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RESEARCH ARTICLE

A DOSE RELATED STUDY ON THE EFFECTS OF TAURINE ADMINISTRATION ON RECOGNITION AND SPATIAL MEMORY FUNCTIONS AND DEPRESSION LIKE SYMPTOMS IN RATS

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Abstract

Taurine is an organic acid widely present in animal tissues and comprises 0.1% of body weight. It is an important ingredient used in energy drinks. It has been reported to have antioxidant properties and it also plays a role in cardiovascular function, development of skeletal muscle, protection against glutamate excitotoxicity and possesses antidepressant-like effects. Present study was designed to study the effect of taurine administration (10mg, 50mg and 100mg) on food intake, locomotor activity, memory function and depression like behavior in rats. Spatial working memory of rats was assessed by WM test and recognition memory of rats was monitored with the help of NOR task. In the present study taurine administration significantly enhanced both spatial and recognition memory functions in rats. Chronic taurine administration at 100mg dose significantly decreased depression like symptoms as evidenced by decrease in immobility time in forced swimming test. Taurine administration dose dependently decreased blood glucose level in blood and increased food intake. In conclusion, taurine has been suggested to have beneficial effects in various behavioral disorders.

Introduction

Taurine (2-aminoethanesulfonic acid) is a semi-essential amino acid which is presentin the body and also used in a wide range of nutritive-tonic drinks which helps in improving health (Lourenco and Camilo, 2002). Taurine is involved in several biological functions such as antioxidation, bile acids conjugation osmoregulation, stabilization of membrane and calcium signaling modulation (Kendler, 1989). Moreover it is important for several vital function like CNS, cardiovascular, skeletal muscle and retinal functions (Oja et al., 2007). High levels of taurine in the brain have been observed to protect brain tissues from cerebral ischemia. Taurine has been reported to have neuroprotective properties (Wu, 2010).

Oxidative stress plays an important role in memory deterioration and taurine has been found to protect the neurons. Since taurine has an antioxidant property so it has protective functions such as scavenging reactive oxygen species, attenuating lipid peroxidation and thus involved in membrane stabilization (Wu et al., 1999). An increase in glutamic acid decraboxylase expression, increased levels of neurotransmitters such as GABA and glutamate, a rise in levels of somatostatin neuropeptide and neurons which are somatostatin-positive have been reported by taurine supplementation (El Idrissi, 2008). Taurine administration can modulate central nervous-motor system instead of causing a diffused inhibition (Paul et al., 1977).

Based on the above consideration, the aim of present study was to investigate the effects of long-term administration of taurine on memory function in rats by twodifferent methods i.e. water maze and object recognition task. Effect of taurine administration on food intake and depression like symptoms was also investigated in the present study. Biochemical effects following taurine administration has also been investigated.

MATERIALS AND METHODS

ANIMALS

24 male locally bred albino Wister rats (200-250 g) purchased from Aga Khan University Hospital were used in the study. All animals were housed individually in a quiet room under a 12 h light-dark cycle (light on at 6:00h) and controlled room temperature ($22^{\circ}C \pm 2$) with free access to standard rodent diet and tap water for at least 3 days before experimentation. All experiments were conducted according to a protocol approved by Local Animal Care Ethical Committee.

DRUGS

Taurine at doses of 10, 50 and 100 mg/kg were injected intraperitoneally (i.p.) for 9 daysinvolumes of 1ml/kg. Control animals were injected with saline (1ml/kg).

EXPERIMENTAL PROTOCOL

Animals were randomly divided into control and three test groups. Controls were injected with saline (0.9%) and other 3 test groups were injected with different doses of taurine (10mg/kg, 50mg/kg and 100mg/kg). Weighed amount of food was given in the hopper of all the cages. Behavioral activities of rats were monitored after 30 min of injection on 9^{th} day.

