Physiology & Behavior 142 (2015) 155–160

Contents lists available at ScienceDirect

Physiology & Behavior

journal homepage: www.elsevier.com/locate/phb

Psychological or physical prenatal stress differentially affects cognition behaviors

Masoud Nazeri [a], Mohammad Shabani [a,*], Samaneh Ghotbi Ravandi [b], Iraj Aghaei [c], Masoumeh Nozari [a], Shahrzad Mazhari [a]

[a] Neuroscience Research Center, Institute of Neuropharmacology, Kerman University of Medical Sciences, Kerman, Iran
[b] Department of Biology, Islamic Azad University of Jahrom, Fars, Iran
[c] Guilan Road Trauma Research Center, Poursina Hospital, Guilan University of Medical Science, Rasht, Iran

HIGHLIGHTS

- Prenatal stress effects on motor function is sex and stressor dependent.
- Motor function was impaired in male and female offspring in a stressor-dependent manner.
- Prenatal stress effects on cognitive function are sex and stressor dependent.
- Anxiety-like behaviors are only altered in female offspring of the stressed mothers.

ARTICLE INFO

Article history:
Received 24 October 2014
Received in revised form 21 January 2015
Accepted 6 February 2015
Available online 7 February 2015

Keywords:
Prenatal physical stress
Psychological stress
Cognitive function
Offspring

ABSTRACT

Introduction: Prenatal stress is proposed as a major risk factor in the development of cognitive impairments in the offspring. The objective of the current study was to evaluate the effect of prenatal physical or psychological stress on the motor and cognitive functions of male and female offspring.
Methods: Adult female rats were stressed during their conception using a novel method to induced whether physical or psychological stress. Animal offspring were then kept until adulthood. Elevated plus maze (EPM) was used to evaluate their anxiety-like behavior. Rotarod and wire grip were used to evaluate muscle strength and balance function. Morris water maze (MWM) and passive avoidance (PA) learning and memory paradigm were used to evaluate the cognitive function of the offspring.
Results: Female offspring of both physical and psychological stress had an increased anxiety-like behavior in the EPM test in comparison to female control rats. Balance function was impaired in physical stressed female offspring in comparison to the control and male offspring. Muscle strength was reduced in physical male and female offspring. Both male and female offspring groups that underwent prenatal physical and psychological stress had an impaired spatial learning and memory. PA learning and memory were impaired in both male and female offspring except for the psychological stress female offspring in PA learning.
Conclusion: Results of our study revealed that prenatal physical or psychological stress have different effects on motor and cognitive functions of the offspring. Male and female offspring were differentially affected by prenatal stress. We suggest more studies to evaluate the role of sex hormones on the effects of prenatal physical or psychological stress on cognitive and motor functions of the offspring.

1. Introduction

Stress during pregnancy has been shown to be associated with cognitive impairments in adulthood of the children. Prenatal stress is considered as a risk factor for psychiatric disorders such as schizophrenia and autism [8,9,12]. Previous animal studies have demonstrated cognitive deficits similar to that observed in schizophrenic patients in the offspring of female exposed to different stressors [4,10].

Glucocorticoids play a prominent role in the development of neural system during fetal period as it is shown that HPA axis is reprogrammed by the stressors during pregnancy [10,20,23]. Though the exact mechanisms are not fully understood, exposure to excessive stress hormones during the fetal period leads to the delayed development of the nervous system and inhibition of neurogenesis in different parts of the brain, which might provide an explanation for the cognitive deficits observed in the offspring [7,14].

