Research Paper

The Effect of Nursing Intervention on the Rehabilitation of Senile Dementia in Rapid Aging Rat Model

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Guo and Bai: Nursing Intervention on Senile Dementia in Rapid Aging Rat Model

In order to study the effect and mechanism of nursing intervention based on music and exercise therapy on cognitive impairment in patients with senile dementia and to provide objective experimental basis for implementing clinical nursing measures, a rapid aging rat model was established. Rats were randomly divided into 5 groups, control group, homologous normal control group, music group, exercise group, music+exercise group to explore the mechanism of nursing intervention based on music and exercise therapy, and then 6 representative patients with mild to moderate senile dementia were selected as research subjects, divided into 3 groups with 2 patients in each group. Then, a nursing intervention based on music and exercise therapy was implemented. The results showed that there was no difference in the escape latent period between the experimental groups on the first day. On the second and third days, the control group had the longest escape latent period, but not significant compared to the other groups. There were no statistical differences between the remaining groups with different nursing interventions ($p>0.05$). Similarly, the escape latent period of the control group was the longest and significant on d 4 and 5 compared to the other groups. And the differences among the music group, the exercise group and the music+exercise group were not statistically significant. In addition, in the clinical evaluation of the rehabilitation effect of the nursing intervention in the senile dementia patients, the scores of the control group were lower than the scores of the experimental groups. Moreover, the experimental group had the largest change in scores before and after nursing intervention in neuropsychiatric symptoms. In the study of the mechanism of action of nursing intervention on senile dementia, it was found that nursing intervention can effectively improve the learning, memory and mimicry ability of rats, and also increased the content of choline acetyltransferase in hippocampus. In other words, the memory level of rats is related to the amount of choline acetyltransferase in the hippocampus. This also showed that nursing intervention had a great effect on the rehabilitation of patients with senile dementia.

Key words: Senile dementia, nursing intervention, rapid aging model, music, exercise, memory ability

With the increasing social pressure, the number of patients with senile dementia is on the rise[1], and people with dementia are attracting greater attention in the medical field. Senile dementia is a clinical syndrome of mental retardation[2]. Patients may have symptoms such as difficulty in speech communication, severe memory loss, dysfunction of time and space, and reduced ability to calculate and discriminate even under conscious status[3]. The incidence of senile dementia is high, the causes of the disease are various, and the incubation period is very long, which is not easy to be detected[4]. The most common typical symptoms of senile dementia patients are decreased mental status, decreased cognitive ability, behavior and emotional disorders, and reduced social adaptability[5]. In recent years, among the elderly population in China, about 6 % suffer from senile dementia. The older the age, the more dementia patients, about 22 % of dementia patients are over 80 y old. This is only the case of senile dementia with obvious symptoms, plus those with mild to moderate senile dementia, the survey data is two or three times more than the above data[6]. Senile dementia is a variety of dementia syndrome caused by aging and physical deterioration of the elderly. The most common three kinds of senile dementia are vascular dementia, Alzheimer's disease, and mixed dementia[7]. The basic biological basis of senile dementia brain disease is the loss and change of brain cells or brain atrophy. Human brain cell population is the master of human thinking, memory, executive function. The variation of the brain cells of the elderly and the loss of mental function will eventually affect the normal life of the elderly[8].

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Nursing interventions based on music and exercise mainly rely on all forms of activity related to music and sports. In the research stage of rehabilitation effect[9], this study was mainly to analyze and understand the clinical manifestations and mental state of patients with senile dementia through clinical observation. And with the help of nursing interventions, through the combination of music and exercise, to understand the language, behavior and memory impairment of senile dementia patients, and improve the language and behavioral dysfunction of patients with senile dementia[10]. Planned implementation of nursing intervention and active psychological counseling for patients can improve mental status, enhance memory, and improve cognitive function. Therefore, it can better promote the rehabilitation effect of patients with senile dementia[11,12]. Based on the above background, the rehabilitation effects of nursing interventions based on music and exercise on patients with senile dementia, and the effects of music and exercise on the memory of rats with rapid aging and the changes of choline acetyltransferase (ChAT) content in hippocampus of rats were studied.