BEHAVIORAL TESTS

Water Maze Test

Spatial memory effects were monitored by Water Maze test designed in our laboratory. We used rectangular maze as used by (Plech et al., 2000) with slight modification. The water maze apparatus used was a rectangular shaped glass tank (90x60 cm) filled with wateropacified by powdered milk. The level was keptupto18 cm. A submerged wooden platform (15x13 cm) was placed hidden 2cm underneath water surface at a fixed location. The experiment was performed after 30 min of injection. A training session of rats was conducted at the start of the experiment in which each rat was placed into the tank facing the wall and was allowed to locate and climb onto the platform. The rat was gently guided towards the platform if it could not find the platform during the specified time and was allowed 10 seconds to stay on the platform. Spatial working memory functions were monitored byrecording the retention latency. Each session was conducted with a cut-off time of 3 minutes.

Novel object recognition task

Cognitive abilities of rats were assessed by using novel object recognition test. The apparatus consists of square box ($45x45x45cm^3$) made of gray painted wood. Familiar objects used in this test were two identical wooden cubes and novel object was a wooden triangle. Three phases including habituation, training and test session were performed in the test. In habituation phase rats were placed in the empty square box for 10 minutes. Training phase was performed after24 hrs.of habituation phase. Rats were trained for 10 minutes with two similar objects. On day three, the test phase conducted by exposing the animal to one of the known object and a novel object, for about 3 minutes. During the test phasetime of sniffing the novel and familiar object was measured. Discrimination index reveals cognitive performance by calculating the difference in exploration time of familiar and novel objects (Antuneset al., 2012).

Forced swimming test The forced swim test apparatus comprised of a glass tank having height of 56 cm and width of 30cm, which contained water at the height of 22 cmand temperature of 25 º C. In this glass tank animals were individually forced to swim for 6 minutes. The height of water was selected so that animal was prevented from touching the bottom of the glass tank and also to prevent its escape from the glass tank. The FST test is commonly used as standard pharmacological model for evaluating depression like symptoms in rats (Porsolt et al. 1978). When the rats are placed in an inescapable chamber which is filled with water then the development of the state of immobility reflects the cessation of persistent escape directed behavior. In the test session animal's swimming behavior was monitored which can be defined as movement throughout the swim chamber (glass tank). The immobility time was monitored. The animal is considered immobile when it makes no further attempts to escape and only tries to keep its head above the water.

STATISTICAL ANALYSIS

Behavioral data were analyzed by one-way ANOVA. Post hoc comparisons were made using the Newman-*k*euls test; p values < 0.05 were considered significant.

RESULTS

Fig 1 shows the effect of taurine administration for 9 days (10mg, 50mg and 100mg) on food intake in rats. Analysis by one-way ANOVA showed a significant effect of taurine administration on food intake ($F=5.65 df= 20, 3$ $p<0.01$). Post hoc analysis revealed that taurine administration significantly increased ($p<0.01$) food intake in taurine treated rats at 50 mg/kg and 100mg/kg. However no significant effect of taurine administration on growth rate was observed Fig.2.

Fig.3 shows the effect of taurine (10mg, 50mg and 100mg) administration for 9 days on memory functions in rats using water maze. Analysis by one-way ANOVA showed a significant effect of taurine administration on memory functions ($F= 29.06$ $df=20,3$ $p<0.01$). Post hoc analysis test showed that working memory of rats was significantly ($p<0.01$) improved following taurine administration. A decrease in time to reach the platform was observed in 10mg/kg treated rats and 100 mg/kg treated rats as compared to controls. While no significant effect observed at 50 mg/kg.

Fig.4 shows the effect of taurine administration for 9 days (10mg, 50mg and 100mg) on depression like behavior in rats using forced swimming apparatus. Analysis by one-way ANOVA showed a significant effect of taurine administration on depression like symptoms ($F=2.21$ $df=20, 3$ $p<0.05$). Post hoc analysis showed that taurine administration significantly decreased ($p<0.05$) depression like symptoms in rats administered at highest dose of taurine (100mg/kg).

Fig.5 shows the effect of taurine (10mg, 50mg, and 100mg) on recognition of known and novel object in rats using novel object recognition task. Analysis by one-way ANOVA showed a significant effect of drug on recognition. Post hoc analysis of both showed that novel object recognition in rats was significantly ($p<0.01$) decreased in 50mg and 100mg treated rats.

