze (alternation behavior) scores in treated groups

* $p<0.05$ (as compared to control)

4. Discussion

Previous studies have reported that DM is associated with neurological complications in both the peripheral and central nervous system. Impairment of learning and memory is also recognized as a complication of diabetes (5). Cognitive deficits in DM can result from metabolic impairment or cerebral vascular complications (6). In animal models of DM, such as the STZ-diabetic rat, spatial learning impairments have also been reported. STZ-diabetic rats also display deficits in cognitive tasks, such as performance in the Morris water maze (7). Although the pathogenesis of these deficits is multifactorial and controversial, but there is strong evidence for the involvement of microvascular dysfunction and oxidative stress due to excess production of oxygen free radicals. In the latter case, since the mammalian hippocampus and cerebral cortex play a pivotal role in a diverse set of cognitive functions, such as novelty detection and memory, these areas are very vulnerable to oxidative damage in STZ-diabetic animals (8). In agreement with this idea, it has been reported that lipid peroxidation enhances in both regions of the brain, which itself leads to a significant impairment in both motor and memory behavioral functions in diabetic animals [9].

In summary, chronic oral administration of NS could enhance the consolidation and recall capability of stored information and spatial memory in diabetic animals.

References

1. Tripathi BK, Srivastava AK. Diabetes mellitus: complications and therapeutics. Med Sci Monit 2006;12:RA130-47

2. Wandell PE. Quality of life of patients with diabetes mellitus. An overview of research in primary health care in the Nordic countries. Scand J Prim Health Care 2005;23:68-74.

3. Jackson-Guilford J, Leander JD, Nisenbaum LK. The effect of streptozotocin-induced diabetes on cell proliferation in the rat dentate gyrus. Neurosci Lett 2000; 293:91-94

4. Biessels GJ, Smale S, Duis SE, Kamal A, Gispen WH. The effect of gamma-linolenic acid-alpha-lipoic acid on functional deficits in the peripheral and central nervous system of streptozotocin-diabetic rats. J Neurol Sci 2001; 182:99-106

5. Parihar MS, Chaudhary M, Shetty R, Hemnani T. Susceptibility of hippocampus and cerebral cortex to oxidative damage in streptozotocin treated mice: prevention by extracts of Withania somnifera and Aloe vera. J Clin Neurosci 2004; 11:397-402.

6. Reagan LP, McEwen BS. Diabetes, but not stress, reduces neuronal nitric oxide synthase expression in rat hippocampus: implications for hippocampal synaptic plasticity. Neuroreport 2002;13:1801-1804.

7. Baydas G, Nedzvetskii VS, Nerush PA, Kirichenko SV, Yoldas T. Altered expression of NCAM in hippocampus and cortex may underlie memory and learning deficits in rats with streptozotocin-induced diabetes mellitus. Life Sci 2003; 73:1907-1916.

8. Lupien SB, Bluhm EJ, Ishii DN. Systemic insulin-like growth factor-I administration prevents cognitive impairment in diabetic rats, and brain IGF regulates learning/memory in normal adult rats. J Neurosci Res 2003; 74:512-523.