MATERIALS AND METHODS

Experimental animals:

Forty adult male rats were obtained and were housed in a clean animal room equipped with air conditioning. The ambient temperature was 20°±3°, and the air humidity was 65±5 %. The rats were given free access to food and water. The weight of all rats was controlled at 27~31 g, these rats were randomly divided into 4 groups of 10 rats each, the control group, the music group, the exercise group and the music+exercise group. In addition, 10 male rats of the same weight were selected as the homologous normal control group (referred to as R group).

Experimental intervention:

For the music group and the music+exercise group, the rats were scheduled with music for one hour each morning and evening, and the melody of the music should be light and the rhythm should be strong. Each time while playing the music, the rats were placed in a fixed position in a fixed room, all the doors and windows were closed, the curtains were drawn, and the indoor conditions were basically the same. In addition, the distance of sound of playing music was 1.5 m away from the rats, the music decibel is 65-75 dB, music was played twice a day, 5 d a week, for a total of 6 w.

Before the formal intervention, the rats in the exercise group and the music+exercise group were trained for swimming adaptation, 10 min each time, once a day for a total of 3 d. At the end of adaptive training, the rats were formally intervened. At 16:00 every day, swimming exercises were performed in a pool of length 100 cm, width 80 cm, height 60 cm and a depth of 50 cm, 15 min each time, once a day, 6 d a week for a total of 6 w. The temperature of the water in the pool was maintained at about 30°, and the indoor temperature was maintained at 23° to 27°. In order to prevent the rats from drowning, the rats were manually controlled to swim. When the rats were in a state of lack of physical strength, the rats were immediately taken out of the pool. After 4 min of rest, the rats were further placed in the swimming pool for swimming experiments until the last time of the experiment is enough for 15 min. A total of 3 rats have drowned in this experiment.

Morris water maze test for spatial learning and memory ability in rats:

Morris water maze training is a classic training method for detecting spatial learning and recall memory in rats. The Morris water maze training included a 5 d positioning navigation test and a 1 d space exploration test[13]. Positioning navigation training, the Morris water maze was divided into 4 quadrants according to the 4 marking points of the water maze. In one of the quadrants, a black platform was placed 2 cm below the water surface and the position was fixed. The black platform has been placed in the same quadrant in the next experiment. The water maze circular pool had a diameter of 150 cm, a height of 65 cm, a water depth of 40 cm, and a water temperature of 22° to 27°. A quadrant was randomly selected as the water entry point of the rat, and the rats were gently placed into the water facing the pool wall. A device of Morris water maze automatically tracks and records the escape latent period of the rat, that is, the time from the rat entering the water to climbing the platform. The time for the rat to find the platform was 2 min. After finding the platform, if the rat stayed on the platform for more than 10 s, it was considered as success of finding the platform. If the rat did not find the platform within 2 min, it was manually guided to the platform for 10 s and the escape latent period was recorded as 2 min. According to the same method, the rats were trained once in 4 quadrants, and the results were tracked and recorded[14]. Space exploration test included after completing the positioning navigation training, the

black platform was removed, and the space exploration experiment was repeated and the number of times the rats climbed onto the platform within 2 min was tracked[15].

ChAT immunohistochemistry:

