Effect of Xingyo-tang on Learning and Memory Performances in Mice

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The effects on memory and learning ability of the Korean herbal medicine, Xingyo-tang(XGT, 神交湯), which consists of Ginseng Radix(人蔘) 4 g, Liriopis Tuber(麥門冬) 40 g, Morindae Officinalis Radix(巴戟天) 40 g, Biotae Semen(柏子仁) 20 g, Dioscoreae Rhizoma(山藥) 40 g, Euryales Semen(芡實) 20 g, Scrophulariae Radix(玄蔘) 40 g, Salviae Miltiorrhizae Radix(丹蔘) 12 g, Poria(茯神) 12 g, Cuscutae Semen(免絲子) 40 g, was investigated. The effects of XGT on learning and memory performance were examined in normal or memory impaired mice by using avoidance tests, Pentobarbital -induced sleep test, fear conditioning task, novel object recognition task, and water maze task. Hot water extract from XGT was used for the studies. Learning ability and memory are based on modifications of synaptic strength among neurons that are simultaneously active. Enhanced synaptic coincidence detection leads to better learning and memory. The XGT-treated (30 mg/100 g and 60 mg/100 g, p.o.) mice exhibit superior ability in learning and memorizing when performing various behavioral tasks. XGT did not affect the passive avoidance responses of normal mice in the step through and step down tests, the conditioned and unconditioned avoidance responses of normal mice in the shuttle box, lever press performance tests, and the ambulatory activity of normal mice in normal condition. In contrast, XGT produced ameliorating effects on the memory retrieval impairment induced by ethanol. XGT also improved the memory consolidation disability induced by electric convulsive shock (ECS). XGT extended the sleeping time induced by pentobarbital dose-dependently, suggesting its transquilizing or antianxiety action. These results suggest that XGT has an improving effect on the impaired learning through the effects on memory registration and retrieval.

Key words : Xingyo-tang, Learning and Memory Ability

Introduction

According to the oriental medical literature, the formula of Xingyo-tang(XGT, 神交湯) first appeared in Bian-Zheng-Ji-Wen(辨證奇聞, A.D. 1687) compiled by Qian Song(錢松) of the Qing(淸) Dynasty of China[1]. XGT consists of Ginseng Radix(人蔘) 4 g, Liriopis Tuber(麥門冬) 40 g, Morindae Officinalis Radix(巴戟天) 40 g, Biotae Semen(柏子仁) 20 g, Dioscoreae Rhizoma(山藥) 40 g, Euryales Semen(芡實) 20 g, Scrophulariae Radix(玄蔘) 40 g, Salviae Miltiorrhizae Radix(丹蔘) 12 g, Poria(茯神) 12 g, Cuscutae Semen(免絲子) 40 g. Each herb distributed in Korea, has been used mainly for medical treatment for more than two thousand years. As Ginseng Radix(人蔘) strengthens vigor, settles our mind and makes the juices, it is very effective to use this for amnesia. Liriopis Tuber(麥門冬) strengthens yin(陰), removes agony, improves digestive system and generates the juices. Morindae Officinalis Radix(巴戟天) is effective to strengthen the kidney by acting on kidney meridian. As Biotae Semen(柏子仁) nourishes the heart and settles mind, it is very effective to heal diseases caused by mind, such as cardiopalmus, cardiagra and so on. Dioscoreae Rhizoma(山藥) strengthens vigor, supplements yin(陰), and makes Jing(精) rich. Euryales Semen(芡實) refresh in the head as it strengthens Jing(精) by making the kidney healthy. As Scrophulariae Radix(玄蔘) is effective to supplement yin(陰) and to cool fever, it strengthens kidney-fluid(腎水) and controls heart-fire(心火). If fever comes to the head, our mind is not clear and memory is easily damaged. Salviae Miltiorrhizae Radix(丹蔘) makes blood circulation smooth, settles mind and removes pitapating, so it heals uneasiness, hyposomnia, cardiagra, and pitapating caused without reason. Because Poria(茯神) is effective to settle the heart and to discharge urine, it remedies mental disorders, such as amnesia or hyposomnia. Cuscutae Semen(免絲子) strengthens the liver and kidney, and enriches Jing(精) and marrow(髓). In oriental

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medicine, XGT has been known to nourishe the heart(養心), settle mind(安神), strengthen kidney-fluid(滋腎陰), control heart-fire(降心火), enriches blood(補血), and replenish vital essence(益精). In Bian-Zheng-Ji-Wen, XGT was used to treat amnesia from the discord of heart and kidney(心腎不交)[1].