Fig.6 shows the effect of taurine (10mg, 50mg and 100mg) on discrimination index in rats by object recognition task. Analysis by one-way ANOVA showed a significant effect of taurine administration on discrimination index ($F=21.05$ $df= 20,3$ $p<0.01$). Post hoc analysis showed that discrimination index was significantly ($p<0.01$) increased in 50mg and 100mgtaurine treated rats indicated improvement of cognition in taurine treated rats.

Fig.7 shows the effect of taurine (10mg, 50mg and 100mg) on glucose levels in rats by standard glucose estimation. Analysis by one-way ANOVA showed a significant effect of taurine administration on glucose levels ($F=13.27 df= 20,3$ $p<0.01$). Post hoc analysis showed that glucose levels in rats was significantly ($p<0.01$) decreased in taurine treated rats in a dose dependent manner.

Fig 1: Effect of taurine administration (10mg/kg, 50mg/kg, and 100mg/kg) on food intake in rats. Values are means ± SD (n=24). Significant difference by Newman keuls test: *p<0.01 compared with controls, +P<0.05 compared with 10mg and –p<0.05 compared with 50 mg rats.

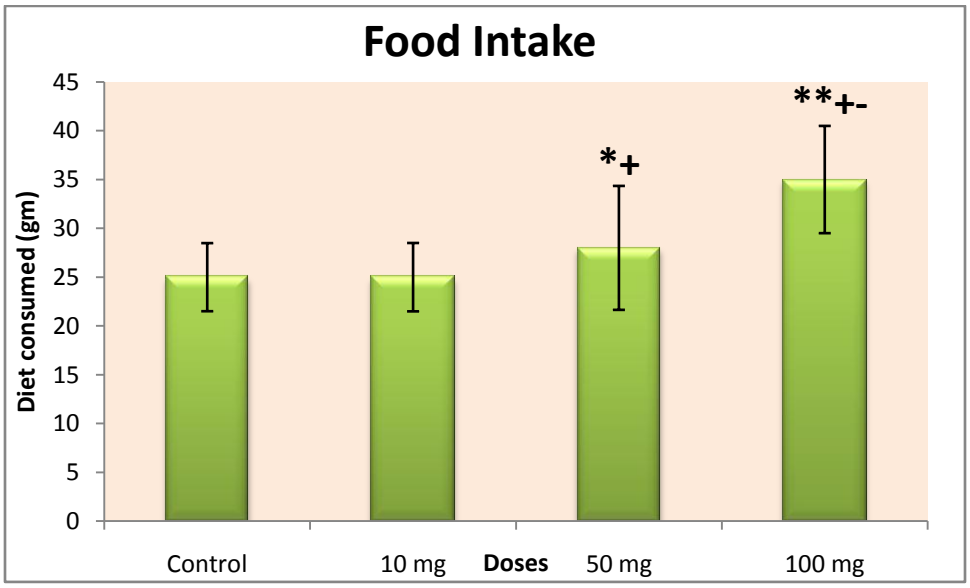


Fig 2: Effect of taurine administration (10mg/kg, 50mg/kg, and 100mg/kg) on growth rate in rats. Values are means ± SD (n=24). No significant effect reported compared with controls.