After the Morris water maze experiment, 5 rats in each group were randomly selected, and 5 % pentobarbital sodium was intraperitoneally injected to anesthetize the rats. After sufficient anesthesia, the rats were sacrificed. Then a scalpel was used to open the thoracic cavity of rat, the rat heart was exposed, and the right atrial appendage was cut. Then a needle was inserted into the left ventricle of the rat and 55 ml of 0.9 % saline was injected, then the left ventricle of the rats was perfused with 140 ml of 5 % paraformaldehyde fixative and after 5 min, the brain was taken out, fixed again with 5 % paraformaldehyde fixative for 1 d. After that, the tissue was dehydrated and embedded with paraffin carefully. A side row of continuous coronary was cut into pieces and adhered to the slides, then fixed, the slice thickness should be 5 μm. Five slices were taken from each rat and immunohistochemistry was performed in strict accordance with the operating instructions. First, the slice was conventionally dewaxed and put into clear water, and then the repair solution was poured into the pressure cooker, and the slide was taken out from the clean water and kept in the repair solution. The pressure cooker was then covered and heated until the pressure cooker sprays at a constant speed. Start timing when the steam was evenly sprayed. After 2 min, pressure cooker was switched off and allowed to cool. When the temperature reached room temperature, the repaired slice was taken out, washed with distilled water, soaked with phosphate buffered saline (PBS) twice each time for 3 min. The slides were immersed in the endogenous peroxidase blocking solution for 12 min and rinsed with PBS. After rinsing, the slides were placed in the goat serum working solution blocking solution, soaked for 12 min and dried. After drying, antirabbit rat ChAT polyclonal antibody was added dropwise, soaked overnight and rinsed with PBS solution on the next day. The appropriate amount of biotin-labeled goat antirabbit secondary antibody working solution was added dropwise, soaked for 12 min and rinsed with PBS solution. HRP-labeled streptavidin was then added dropwise, soaked for 12 min and continued to rinse with PBS solution. In the DAB color development, the coloring solution was applied to the tissue section, the color development time was 3 min and the color development time was controlled under the microscope to achieve the best color development effect and the color development was terminated by washing under tap water. Finally, conventional dehydration was carried out. Finally, the tissue section was observed under a microscope.

Extraction of hippocampal tissue protein:

After the Morris water maze test, 5 rats were randomly selected from each group. The rats were anesthetized with 5 % sodium pentobarbital and sacrificed. The rats were placed on ice cubes to separate brain tissue and the hippocampus tissues were taken out, washed with PBS solution, placed in an EP tube prepared in advance and quickly placed in liquid nitrogen for cryopreservation. At the time of further processing the hippocampus tissue was taken out from the liquid nitrogen and placed in an EP tube for weighing. After weighing, the cell lysate was added to the EP tube, mixed thoroughly and the hippocampus tissue was disrupted by an ultrasonic breaker, the EP tube was placed in an ice box for 10 min, transferred to a refrigerator at -4±2° and frozen for 30 min. Then, the mixture was centrifuged at 12 000 rpm for 15 min in a low-temperature high-speed centrifuge, and the supernatant was taken to measure the protein concentration using the BCA method.

Mini mental state examination scale and neuropsychiatric questionnaire:

The mini mental state examination scale is an examination scale that comprehensively evaluates computing ability, memory, behavioral mimicry ability and comprehension ability of patients. It is also the most commonly used and most effective screening scale for senile dementia patients in the world. The mini mental state examination scale included five major aspects, orientation, memory, attention and computing power, recall ability and language ability. The total score is 30 points, 1 point for each question, a total of 30 questions. Under normal circumstances, the degree of education can seriously affect the test result of the normality of the subject. Less than 24 points was identified as cognitive dysfunction, of which illiteracy group ≤17 points, a primary school culture group ≤20 points, and a remaining middle school culture or other group ≤24 points.

The neuropsychiatric questionnaire has been the most general and commonly used mental condition questionnaire in China. It mainly includes twelve aspects: delusion, hallucination, agitation, negative psychological, anxiety, apathy, disinhibition, emotional

instability, abnormal behavior, sleep, appetite and eating disorders. During the care of the nursing staff, each behavior was scored according to the severity and frequency. The 12 aspects were observed one by one, and scored one by one. Finally, the scores of the 12 aspects were added together to be the total score. If any of these behaviors occur, the score of the neuropsychiatric questionnaire is considered to be >0. If any item has a neuropsychiatric questionnaire score of ≥4, it is considered to be clinically significant.

Statistical analysis:

All data were processed using SPSS 19.0 statistical analysis and the data were expressed as mean±standard deviation. The two-way analysis of variance (ANOVA) of repeated measures was used to analyze the data of Morris water maze positioning navigation. The least significant difference (LSD) test was used to test the difference between the groups, P<0.05 was considered as statistically significant. Morris water maze space exploration experimental data, immunohistochemical optical density data and Western Blot gray scale ratio were analyzed by one-way ANOVA. LSD test was performed when the difference between the two groups was significant. P<0.05 was considered as statistically significant. The interaction effect between music therapy and exercise therapy was analyzed. Two factors and two levels were analyzed using factorial design analysis of variance.