According to other papers, the causes of amnesia are the discord of the heart and kidney(心腎不交), insufficiency of the heart and spleen(心脾不足), the lack of blood(血虛), damage of the kidney(腎虛), phlegm(痰)[2]. To remedy amnesia and promote memory, it is demanded to nourishe the heart(養心), strengthen the kidney(滋腎), settle mind(安神), and replenish vital essence(益精)[3]. Therefore, XGT has been considered to improve memory and to regulate physiological activities. Of these effects, author was interested in the anti-amnesic effect of XGT. Scarcely any paper introduces the experiments on the effects of XGT on memory processes. This paper describes the effects of XGT on memory and learning processes, by using the passive and active avoidance performance tests, Pentobarbital-induced sleep test, fear conditioning task, novel object recognition task, and water maze task. Thus, the results indicate that oriental medication, which contributes to improve intelligence and memory, is feasible in mammals.

Materials and Methods

1. Animals

The C57B/6 mice were used as experimental animals. Also, male mice of ddY-strain of 5-6 weeks old (KRIBB, Tawjon, Japan) were used. Ten mice were kept in one cage in a room where the temperature and humidity were controlled for a week before the experiment.

2. Isolation of hot water extract from XGT and Chemicals

XGT, which is consisted of 10 herbs, was extracted by boiling extraction[1]. The composition and ingredients of XGT are listed in Table 1. They were added to 500 ml of water, boiled for 2h, filtered, and concentrated to 10 ml. Finally, 10 g of extract was obtained from about 268 g of XGT. The extract was lyophilized. Aliquots (50 mg) were separately stored at -20 ℃ for next experiments. The aqueous extract of XGT and its 10 composed oriental medicinal herbs, which were massproduced as for clinical use, were kindly provided by the Oriental Medical Hospital of Dongguk University (Kyungju, Korea). Two doses of XGT, i.e. 30, 60 mg/100 g, oral administration were used in the experiments, at which doses no changes in the general behaviours and pain sensitivity of mice were observed. Scopolamine hydrobromide, ethanol, chlorpromazine hydrochloride and pentobarbital-sodium salt were obtained from commercial sources.

Table 1. Composition of Xingyo-tang(XGT)

Herb Medicine Name	Herbs	Scientific Name	Dose(g)
Ginseng Radix	人蔘	*Panax ginseng*	4
Liriopis Tuber	麥門冬	*Liriope platyphylla*	40
Morindae Officinalis Radix	巴戟天	*Morinda officinalis*	40
Biotae Semen	柏子仁	*Biota orientalis*	20
Dioscoreae Rhizoma	山藥	*Discorea opposita*	40
Euryales Semen	芡實	*Euryale ferox*	20
Scrophulariae Radix	玄蔘	*Scrophularia buergeriana*	40
Salviae Miltiorrhizae Radix	丹蔘	*Salvia miltiorrhiza*	12
Poria	茯神	*Poria cocos*	12
Cuscutae Semen	兎絲子	*Cuscuta chinensis*	40
Total			268

3. Passive avoidance performances

1) Step through test

The chamber apparatus had a partition wall with a hole, which divided the chamber into two compartments, one bright and the other dark. As soon as a mouse entered the dark compartment from the bright one, a punishing electric shock was given through the foot grids. The time required for the mouse to enter the dark compartment was recorded. On the first day, each mouse received a learning trial, teaching it that if it would enter the dark compartment, it would be to be punished. Twenty four hours later, 10 mice were placed again in the bright compartment, and were left there for 300 sec. The latency and the number of mice which did not enter the dark compartment were recorded[4].