* Corresponding author at: Neuroscience Research Center, Institute of Neuropharmacology, Kerman University of Medical Sciences, Kerman 76198-13159, Iran.
E-mail addresses: shabanimoh@yahoo.com, shabani@kmu.ac.ir (M. Shabani).

http://dx.doi.org/10.1016/j.physbeh.2015.02.016
0031-9384/

It is previously demonstrated that prenatal stress increases the anxiety-like behaviors and post-natal handling leads to low-anxiety in rats. Though studies have attempted to assess the anxiety-like behaviors and cognitive function of the prenatally stressed rats, there is still a lack of evidence for the effect of different prenatal stressors on the adolescent offspring cognitive functions [3,10–12]. It is previously shown that different stressors have diverse effects on cognition and other function of the animals. Proposed mechanisms for these differences include the activation of different brain regions and involvement of different neurotransmitters and also the level of threat that each stressor evokes in the animals [9,15]. Considering the importance of stressor type, it seems rational to evaluate the effect of prenatal physical or psychological stress on the cognitive function of the offspring to see whether any of them is more harmful than the other one or not.

Thus, the objective of the current study was to evaluate the effect of prenatal physical or psychological stressor on cognitive and motor functions of the adolescent male and female offspring. We evaluated the effect of prenatal physical or psychological stress on spatial and fear learning and memory and we also assessed motor and balance functions of the animals.

2. Methods and materials

Female rats with no experience of sexual activity were used in the current study. They were caged in the groups of four with free access to food and water. Animals were kept under standard conditions according to the guidelines provided by Kerman University of Medical Sciences, Kerman, Iran. Maximum effort was made to minimize pain and discomfort for the animals.

2.1. Experimental procedure

Female rats were introduced to a sexually active male rat in their first day of estrous cycle. Samples were made from the vaginal content for three consecutive days to verify mating.

Female rats were then exposed to two different stressors. A five by four house aquarium (each house: 25 * 30 * 45 cm) made of glass was used to stress the animals physically or psychologically. The stress procedure was commenced at day 6 of conception and continued for the next 10 days.

Rats of the physical stress group were placed in one of the houses of aquarium which was connected to an electric pump that filled the house with water (20 ± 2 °C) so that the animal had to swim in the chamber. After 5 min of swimming, the water was emptied and again after 10 min, the house was again filled with water. This procedure lasted for 1 h. The other groups of rats receiving psychological stress were placed in the other houses of the aquarium watching other animals receiving swim stress.

There were 10 female rats in each group (control, physical or psychological stress). Rats were delivered and the number of offspring, their weight, mortality rate and sex distribution were recorded. Two male and 2 female offspring were randomly selected from each rat and then they were caged together in groups of four. Offspring of the same mother were caged together and the behavioral assays were performed at day 40 post-partum.

Each offspring group consisted of 10 animals. Animals underwent behavioral assays in the following order with a two hour interval among each test performed: open field test, plus maze test, rotarod, wire grip test and shuttle box or morris water maze (the last two assays were performed in separate groups of study due to the nature of the procedure).

2.2. Open field test

The open field was an arena (90 * 90 * 30 cm) made of Plexiglas. Horizontal and vertical activities of the animals within a 5 minute period were recorded and analyzed using Ethovision software. The following parameters were recorded for each animal: velocity, rearing and grooming, time spent in center and periphery of the arena and total distance moved [2].

2.3. Plus maze test

The elevated plus maze was used to assay the anxiety-like behavior of the animals. It was made of wood and consisted of two open arms and two closed arms (50 * 50 * 50 cm). Animals were placed in the middle of the maze and their number of entrance into the open and closed arms and time spent in each arm was recorded using a camera installed above the maze.

2.4. Rotarod

An accelerating rotarod apparatus (Hugo Sachs Electronik, Germany) was used to evaluate the balance and motor functions of the offspring. The trial started from a speed of 10 rounds per minute (rpm) to the maximum speed of 60 rpm. Three trials were performed for each rat with a maximum duration of 300 s with a 30-min intertrial. The duration that each rat spent on the rod maintaining its balance without falling was recorded as a measure of motor coordination and balance [19].

2.5. Wire grip test

This test was used to assay the muscle strength of the animals. Animals' hands were put on the wire and when the animal grasped the wire, it was released and time spent to fall from the wire was recorded for each rat [1].

