Enhancing Effect of Monosialoganglioside GM1 on Learning and Memory in Aged Rats

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1 Introduction

Gangliosides are found at high concentration in CNS, and are essentially combined with neuronal membrane[1, 2]. The chemical structures of gangliosides have been determined[3]. They are a family of molecules consisting of a lipid portion anchored in the plasma membrane and a carbohydrate portion on the outer cell surface containing one or more sialic acid residues. The hydrophilic carbohydrate portion is related to the regulation of Ca^{2+} channel[4]. Exogenous ganglioside administration may have facilitatory effects on CNS regeneration and especially on synaptogenesis[5, 6]. Recently, it was reported that exogenous gangliosides have some enhancing effects on learning behavior of rats of different ages (from neonatal to aged rats). The present work is aimed at studying the effect of monosialonganglioside GM1 on learning ability and memory retention of aged rats.

2 Methods

Twenty-one aged (25—26 months old) Sprague-Dawley rats, weighing 650—810g, were used, and randomly divided into 2 groups: GM1-treated and control groups. GM1-treated animals received daily injection of GM1 (10 mg/kg/day, i.p.), and control animals received saline in the same volume. After 7 consecutive daily injections, animals were trained to perform light-dark discrimination task. Monosialoganglioside GM1 used was provided by Fidia Research Lab, Italy.

In the experiments the behavioral model of light-dark discrimination with food reward was used. The procedure of training is as follows: 2 weeks before training, in order to lighten the body weight of rats, the diet of animals was controlled. The body weight of rats was required to reduce to 80% of former body weight. In the period of behavioral experiments the body weight had to be kept at this level. The behavioral training was carried

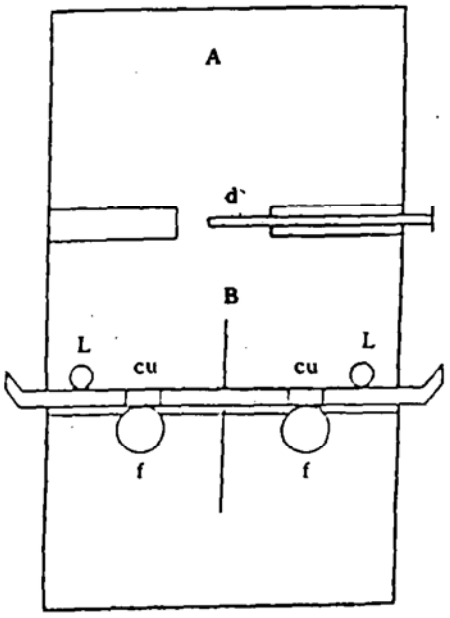

Fig. 1. Diagram of light-dark discrimination box with food reward. L, Signal lamp; f, small dish; d, movable door; cu, small curtain.

out in a light-dark discrimination box (Fig. 1). At the beginning of the experiment, the rat was in compartment A, and a small pellet of food (45 mg) was put in the left or right small dish f. One of the signal lamps was turned on to indicate the food reward. Five seconds later door d was removed, the rat could run from compartment A to compartment B. If the rat ran to the lightened side through the curtain cu, it could get the reward, the small pellet of food. This was a correct response. If the animal ran to the dark side, it could not get food. This was considered a wrong response. After responding (correctly or wrong) the signal lamp was turned off, and the rat was pushed back to compartment A gently. Thus one trial was completed. The signal lamps were turned on alternatively according to Gellerman's table. The average intertrial interval was 1 min, and 20 trials were given in every session. The percentage of correct responses reaching 80% for 3 consecutive days was considered as the learning criterion. All data were expressed as mean $\pm$ S.D. Statistical comparisons between different groups were made with Student's *t* test. $p<0.05$ was considered statistically significant.

3 Results and Discussion

In the present work, the effect of monosialoganglioside GM1 on learning ability of aged rats was investigated, and the memory retention was determined after skipping 3 weeks of training. After 10 days of training to perform light-dark discrimination with food reward, 9 out of 10 GM1-treated aged rats reached the learning criterion, while only 4 out of 11 control aged rats reached the learing criterion. After the continuous training all the animals could reach the learning criterion, and the numbers of trials for GM1-treated and control rats to reach the learning criterion were 104 ± 42.9 and 168.6 ± 42.7, respectively. The difference between them was statistically significant ($p<0.01$, Table 1). The results show that monosialoganglioside GM1 has enhancing effect on learning ability of aged rats, and this task is not so easy for aged rats to learn.

In order to investigate the effect of GM1 on memory retention the experiments were carried out after skipping 3 weeks of training. Twenty trials were given for each daily session. The results are shown in Table 1. The percentages of memory retention for GM1-treated and control aged rats were $98.9\pm2\%$ and $91.4\pm10.2\%$, respectively, the difference between them was statistically significant ($p<0.05$). The percentage of memory retention was calculated by the following formula:

$$\text{Percentage of memory retention} = \frac{\text{Number of correct responses during the memory retention test}}{\text{Mean number of correct responses in the last 3 days of training}} \times 100\%.$$

The results show that monosialoganglioside GM1 has enhancing effect not only on learning ability, but also on memory retention in aged rats.

Table 1 Enhancing Effects of Monosialoganglioside GM1 on Learning and Memory of Aged Rats[a)]

Group	Learning ability (number of trials reaching the criterion)	Memory retention (% of memory retention after 3 weeks)
GM1-treated	104±42.9(10)	98.9±2(10)
Control	168±42.7(11)	91.4±10.2(11)
	$p<0.01$	$p<0.05$

a) The data are expressed as $X\pm SD$, and the number in parentheses represents the number of animals used.

The decline in learning and memory abilities is a main aspect of brain function deficiency during aging. So it is important to search for enhancing agents for learning and memory abilities against aging. A number of works[5, 6] reported that gangliosides have some facilitatory effects on synaptic plasticity in CNS, and the synaptic plasticity is considered the neural basis of learning and memory processes. Thus we suggest that exogenous gangliosides may have enhancing effects on learning and memory processes. Our recent work has shown that exogenous gangliosides can enhance the learning ability (acquisition) of rats of different ages[7], including the aged rats[8]. In the present study the effect of one kind of gangliosides, monosialoganglioside GM1, was investigated in the behavioral model with food reward, and the same results were obtained. It provides further leads in searching for learning and memory enhancing agents.

There are several kinds of gangliosides in brain, and at least 7 representative brain gangliosides. The differences in their chemical structures are expressed as the different contents of sialic acid residues and different carbohydrate components. So it is worthy to study their functional difference and the relationship between them. In the present work, the effect of monosialoganglioside GM1 has been studied. The dosage of monosialoganglioside GM1 used in the experiments is approximately 1/5 of total bovine brain gangliosides (equivalent to the content percentage of GM1 in total bovine brain gangliosides, i.e. 21%). Its enhancing effect on learning and memory is very significant. This result indicates that monosialoganglioside GM1 may play a main role in the behavioral effects of gangliosides. Consequently, it is undoubted that the thorough study of mechanisms of enhancing effects of monosialoganglioside GM1 on learning and memory will be important for clarifying the neural function of gangliosides. On the other hand, since gangliosides have the same enhancing effect on learning ability and memory retention in different behavioral models and in rats of different ages, it is suggested that gangliosides probably influence the learning and memory processes. Moreover, as gangliosides are

endogenous substances, they are possibly involved in normal learning and memory processes. So the study on mechanisms of effects of gangliosides will be helpful to clarify the neural mechanisms of learning and memory.

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