2) Step down test

A rectangular box with its floor grids connected to a electric stimulator was used. It was to give a punishing shock, when a mouse left the rubber platform placed in a corner of the box. On the first day, each mouse was given a learning trial for 10 min. During the latter 5 min of the learning trial, the number of stepping down events (number of errors) and the number of mice which did not step down (successful mice) were counted. Tewnty four hours later, the 3 min testing trial was given to them and the number of errors and the number of successful mice were also counted[5].

3) Experimental procedures

(1) Effects of XGT on memory processes in normal mice

XGT was orally administrated 30 min prior to the learning trial. It was immediately after the learning trial or 30 min before the testing trial to demonstrate the effects of XGT on memory registration, consideration or retrieval processes respectively. 12 mice were randomly used for each group.

(2) Effects of XGT on memory impaired mice

Mice were randomly divided into different groups ; a control group and two experiment groups. One is treated with

30 mg/100 g XGT and the other with 60 mg/100 g XGT. 12 mice were used for each group.

① Memory registration impairment

10 min after the administration of XGT, 30% ethanol (10 ml/kg, p.o.) or scopolamine (0.5 mg/kg, i.p.) were given to the mice to interrupt memory registration process. 20 min later, the learning trial was given to them.

② Memory consolidation impairment

XGT was give 30 min before the learning trial. ECS (0.4 m/s in width, 100 Hz, 94 mA for 0.2 sec) was injected to the mice through the ears immediately after the learning trial in order to impair the memory consideration process.

③ Memory retrieval impairment

On the first day, the learning trial was given to mice. Next day, 10 min after the treatment with XGT, 40% ethanol (10 ml/kg, p.o.) or ECS (0.4 m/s in width, 100 Hz, 80 mA for 0.2 sec) was given to the mice to impair the memory retrieval process. 20 min later, the testing trial was given.

4. Active avoidance performances

1) Shuttle box test

Two sets of infra-red beams were arranged apart from the long side of the shuttle box apparatus. A buzzer and a lamp were set on the ceiling and the grid floor of the box connected with an electric stimulator. The procedure of one trial was as the following : (1) 40 sec interval ; (2) 10 sec for conditional stimulation (CS), (warning buzzer and the lamp were on during this CS period) ; (3) 10 sec for unconditioned stimulation (US), (electric stimulation-an intensity of 36 V, AC-as well as buzzer and lamp were on during the US period). If a mouse interrupted both of two infra-red-beams during the CS or US period, the electric shock was canceled immediately. The photobeam interruption during the CS period was considered as a conditioned avoidance response (CAR) and in the US period as an unconditioned avoidance response (UAR). The trial without interruption in CS and US period was considered as a failure. The movement of a mouse which was irrelevant to CAR or UAR was counted as spontaneous motor activity (SMA)[6].

2) Lever press test

A stainless steel lever was vertically set at one side of the lever press test chamber. A buzzer and a lamp were set on the ceiling and the grid floor where an electric stimulator was connected. The parameters, time schedule and data analysis were similar to the one for the shuttle box test except that mice were to press the lever instead of interrupting the infra-red beam to avoid the electric stimulation in this test[6].

3) Experimental procedures

(1) Effects of XGT on memory registration

XGT was orally administrated 15 min prior to the test. Shuttle box and lever press performances were tested at the same time once a day for 7 days. The number of animals in each group was 8.

(2) Effects of XGT on memory retrieval

After several days of training, the mice which showed over 80% of CAR in the shuttle box test and over 50% of CAR in the lever press test were selected. The shuttle box and lever press tests were given to them in order to determine their basal performance levels for the following 3 days. On the 4th day, 15 min after the XGT administration, the two tests were conducted for 1 hr. The data of the 4th day test was compared with the one of the 3rd day test. Six or seven mice were used for one group.

5. Pentobarbital-induced sleep

Fifteen min after a saline, chlorpromazine (2 mg/kg, i.p.) or XGT administration, pentobarbital (50 mg/kg, i.p.) was given to the mice. The sleep duration (the time from the disappearing of the light reflex to the recovering of the reflex) was measured[6]. The number of animals in each group was 9.