2.6. Morris water maze

In a separate group of animals (n = 10 for each group), MWM was performed to evaluate spatial learning and memory. The test chamber was a circular water tank (140 cm wide, 45 cm high) surrounded by visual cues visible to the animal. A platform, either visible or submerged (15 cm wide and 35 cm height) was placed 1.5 cm above or below the water surface. Water temperature was set between 21 and 23 °C. Behavioral data for MWM was collected using Ethovision automation software (Noldus information Technology, Netherlands). Each rat was tested in three blocks of trials and each block was comprised of four trials commencing from different points. The inter-block interval was at least 30 min for each rat. All the experiments were performed between 8:00 AM and 12:00 PM. Rats were put in one of the quadrants of the water tank with their face toward the maze. The location of the platform did not change in the acquisition trial. Rats were observed for 60 s to find the platform, when it found the platform, a 20–30 second break was given to the rat on the platform. The animal was returned to its cage and again, after 20–30 s, the rat was put into the water. Time and distance traveled by the animal to find the platform were recorded by the software. To assess the spatial memory of the animals, a single probe trial was performed 2 h after the last block of trials. In the probe trial, the platform was removed from the tank and animals were allowed to swim for 60 s in the tank. Distance and time spent in the target quadrant were recorded for each rat as the indicator of spatial memory retention [1,18].

2.7. PA learning

A shuttle-box device with dimensions of 100*25*25 which consisted two parts was used. First, animals were placed in a light area of the shuttle-box and then the door was opened and the animal was allowed to go to the dark sector, then the door was closed without electric shock and the animal was returned to its cage. 30 min later, this step was repeated again and the third time that the animal entered dark

sector, an electric shock was administered to the animal (0.5 Å, 5 ms) then the animal was returned to its cage. 24 h after training, the test was performed to assess memory; in this step animal was placed in a light arena of the shuttle-box apparatus. After 30 s, the door was opened and the time spent to enter the dark sector was recorded as retention time (Step-through latency (STL). Total dark complement (TDC) and number of entrance into dark sector were recorded in 300 second duration as an indicator of contextual learning [13,17].

Data were analyzed using SPSS 16 (IBM, USA). Two-way ANOVA was separately performed for each types of stress to compare different groups of both sexes. In order to assess the effect of stress on motor and cognitive behaviors in male and female rats, a separate two-way ANOVA test was performed on data of each behavioral test. When a main effect of factors on behavioral variables was detected ($p < 0.05$), appropriate post-hoc analysis was performed to evaluate significant differences. $p < 0.05$ was considered statistically significant. The results are expressed as the mean ± SEM.

3. Results

3.1. The effect of prenatal stress on mobility and anxiety-like behaviors

Data of the open field test revealed no significant difference among groups of study in both male and female offspring ($p > 0.05$) (data not shown).

Male offspring that were exposed to prenatal physical or psychological stress did not show any significant difference in elevated plus maze test in comparison to the control male rats ($p > 0.05$, ANOVA). Female offspring of the physical and psychological prenatal stress had a decreased number of entrances into the open arms in comparison to the control rats (Fig. 1.A–F). The two-way ANOVA of the anxiety-like