RESULTS AND DISCUSSION

After a 6-d Morris water maze test, the latency required for rats to find an underwater platform during the first 5 d of positioning navigation training is shown Table 1. As the number of training days increased, the escape latent period of each group of rats gradually decreased, and the downward trend of each group began to slow down on the third day. There was no statistical difference in escape latent period between the groups on d 1 (p>0.05). On d 2 and d 3, the escape latent period of each group was significantly different. The control group was compared with the other four groups. The escape latent period of the control group was (94.2±10.7, 70.5±9.3) and escape latent period is the longest, the result was statistically significant (p<0.05). There was no significant difference between the other four groups (p>0.05). On d 4 and 5, the escape latent period of the control group was still the longest compared with the other groups, which were respectively 55.4±8.2 and 40.5±6.4, the result was statistically significant (p<0.05). Compared with the other groups, the escape latent period of the R group 25.3±5.5 and 16.2±5.3 were the shortest (p<0.05). The results showed that with the increase of training time, the influence of nursing intervention based on music and exercise on the escape latent period of rats was more and more obvious.

After 6 d of Morris water maze test, the black platform was removed on the d 6 and the rats were tracked. The number of times the rats crossed the platform within 2 min is shown in the following Table 2. It can be observed from the table that the difference between the control group and the other four groups was statistically significant (p<0.05). In the same period of time, rats in the R group had the highest number of platform crossings, and the difference was statistically significant compared with the other four groups (p<0.05). The number of platform crossings of the music group, the exercise group, and the music+exercise group were 8.96±1.89, 7.85±2.34 and 9.63±2.28, and the values were not different from each other. Fig. 1 shows the interaction effect between music therapy and exercise therapy. After statistical analysis, the difference is not statistically significant (p>0.05), and there is no interaction effect between the two. The results showed that the memory of fast aging rats can be improved by the intervention of music and exercise, but even if it was not as good as the learning and memory ability of normal rats of the same age. It also showed that the comprehensive intervention of music and exercise was better than the individual intervention.

Table 3 shows the average optical density value of ChAT proteins of each group, and fig. 2 is a schematic diagram of protein expression of ChAT in the rat hippocampus. As can be observed from Table 3, the

TABLE 1: MORRIS WATER MAZE ESCAPE LATENCY PERIOD (X±S)

Group	Control group	R group	Music group	Sports group	Music and Sports Group
First day	113.2±8.9	98.5±7.9	101.6±10.3	97.2±9.8	97.1±9.8
Second day	94.2±10.7	62.1±10.1	76.2±10.4	80.5±10.7	69.3±9.6
On the third day	70.5±9.3	40.3±8.8	46.3±9.2	48.2±9.8	44.5±7.9
The fourth day	55.4±8.2	25.3±5.5	33.1±7.0	33.4±7.2	30.7±4.8
The fifth day	40.5±6.4	16.2±5.3	23.4±6.3	26.0±5.5	23.4±5.8

average optical density value of the ChAT protein in the control group was 0.0570±0.0039, which was the lowest, and the difference was statistically significant compared with the other four groups ($p<0.05$). The average optical density of the ChAT protein in the R group was the highest 0.1102±0.0048, and the difference was statistically significant ($p<0.05$). The mean optical density values of ChAT protein in the music group, exercise group and music+exercise group were similar, and the difference was not statistically significant ($p<0.05$). The results showed that music intervention, exercise intervention and music+exercise intervention can significantly affect the content of ChAT in rat hippocampus.