6. Fear conditioning task

Author used a fear conditioning shock chamber (10 × 10 × 15 inches high) and TruScan multi-parameter activity monitors (Coulbourn Instruments). The conditioned stimulus (CS) used was an 85dB sound at 2,800 Hz, and the unconditioned stimulus (US) was a continuous scrambled foot shock at 0.75 mA. After the CS/US pairing, the mice were allowed to stay in the chamber for another 30 sec for measurement of immediate freezing. During the retention test, each mouse was placed back into the shock chamber. The freezing response was recorded for 3 min (contextual conditioning). Subsequently, the mice were put into a novel chamber and monitored for 3 min before the onset of the tone (pre-CS). Immediately after that, an identical tone to the CS was delivered for 3 min and the freezing response was recorded (cued conditioning)[7].

7. Novel object recognition task

The mice were individually left to an open-field box (20 × 20 × 10 high inches) for 3 days. During training sessions, two novel objects were placed into the open field. Each mouse was allowed to explore for 5 min. The time spent in exploring each object was recorded. During retention tests, the mice were placed back into the same box. One of the objects, that were used during the training sessions, was replaced to a novel

object and allowed to explore freely for 5 min. A preference index, that is a ratio of the amount of time spent exploring any one of the two objects (training session) or the novel one (retention session) over the total time spent exploring both objects, was used to measure recognition memory[8].

8. Water maze task

The water maze apparatus is a circular pool (1m in diameter). The procedure of the task was essentially as described[9]. The training protocol consisted of six sessions (4 trials per session per day). A videocamera traced the navigation of the mice. The escape latency to the platform was recorded. In addition, author performed two transfer tests. The first one was done at the end of the third session. The second one was done at the end of the last session. During the transfer test, the platform was removed and the mice were allowed to swim in the pool for 60 sec. The time spent in each quadrant was recorded[10].

9. Statistics

The results of the rate of the successful mice in step down test were analyzed by the chi-square test, the CAR and SMA data in the memory retrieval tests by the paired t-test, the sleep prolongation test and water maze task by Student's t-test, the cued fear conditioning task by ANOVA test, and the novel object recognition task by Dunnett's test. All the other data used the Mann-Whitney's U-test.

Results

1. Effects of XGT on passive avoidance performaces

1) Normal mice

In case of normal mice, XGT did not affect the latency in the step through test, and the number of errors in the step down test. The percentage of failure mice in both tests suggested that XGT had no effect on passive avodance performances for normal mice (data not shown).

2) Memory impaired mice

XGT neither ameliorated the memory registration impairment with 30% ethanol or scopolamine, nor improved the memory consolidation deficit and memory retrieval disturbance induced by ECS, when the step down tests were performed. In the step through test, there was not positive effects and significant difference (data not shown). In case of mice that had a memory retrieval impairment induced by 40% ethanol, at doses of 30 mg/100 g and 60 mg/100 g, it significantly decreased the number of errors (Fig. 1) and increased the percentage of successful mice in the step down test (Fig. 2).

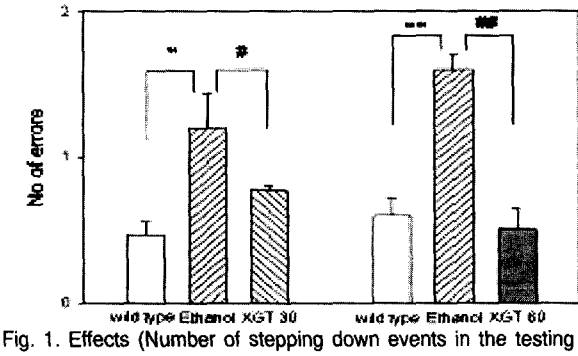

Fig. 1. Effects (Number of stepping down events in the testing trial) of XGT on memory retrieval impairment induced by 40% ethanol in the step down tests. Ethanol : mice orally treated with 40% ethanol 20 min before the testing trial (n=12). XGT 30 and 60 : 30 mg/100 g or 60 mg/100 g XGT was orally given 30 min before the testing trial (XGT 30, n=12 ; XGT 60, n=12). Data expressed as mean ± S.E. * : P<0.05 ; ** : P<0.01 vs wild type, # : P<0.05 ; ## : P<0.01 vs ethanol, Mann-Whitney's U-test.