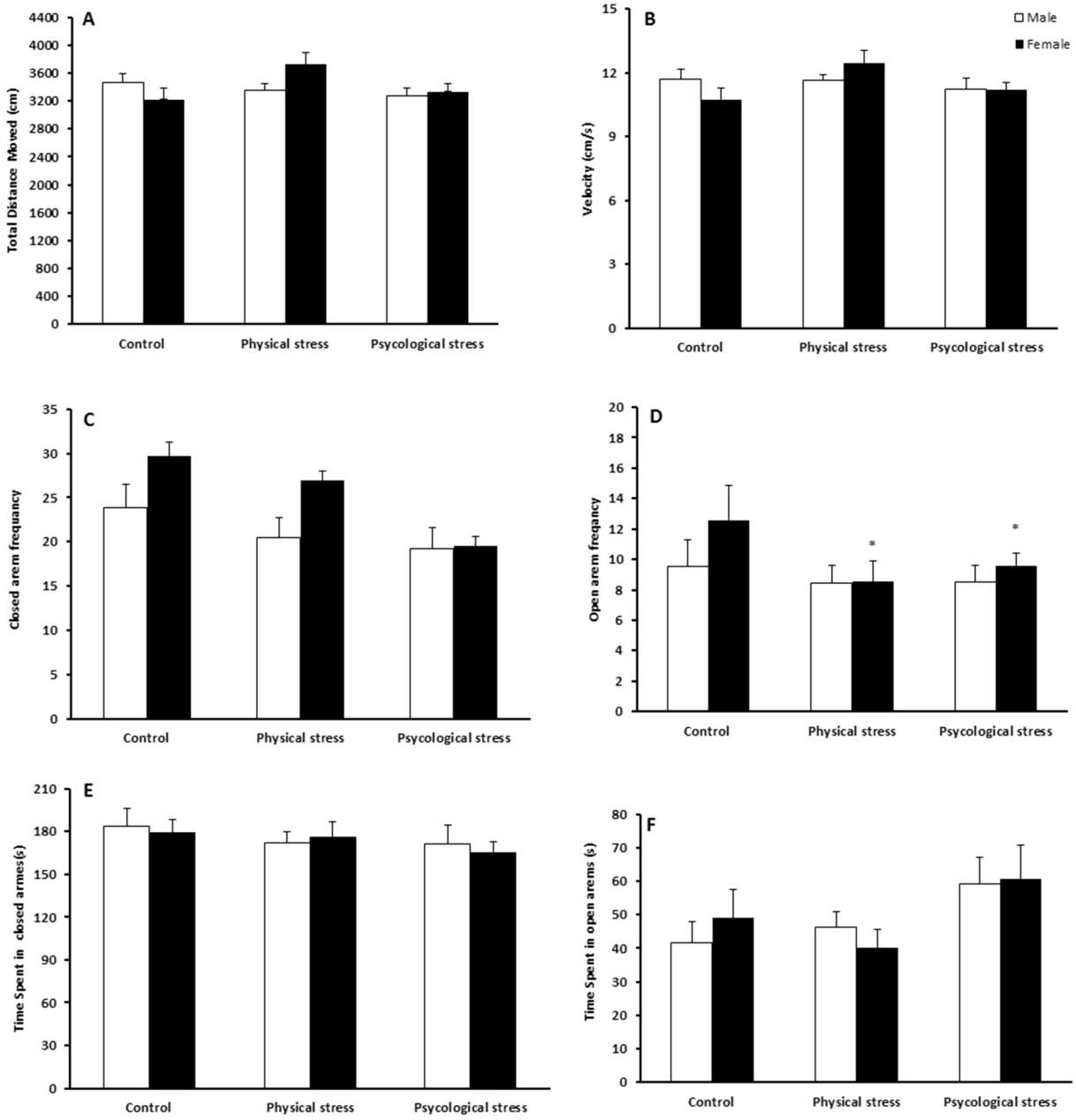

Fig. 1. Anxiety-like behavior of the male and female offspring in comparison to their controls and other sex group. There is only a significant difference in number of entrance into the open arms, declaring an increased anxiety-like behavior for female physical and psychological stress group (D).

behaviors in plus maze didn't show significant interaction of group (stress type) × sex ($F_{(2, 67)} = 2.81$, $p > 0.05$, Fig. 1).

3.2. Effect of prenatal physical or psychological stress on balance and motor function

No significant changes were observed in the time on rod during trials in male offspring ($p > 0.05$). While female offspring of the physical stress group had a decreased time spent on rod in comparison to the matched male stress and control rats [$F_{(2, 67)} = 9.3$, $p < 0.05$, two-way ANOVA (sex * stressor)]. There was also a significant difference between female physical stress offspring and psychological stress offspring in time spent on rod, so that only physical stress had a significantly reduced time (Fig. 2.A).