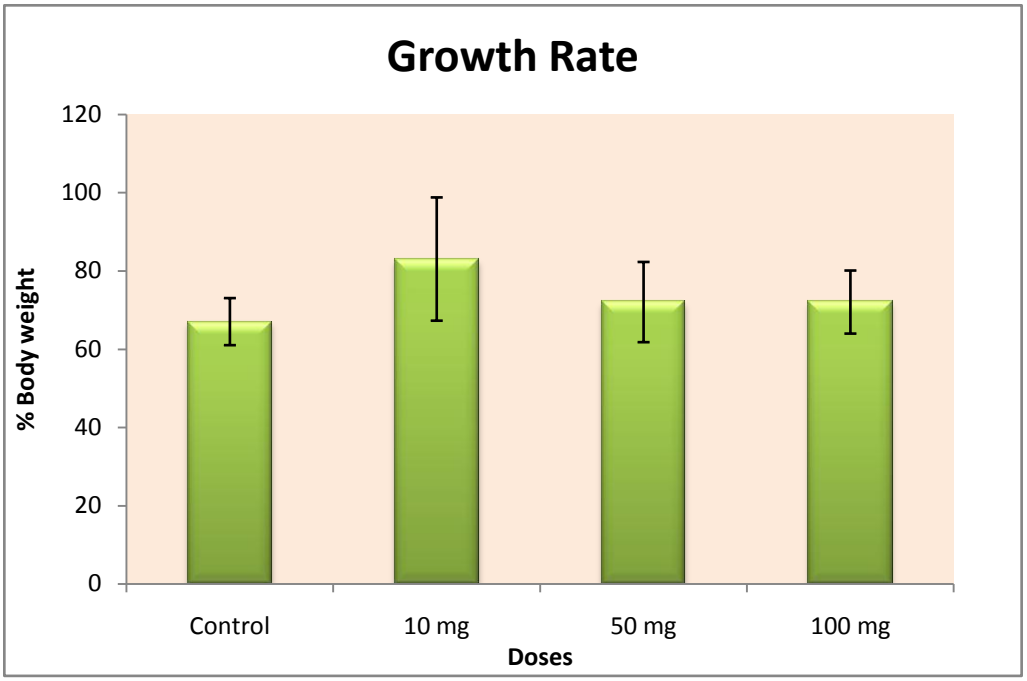


Fig 3: Effect of taurine administration (10mg/kg, 50mg/kg, and 100mg/kg) on memory functions of rats using water maze. Values are means ± SD (n=24). Significant difference by Newman keuls test: *p<0.01 compared with controls, +p<0.01 compared with 10mg and –p<0.01 compared with 50 mg rats.

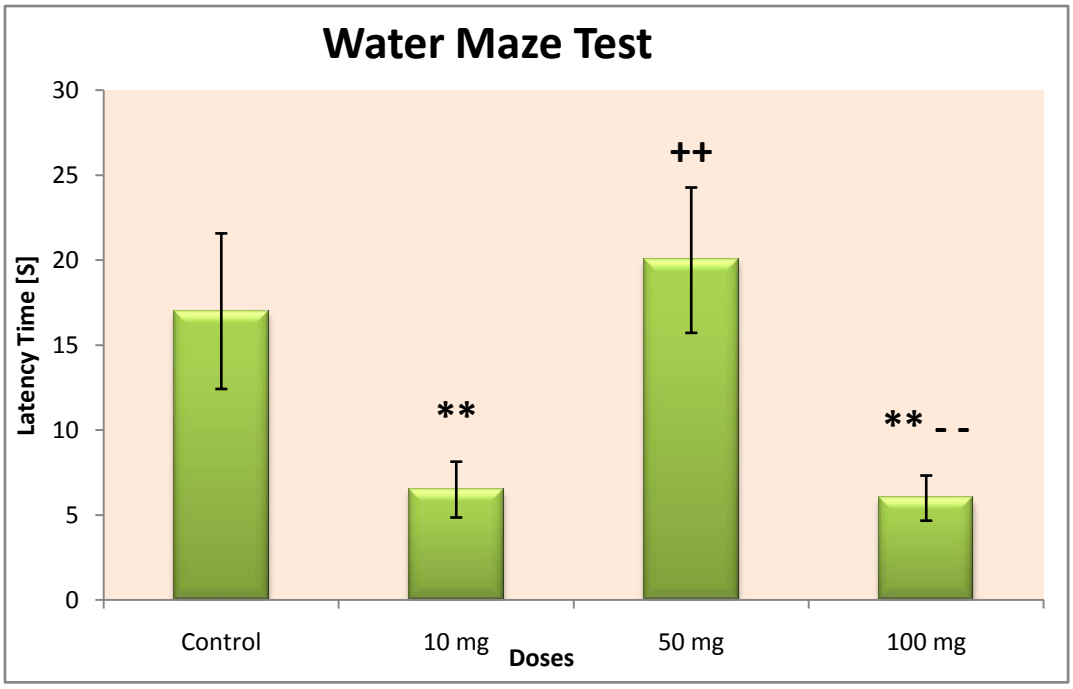


Fig 4: Effect of taurine administration (10mg/kg, 50mg/kg, and 100mg/kg) on depression in rats using force swimming apparatus. Values are means ± SD (n=24). Significant difference by Newman keuls test: *p<0.05 compared with controls.