TABLE 2: MORRIS WATER MAZE CROSS PLATFORM NUMBER (X±S)

Group	Number of platform crossings
Control group	4.53±5.71
R group	18.32±3.89
Music group	8.96±1.89
Sports group	7.85±2.34
Music and Sports Group	9.63±2.28
F	21.342
P	0.003

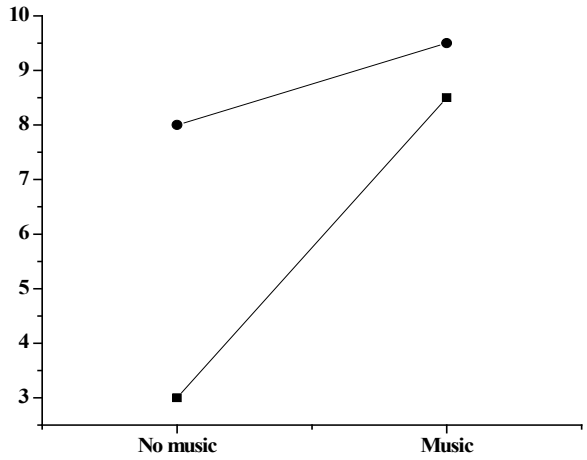

Fig. 1: Space exploration experiment interaction effect of music therapy and exercise therapy
—■— No sports, —●— sports

Through music and exercise intervention, the expression of ChAT protein in the hippocampus of rats with rapid aging increased significantly. The results are shown in Table 4. As can be observed from the fig. 3, compared with the other four groups, the expression of ChAT protein in the control group was the lowest, and the difference was statistically significant ($p<0.05$). Compared with the other four groups, the expression of ChAT protein in R group was the

TABLE 3: THE AVERAGE OPTICAL DENSITY VALUE OF THE HIPPOCAMPUS CHATPROTEINS (X±S)

Group	Average optical density
Control group	0.0570±0.0039
R group	0.1102±0.0048
Music group	0.0813±0.0067
Sports group	0.0803±0.0066
Music and sports group	0.0797±0.0029
F	23.531
P	0.004

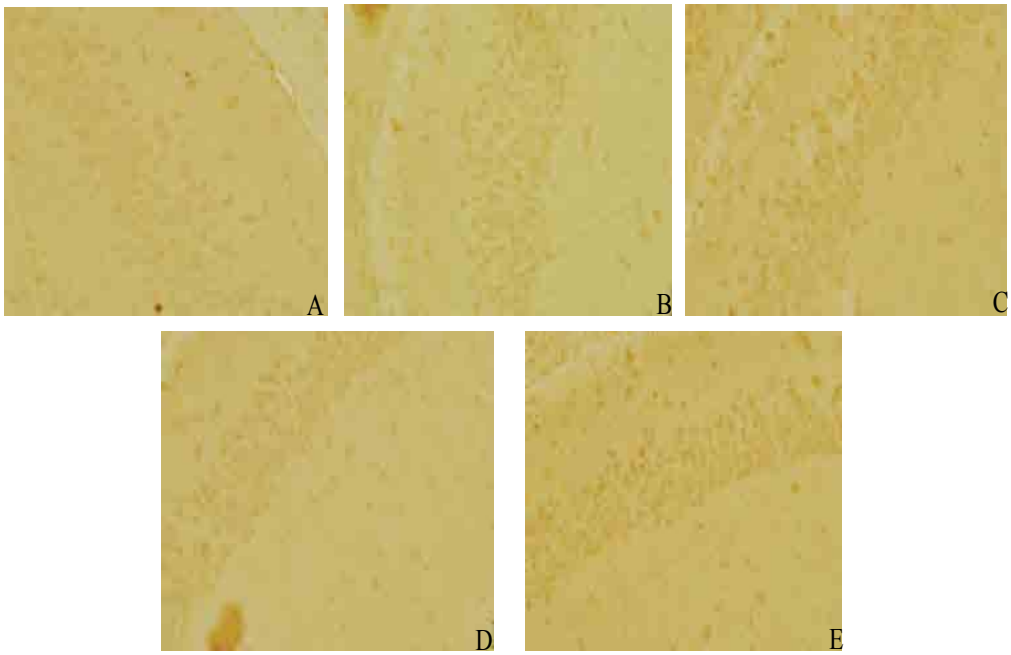

Fig. 2: The distribution of the hippocampus chat protein
(A) control group, (B) R group, (C) music group, (D) exercise group, (E) music and exercise group

highest, and the difference was statistically significant ($p<0.05$). Compared with the music+exercise group, the expression of ChAT protein in the music group and the exercise group was slightly different, which was statistically significant ($p<0.05$). After statistical analysis, there was an interaction between music intervention and exercise intervention, which was statistically significant. The final results indicated that music intervention and exercise intervention can increase the content of ChAT protein in the hippocampus of rapidly aging rats, and the combined effect of music and exercise was more obvious than the intervention of the single one.