3.3. Effect of prenatal stress on muscle strength

Time to fall was significantly reduced in both male and female offspring that underwent physical prenatal stress in comparison to their control groups. Male offspring of the psychological stress group also had an impaired muscle strength in comparison to their control group, while female psychological offspring group had a normal time to fall in comparison to their physical stress group [$F_{(2, 67)} = 6.05$, two-way ANOVA (sex * stressor) (Fig. 2.B)].

3.4. Effect of prenatal stress on spatial learning and memory

Female and male offspring of the physical stress group had an increased time and distance traveled to reach the platform, revealing an impaired spatial memory in comparison to their control groups. While only male offspring of the psychological stress group had an increased time and distance traveled in comparison to their control group and female equivalent group (two-way ANOVA (sex * stressor)) (Fig. 3.A–B). Swimming speed was not altered in all groups of study (Fig. 3.C). Percentage of time spent in correct quadrant was significantly reduced in male and female physical stress groups in comparison to their control groups. It was also reduced in the female psychological female offspring group in comparison to the male offspring (two-way ANOVA (sex * stressor)) (Fig. 3.D). Time spent in correct quadrant was significantly reduced in all groups with no interaction of sex and stressor type (Fig. 3.E). The number of crossing in correct quadrant was reduced in male and female physical stress and female psychological stress groups in comparison to their respected control groups ($p < 0.05$, two-way ANOVA (sex * stressor).

3.5. Effect of prenatal psychological or physical stress on passive avoidance learning

Number of shocks received on the first day was significantly increased in both male and female physical stress groups, while it was only increased in male psychological stress group (Fig. 4.A). The two-way ANOVA of the learning phase on shuttle box test showed significant interaction of stress type × sex ($F_{(2, 67)} = 4.1$, $p < 0.05$, Fig. 4.A). Male offspring of the psychological stress group had an impaired learning strength in comparison to their matched female group (Fig. 4.A).

STL was significantly reduced in both male and female physical and psychological stress groups in comparison to their control groups (Fig. 4.B).

4. Discussion

Results of the current study imply a role for the type of stressor applied prenatally and the role of sex hormones in response of the offspring prenatally exposed to different stressors. Female offspring had an increased anxiety-like behavior in comparison to their control groups. Balance and motor functions of the offspring were also impaired in female groups. Spatial and passive avoidance learning and memory were also altered in a sex and stressor-type dependent manner.

It was previously demonstrated that prenatal stress leads to changes in the cognitive function of the offspring [7]. It is also proposed that prenatal stress might lead to psychological disturbance and in some cases, it is suggested that prenatal stress might be a major risk factor for the development of schizophrenia in the offspring [4,5,10]. Though the exact mechanisms are not clearly defined yet, it seems that excessive secretion of the stress hormones during pregnancy and exposure of the fetus to a high level of these hormones might alter the function of CNS and lead to changes in the development of the nervous system that eventually leads to cognitive impairments in adulthood [15,20].

Markham et al. [10] demonstrated the effects of prenatal stress on cognitive function of male and female rats [10]. Spatial learning and memory and passive avoidance learning and memory were negatively affected by prenatal stress in their study, which is consistent with our findings. We have shown whether prenatal physical or psychological stress leads to impairments in learning and memory of adult male offspring in both spatial and contextual fear memory paradigms [10]. The interesting finding of our study is whether physical or psychological maternal stress during pregnancy differentially affects the cognitive function of the offspring. The finding that different stressors might evoke different responses has been demonstrated in previous studies (e.g. in the study performed by Pacak et al. 1998 [16]), but no study