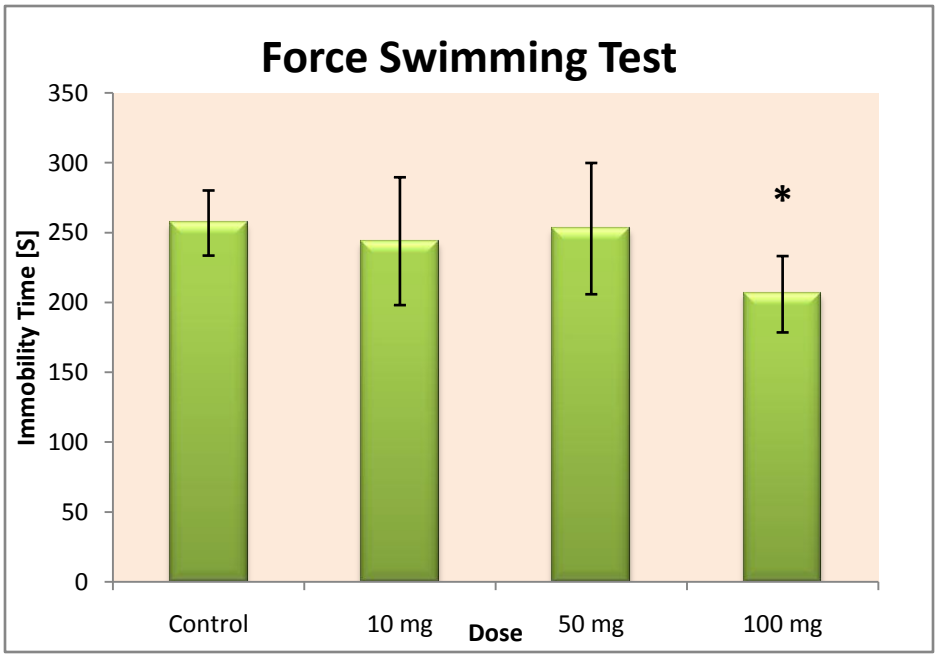


Fig 5: Effect of taurine administration (10mg/kg, 50mg/kg, and 100mg/kg) on recognition memory in rats using novel object recognition task. Values are means ± SD (n=24). Significant difference by Newman keuls test: *p<0.01 compared with controls. +p<0.01 compared with 10mg.