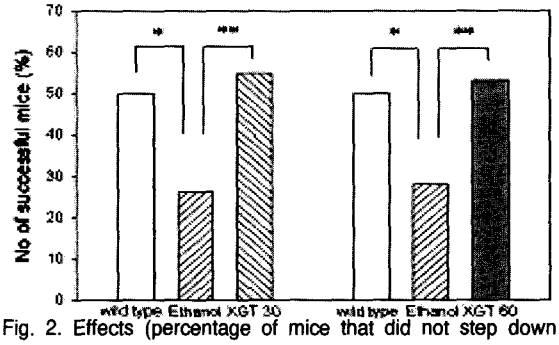

Fig. 2. Effects (percentage of mice that did not step down in the testing trial) of XGT on memory retrieval impairment induced by 40% ethanol in the step down tests. Ethanol : mice orally treated with 40% ethanol 20 min before the testing trial (n=12). XGT 30 and 60 : 30 mg/100 g or 60 mg/100 g XGT was orally given 30 min before the testing trial (XGT 30, n=12 ; XGT 60, n=12). Data expressed as mean ± S.E. * : P< 0.05 vs wild type, ** : P<0.01 vs ethanol, chi-square test.

2. Effects of XGT on active avoidance performaces in normal mice

In the memory retrieval tests, there was partially a significant difference in CAR, SMA and errors between the wild type and XGT treated group (Table 2).

Table 2. Effects of XGT on memory retrieval process in active avoidance performances

Treatment		CAR (%)		SMA (No of movement)	
		Pre	Post	Pre	Post
shuttle box test	wild type	76.3±5.2	79.4±2.1	36.2±4.3	38.3±6.2
	XGT 30	83.6±8.4	81.7±8.7	40.7±4.4	25.6±8.5
	XGT 60	82.3±5.5	83.5±9.5	33.8±2.3	26.5±3.4
lever press test	wild type	64.4±3.3	73.6±5.7	65.3±4.6	87.7±13.1
	XGT 30	52.5±5.6	79.7±8.6*	111.2±23.4	82.4±8.8*
	XGT 60	61.3±6.4	64.5±7.6	118.6±21.5	73.3±21.4*

After the training of shuttle box and lever press tests, well-learned mice were selected. The basal performance levels were determined (Pre). Then CAR and SMA were measured 15 min after oral administration of XGT (Post). XGT 30 and 60 : 30 mg/100 g or 60 mg/100 g XGT was orally given 15 min before the testing trial. (wild type, n=7 ; XGT 30, n=6 ; XGT 60, n=6). Data expressed as mean ± S.E. * : P<0.05 vs Pre, paired t test.

3. Effects of XGT on pentobarbital-induced sleep

The pentobarbital-induced sleeping time was significantly increased by XGT at a dose of 60 mg/100 g, but the extract at a dose of 30 mg/100 g did not. Chlorpromazine (2 mg/kg, i.p.) as an active control, remarkably increased the sleeping time (Table 3).

Table 3. Effects of XGT on pentobarbital-induced sleep

	Sleeping time (min)
Saline	42.2±4.3
Chlorpromazine	9.3±8.8**
XGT 30	50.3±4.5
XGT 60	54.4±6.4*

Pentobarbital (50 mg/kg, i.p.) was administrated 15 min after chlorpromazine (2 mg/kg, i.p.) or XGT (30, 60 mg/100 g, p.o.) treatment (Saline, n=9 ; Chlorpromazine, n=9 ; XGT 30, n=9 ; XGT 60, n=9). Data expressed as mean ± S.E. * : P<0.05 ; ** : P<0.01 vs Saline. Student's t-test.

4. Enhancement of cued fear memory after training to XGT-treated mice (Cued fear conditioning 1 hr, 1 day and 10 days after training)

One-way ANOVA indicated that freezing in response to the tone was also significantly elevated in XGT-treated mice, compared with that in controls when tested at 1 hr ($P<0.05$), 1 day ($P<0.01$) or 10 days ($P<0.05$) after training (Fig. 3, 4, 5). A statistic analysis shows the significant difference between wild type and either of XGT-treated mice ($P<0.05$, respectively). As the minimal amount of current that is required to elicit three stereotypical behaviours (flinching, jumping and volcalizing) were similar in wild type and XGT-treated mice, the enhanced contextual and cued fear memories in XGT-treated mice were not due to altered nociceptive responses. (data not shown).