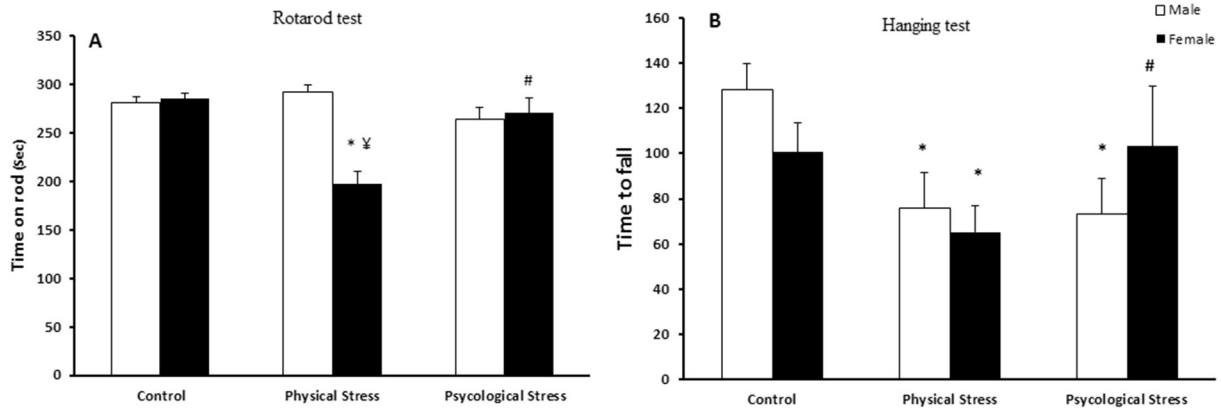

Fig. 2. A) Time on rod was significantly reduced in female offspring that underwent physical stress in comparison to their control and male group. Psychological stress did not alter time on rod in both male and female offspring, though there was a significant difference between female offspring of physical and psychological stress groups. B) Time to fall was significantly reduced in male and female offspring of the physical stress group. There was also a significant reduction in time to fall of the male psychological stress group. *$p < 0.05$, two-way ANOVA controlling for interaction of sex × stressor in comparison to the control group. #$p < 0.05$ in comparison to the same sex in other stressor group. ¥$p < 0.05$ in comparison to the male offspring of the same stressor.