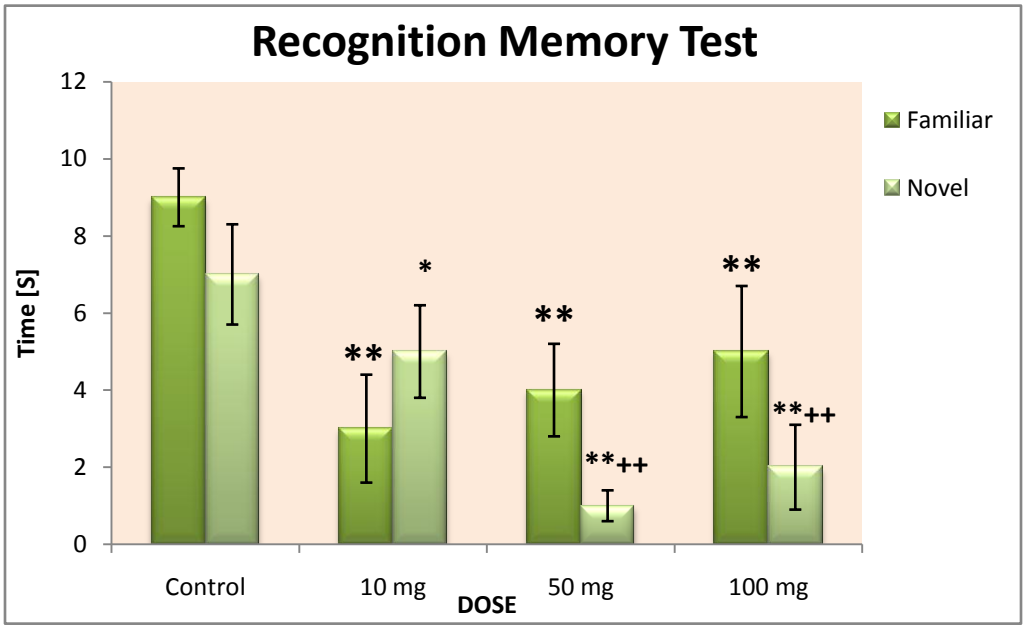


Fig 6: Effect of taurine administration (10mg/kg, 50mg/kg, and 100mg/kg) on discrimination index in rats using novel object recognition task. Values are means ± SD (n=24). Significant difference by Newman keuls test: *p<0.01 compared with controls.

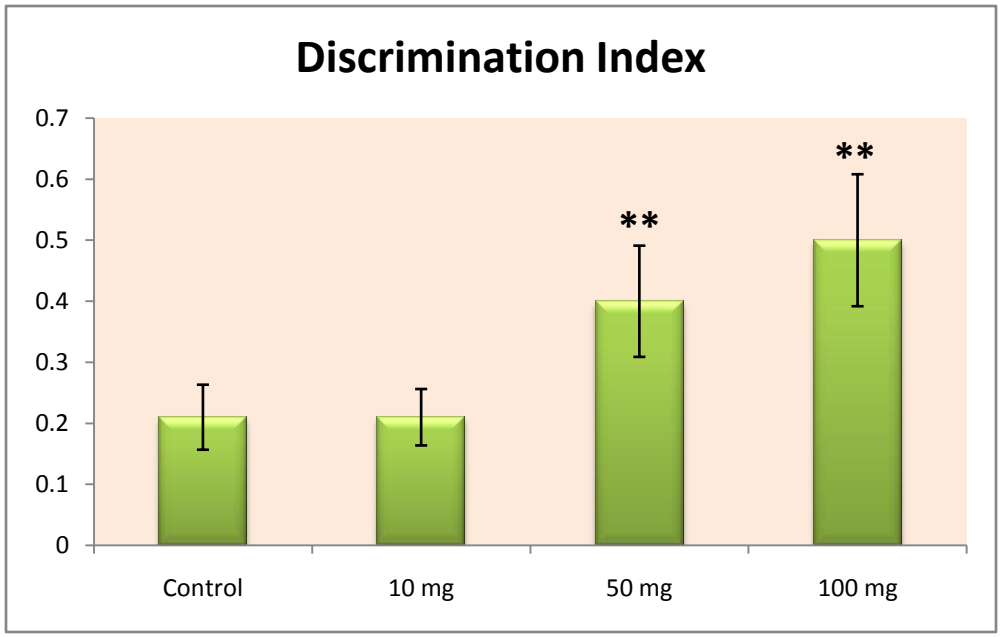
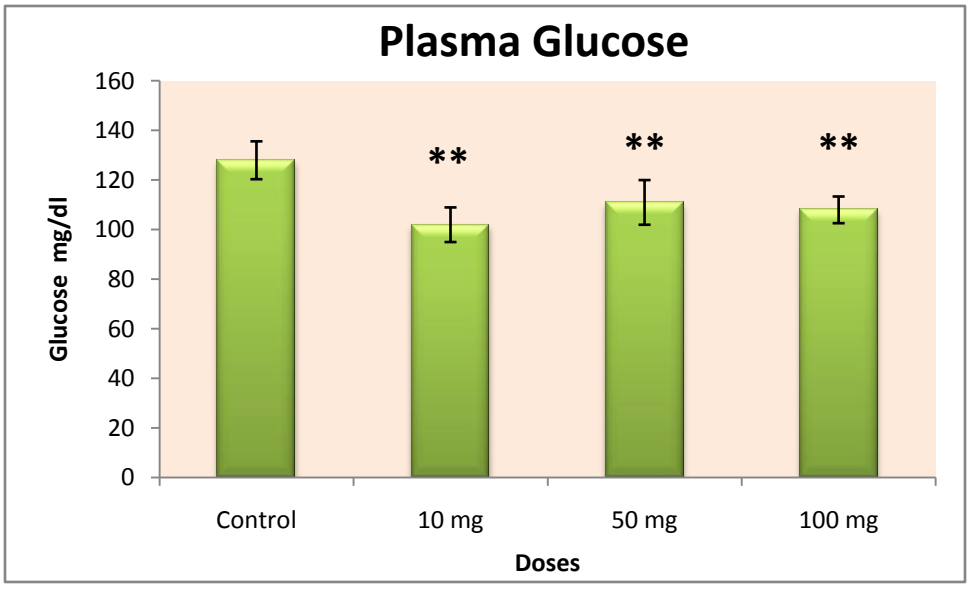