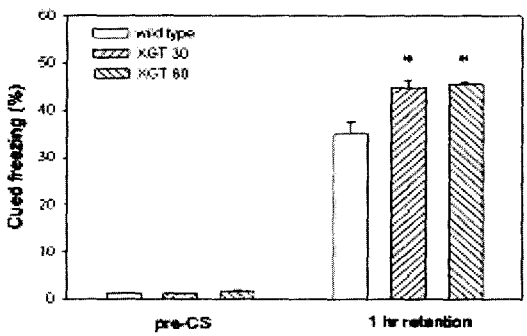

Fig. 3. Enhancement of cued fear memory of 1 hr after training to XGT-treated mice (Cued fear conditioning 1 hr after training). XGT 30 and 60 : 30 mg/100 g or 60 mg/100 g XGT was orally given 15 min before the testing trial (wild type, n=7 ; XGT 30, n=6 ; XGT 60, n=6). Data expressed as mean±S.E. * : P<0.05 vs wild type, ANOVA test.

5. Enhanced novel object recognition memory (Exploratory preference in the training session and retention test) in XGT-treated mice

To increase the difficulty of this task, author used a 5 min training protocol as it was described in Materials and

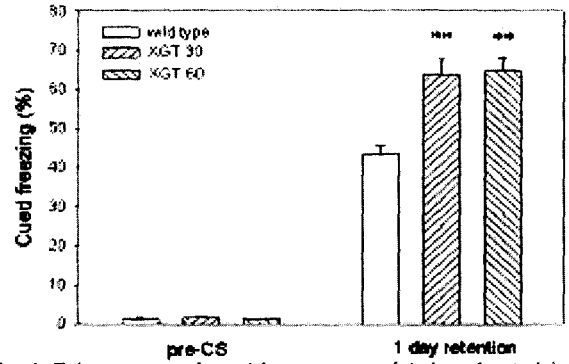

Fig. 4. Enhancement of cued fear memory of 1 day after training to XGT-treated mice (Cued fear conditioning 1 day after training). XGT 30 and 60 : 30 mg/100 g or 60 mg/100 g XGT was orally given 15 min before the testing trial (wild type, n=7 ; XGT 30, n=6 ; XGT 60, n=6). Data expressed as mean±S.E. ** : P<0.01 vs wild type, ANOVA test.

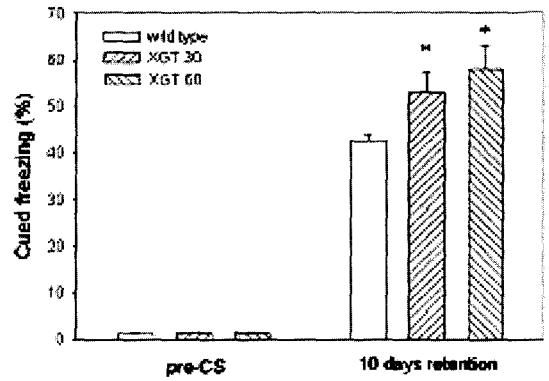

Fig. 5. Enhancement of cued fear memory of 10 days after training to XGT-treated mice (Cued conditioning 10 days after training). XGT 30 and 60 : 30 mg/100 g or 60 mg/100 g XGT was orally given 15 min before the testing trial (wild type, n=7 ; XGT 30, n=6 ; XGT 60, n=6). Data expressed as mean±S.E. * : P<0.05 vs wild type, ANOVA test.

Methods. During training, there was no significant difference in the amount of the time which the mice spent in exploring the two novel objects (as shown in Fig. 6), indicating that both types of mice have the same curiosity and motivation to explore the objects. During the retention test, one of the familiar objects used in the training session was replaced with a third novel object, and animals were allowed to explore for 5 min. Both XGT-treated mice and wild type mice exhibited similar preference towards the novel object in the 1 hr retention test (Fig. 7). This indicates that all groups were equally able to retain the memory of the old object for 1 hr.