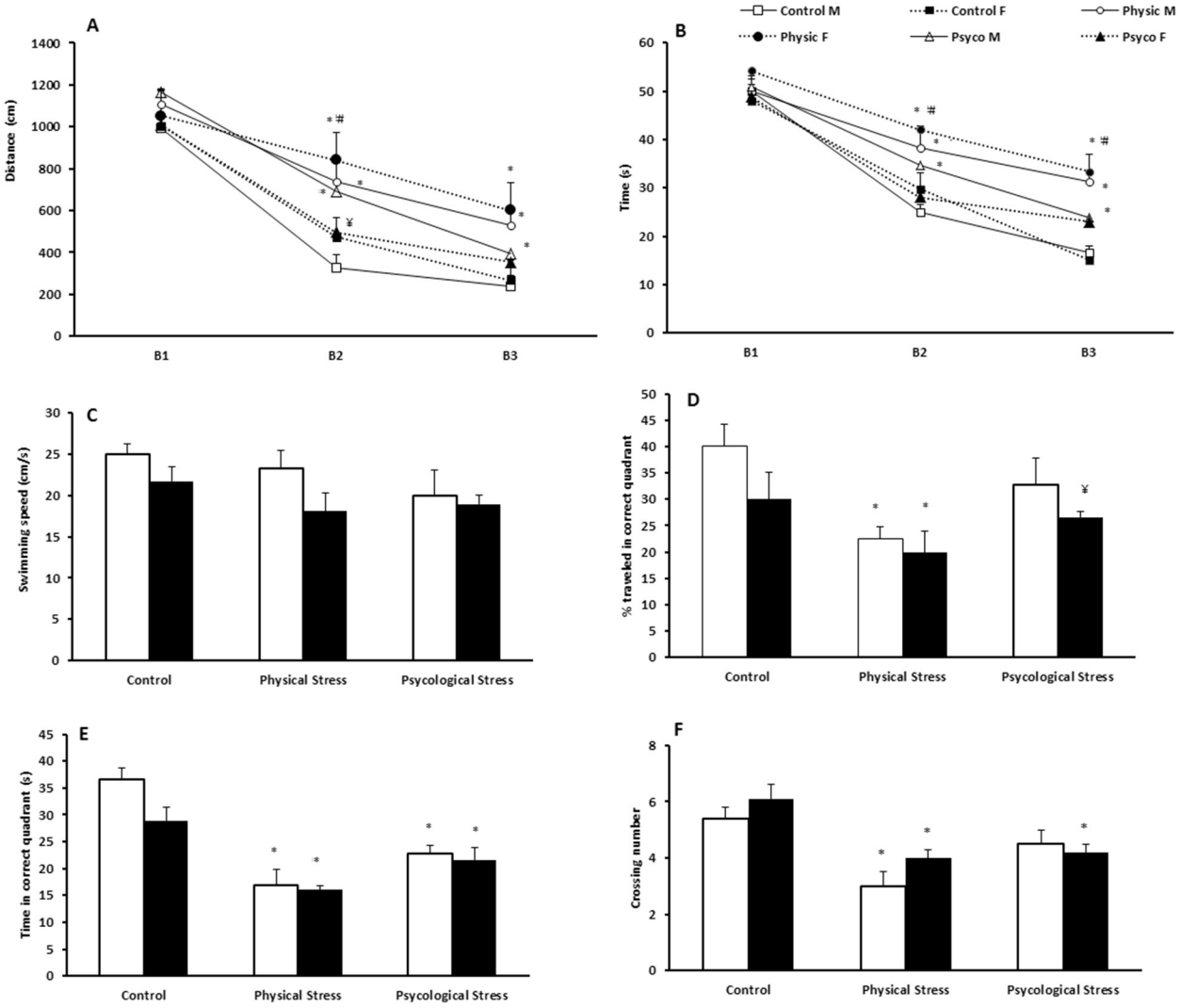

Fig. 3. A and B) An increased distance traveled and time spent to reach the platform were observed in both physical and psychological stress male and female offspring. C) No significant difference was observed in swimming speed in all three groups of study. D) A reduced percentage of time traveled in correct quadrant was observed in physical stress male offspring, declaring an impaired spatial memory in this group. E) A reduced time spent in correct quadrant was observed in both male and female physical and psychological stress offspring. F) Number of crossing in correct quadrant was reduced in both male and female physical stress groups, while it was only reduced in female psychological group. *$p < 0.05$, two-way ANOVA controlling for sex × stressor interaction. #$p < 0.05$ as compared to the same sex group in other stressor group. ¥$p < 0.05$ as compared to the male offspring of the same stressor group. B1, B2 and B3: three consecutive trials.