Fig 7: Effect of taurine administration (10mg/kg, 50mg/kg, and 100mg/kg) on glucose levels in rats. Values are means ± SD (n=24). Significant difference by Newman keuls test: *p<0.01 compared with controls.



DISCUSSION

In the present study, chronic taurine administration for 9 days significantly enhanced the memory functions of rats in water maze test. Taurine treated rats took less time to reach the hidden platform after 1h of training session in water maze test as compared to control rats. The improved recognition memory retention was also exhibited by taurine treated rats in novel object recognition task as evidenced by increased discrimination index value observed at highest dose of taurine. Taurine treated rats spent significantly more time with novel object as compared to control

rats in the current study. Chronic taurine administration at 100 mg/kg for 9 days significantly decreased ($p<0.05$) depression like symptoms in rats. However in depression like symptoms were not observed at 10 mg/kg and 50 mg/kg dose of taurine.

Several theories suggest that taurine affects brain chemicals and also improves cognitive function. It has been hypothesized in this study that taurine influences the activities of neurotransmitters in the brain. Previous studies reported that its administration suppresses and delays the ability of learning and memory in rats (Ito et al., 2012) while other studies reported no effect on learning and memory following taurine administration (Ito et al., 2009). Earlier reports showed that taurine affects learning by improving both memory acquisition and memory retention and it fight the effects of aging in older rats (El. Idrissi, 2009). However, the current study reports that administration for 9 daysenhanced both spatial memory functions and recognition memory compared to control rats.

Previous studies have reported that taurine has an antidepressant-like effect and an ability to change depression-related signaling cascades in the hippocampus (Iio, 2012). Numerous studies indicate that taurine has a general depressant effect on the CNS (Barbeau et al., 1975) and may exert a generalized depressant activity on neural excitation. Results of the present study show that taurine administration significantly decreased depression like symptoms in rats only at the highest dose of taurine. However this decrease in depression like symptoms was not observed at 10 mg/kg and 50 mg/kg dose of taurine.

Taurine supplementation helps to prevent the onset of diabetes mellitus in experimental models of both insulin dependent and insulin independent pathways. Beneficial role of taurine is mediated via their ability in reducing glycooxidation and preventing the generation of intracellular reactive intermediate. Taurine stimulated glucose uptake in a dose-dependent manner by activating AMPK signaling (Manna et al., 2013). Taurine administration has been shown to produce antidiabetic effect by stimulating insulin-independent glucose uptake in rat skeletal muscle (Cheong and Chang, 2013). It has also been reported before that taurine protect against streptozoticin-induced hyperglycemia (Tokunaga et al 1979). Present study reports that taurine administration for 9 days significantly decreased glucose levels in a dose dependent manner.

In conclusion the assessment of memory by two different methods WM and NOR task further confirms the beneficial effects of taurine administration on memory functions.The increase food intake of taurine injected rats at all doses in our study further emphasizes that taurine supplementation proves to be a good appetizer. Further experiments are needed to confirm the neurochemical mechanism involved following taurine administration.

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