However, when retention tests were conducted a day later (Fig. 7), XGT-treated mice exhibited much stronger preference for the novel object than the wild type mice did, indicating that XGT-treated mice had better long term memory. A statistical analysis which used Dunnett's test reveals a significant difference between wild type and XGT-treated mice at the 1 day ($P<0.05$), but not between the two XGT-treated mice. The enhanced long term memory is, therefore,

independent of the XGT-treated methods. However, 3 days and a week after training, the preference that XGT-treated mice showed, also returned to the basal level.

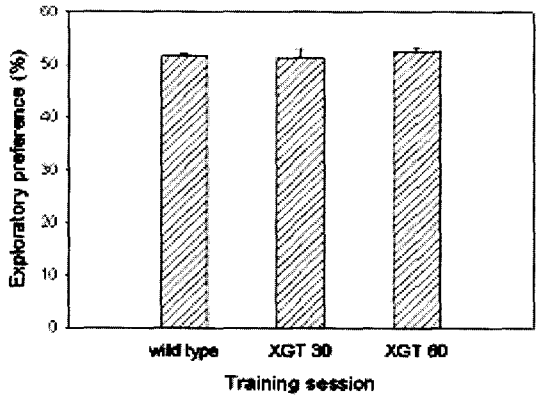

Fig. 6. Enhanced novel object recognition memory in XGT-treated mice : Exploratory preference in the training session. The base line is 50% corresponding to preference at chance. The amount of time spent in exploring two objects was the same for XGT-treated mice and wild type mice (wild type, n=7 ; XGT 30, n = 9 ; XGT 60, n=8). XGT 30 and 60 : 30 mg/100 g or 60 mg/100 g XGT was orally given 15 min before the testing trial. Table shows the temporary feature of the enhanced long term memory in the XGT-treated mice. Data expressed as mean± S.E.

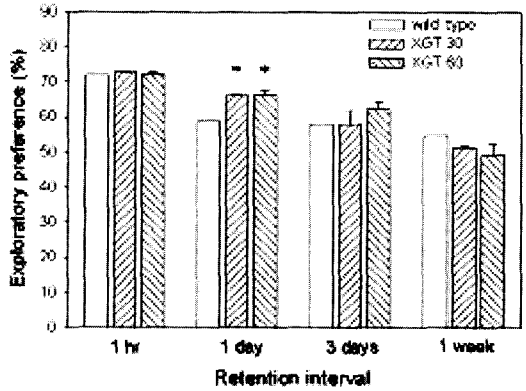

Fig. 7. Enhanced novel object recognition memory in XGT-treated mice : Exploratory preference in retention test. The base line is 50% corresponding to preference at chance. The amount of time spent in exploring two objects was the same for XGT-treated mice and wild type mice (wild type, n=7 ; XGT 30, n = 11 ; XGT 60, n=8). XGT 30 and 60 : 30 mg/100 g or 60 mg/100 g XGT was orally given 15 min before the testing trial. Table shows the temporary feature of the enhanced long term memory in the XGT-treated mice. Data expressed as mean±S.E. * : P<0.05 vs wild type, Dunnett's test.

6. Enhancement of spatial learning in XGT-treated mice (Escape latency in water maze training)

As shown in Fig. 8, the latency to escape to the platform in both wild type and XGT-treated mice decreased in the following training sessions. However, there was a significant group difference in 2nd and 4th session ($P<0.01$), indicating that spatial learning in XGT-treated mice was faster than the one in wild type mice. Moreover, a statistic analysis revealed a significant difference at the third session ($P<0.05$), confirming better learning in XGT-treated mice.