As can be observed from the Table 5, the average value of the neuropsychiatric questionnaire in the experimental group was 28.16 before the intervention of the experimental patients. After a period of nursing intervention, the average score of the neuropsychiatric questionnaire was 8.85. It can be concluded that nursing intervention based on music and exercise can significantly change the memory ability and cognitive function of patients with senile dementia, which indicated that the nursing intervention based on music and exercise had a positive influence on the recovery of cognitive function in patients with senile dementia and there was a clear rehabilitation effect for patients with senile dementia.

TABLE 4: THE GRAY THAN OF HIPPOCAMPUS CHAT (X±S)

Group	Gray value
Control group	0.9538±0.2413
R group	3.5132±0.3757
Music group	2.1053±0.2461
Sports group	2.5730±0.2187
Music and Sports Group	2.4379±0.1362
F	39.48
P	0.002

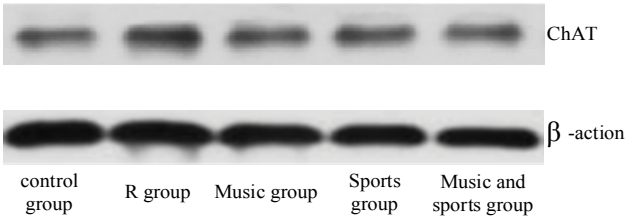

Fig. 3: The expression amount of hippocampus ChAT

TABLE 5: DESCRIPTIVE STATISTICS OF PAIRED SAMPLES BEFORE AND AFTER NURSING INTERVENTION

	Mean	N (Sample size)	Standard deviation (SD)
Before/after MMSE	11.2	3	7.59
	10.87	3	8.63
Before/after NPI	8.85	3	7.98
	28.16	3	21.46

The memory cognitive ability of patients with senile dementia is related to the ChAT content of memory-related brain regions. Therefore, this experiment studied the effects of music and exercise intervention on ChAT content in the hippocampus of rapidly aging rats by protein extraction and immunohistochemistry. Experiments showed that the levels of ChAT in the hippocampus of the rats with music and exercise intervention were significantly elevated, and the memory cognitive function of the rats was related to the ChAT content in the hippocampus of rats. This is consistent with results of previous studies on the proportional relationship between memory and cognitive function in rats and the content of ChAT in memory-related brain regions. The experimental results of ChAT content showed that the content of ChAT in hippocampus of rats with rapid aging was significantly different from that of the control group and R group by music intervention, exercise intervention and music+exercise intervention ($p<0.05$). This indicated that music intervention, exercise intervention and music+exercise intervention can significantly increase the content of ChAT in rat hippocampus to improve memory and cognitive function in rats. The effect of combined intervention is more obvious than treatment alone. In the post-stage clinical nursing observation, this study used a combination of music and exercise to enhance the understanding of patients with senile dementia. Through careful clinical evaluation of the subjects and appropriate self-regulation and reinforce of intervention, the patient can effectively regulate self-emotion, improve language expression, social communication and the ability to communicate with others, thereby to improve their memory and achieve physical coordination. In summary, the following conclusions were drawn.

Firstly, music intervention and exercise intervention can improve the learning and memory ability of rats with rapid aging, and increase the content of ChAT in the hippocampus of rats with rapid aging. The effect of music intervention and exercise intervention on improvement of the learning and memory ability of

rats with rapid aging may be relative to the increase of the content of ChAT in the hippocampus of rats with rapid aging.

Secondly, nursing interventions based on music and exercise can relax the patient's mood, regulate the patient's internal emotional state, and improve cognitive dysfunction in patients with senile dementia, thus helping to restore the patient's physical symptoms and achieve good therapeutic results.

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