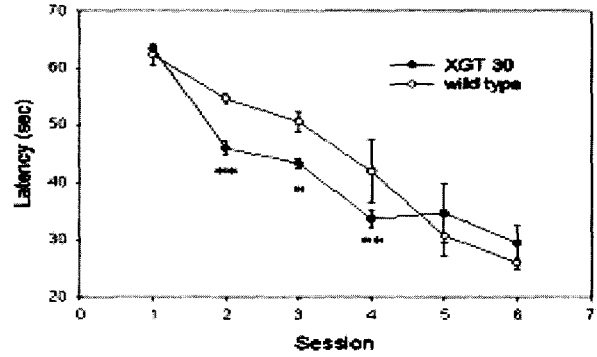

Fig. 8. Enhanced performanec in the hidden-platform water maze task by XGT-treated mice (Cued fear conditioning 1 hr after training). Escape latency in water maze training (wild type, n=10 ; XGT 30, n=16). XGT 30 : 30 mg/100 g XGT was orally given 15 min before the testing trial. Data expressed as mean ± S.E. ** : P<0.01 ; * : P<0.05 vs wild type, student's t-test.

Discussion

In oriental medical theory, the human body consists of four elements ; essence (精), energy (氣), spirit (神) and blood (血). Among these elements, spirit is considered as the concept of vital energy and mind. Especially, from the Jang-Fu (臟腑) physiological point of view, the memory is closly related to the function of the heart and kidney[11]. Becuase of it, wisdom and good memory can be achieved when the heart and kidney complemented each other. People easily forget what they said and do not memorize what they did because a function of the heart and kidney are not smooth.

As human intelligence comes from a smooth circulation of the heart and kidney, if kidney-fluid (腎水) nourishes mind and heart-fire (心火) nourishes the kidney, the intelligence gets richer. When heart-fire (心火) is too strong, kidney-fluid (腎水) drys out, and then heart-fire (心火) gets more prosperous. If the heart and kidney can not interact each other, men can not feel clear in their head and have amnesia[1].

XGT, which is consisted of medicinal herbs to settle heart, supply energy and blood, and nourish kidney, is effective to increase memory and learning ability. Many memory impairment models have been established and used in the studies of memory and learning process[12-14]. Five of such models were used in this work ; 30% ethanol-induced and scopolamine-induced memory restriction deficit mice, 40% ethanol-induced memory retrieval impairment mice, ECS-induced memory consolidation deficit mice and ECS-induced memory retrieval deficit mice.

XGT improved only the memory retrieval deficit induced by 40% ethanol, which suggested that XGT might interrupt the

action of ethanol. The neurotoxicity of ethanol has been well studied[9,15,16]. Ethanol induces short and long term memory impairment. The administration results of ethanol before and after the tests suggested that the ethanol-induced memory deficit was due to its effect on the neurotransmitters, especially cholinergic and adrenergic, and that the neocortex might be the major taget of ethanol in the brain[12,17]. In the present experiment, XGT improved the memory impairment induced by ethanol but not the memory disorder induced by scopolamine.

XGT prolonged the sleep time induced dependently by pentobarbital dose. It suggests that XGT possesses a psychotropic effect, because antipsychotropic, transquilizing or antianxiety drugs are known as prolonging the barbital-induced sleep. The obtained results lead author to the speculation that XGT is clinically useful for the treatment of memory deficits caused by alcoholism. To test whether the selective enhancement of responses to stimuli at 10-100 Hz represents an optimal plasticity curve, author conducted various learning tasks relevant to the forebrain regions. Results indicate that neural activities at the 10-100Hz range in the forebrain may be crucial for coding and storage of learned information.

In addition, author tested spatial learning to XGT-treated mice using the hidden-platform water maze, which requires the recognition memony in the hippocampus[17,18]. There was a significant difference among groups, indicating that spatial learning to XGT-treated mice was faster than one of wild type mice. Visual recognition memory is evolutionarily conserved in species including humans and rodents and requires the hippocampus[5,9,19]. These results would provide evidences for the clinical application of XGT to amnesia or the decreased memory performance. Thus, this study reveals a strategy for the creation of other oriental medically treated mammals with enhanced intelligence and memory.

Generally, amnesia has been shown more in old men than others, and closely related with the function of the heart and kidney. In case of a child, the insufficient memory also results from the disorder of the heart and kidney. The insufficient memory in a child is considered not to be full and in an old man, it is considered to decline by degrees[11]. In this point, XGT may be effective to promote memory of a child. The loss of memory and failure in study raise problems for a child in mentality, character and society. Although further research is required to elucidate its effects of XGT on memory and learning processes, the results presented in this paper would provide fundamental data for the study about the effects of XGT on the central nervous system.

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