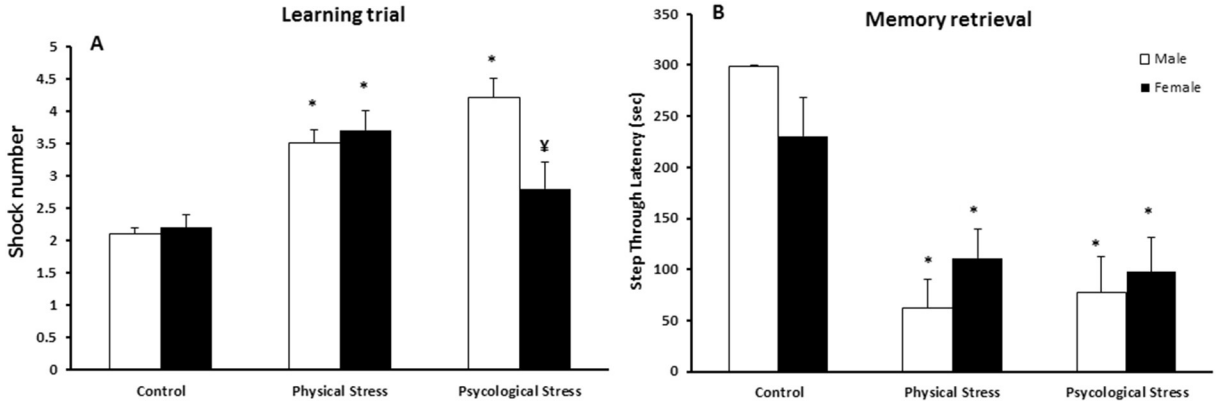

Fig. 4. A) An increased number of shocks was observed in both male and female physical stress offspring. There were also an increased number of shocks received in male psychological stress group, while female offspring did not show such an increase. B) A decreased step through latency (STL) was observed in male and female physical and psychological stress groups in comparison to their controls. *$p < 0.05$, two-way ANOVA controlling for sex × stressor interaction. ¥$p < 0.05$ in comparison to the male offspring of the same stressor group.

has evaluated the effect of prenatal physical or psychological prenatal stress on cognitive function of the offspring which is the novelty of our research.

Impaired memory of adult offspring could be attributed to the impairments of neurogenesis in the hippocampus of the animals, as demonstrated by Lemaire et al. [7]. They have proposed a neurodevelopmental basis for learning and memory impairments in the offspring that have been prenatally stressed. We propose further studies to evaluate the effect of prenatal physical or psychological stress on neural development of the hippocampus and amygdala, two centers in the brain that are heavily involved with spatial and contextual learning and memory [7]. Prenatal stress might also predispose the animals to the negative consequences of aging, as demonstrated by Vallee et al. [22]. This predisposition might be due to changes in the stress regulatory system during adolescence and adulthood of the animals, though further research is needed to clarify the exact mechanisms involved.

Yang et al. [24] have demonstrated that prenatal physical stress (footshock) alters synaptic plasticity in the hippocampus of the offspring [24]. They have demonstrated a decreased long-term potentiation (LTP) and increased long-term depression (LTD) in the male offspring and also impairment of spatial learning in the rats, which is consistent with our findings [24]. Though we did not evaluate the electrophysiological parameters of the rats, we suggest further studies to see whether physical or psychological prenatal stress could change the LTP and LTD of hippocampal formation in a diverse manner or not.

That male rats are more susceptible to the effects of prenatal stress on spatial and learning has been demonstrated by Tavassoli et al. [21]. In the current study, prenatal physical or psychological stress differentially affected the cognitive function of the animals. Though the data presented in the current study might not totally confirm the findings by Tavassoli et al. [21], it would provide a new insight into the importance of stressor type.

It is proposed that sexual dimorphism during brain development period has an important impact on the susceptibility of the brain to further environmental stressors [3]. Results of the current study implicate an important role for sex hormones in the response to prenatal physical or psychological stress. This finding might provide new documents for the pre-clinical studies on affective disorders, considering the fact that previous studies have implicated an important role for sex hormones on the development of affective disorders [6,10,21].

Our study has some limitations which should be considered in future studies. We did not check the estrous cycle of the female rats and therefore it might contribute to the variability of data in female rats. Though we caged the animals together in groups of four, we suggest more studies on the effect of sex hormones on response to prenatal physical or psychological stress. That the HPA axis response to physical or psychological prenatal stress is different or not should be tested in further studies. Motor function impairments observed in the animals might contribute to the impairments observed in cognitive function of the animals, though this hypothesis should be tested.

5. Conclusion

The effects of prenatal exposure to physical or psychological stress on anxiety-like behaviors, motor function and learning and memory were evaluated in adolescent male and female offspring. Results of our study suggest a sex and stressor-dependent response to prenatal stress. We suggest further studies to elucidate the possible mechanisms involved to provide better preventive and treatment modalities for at risk populations.

Conflict of interest

The authors declare no conflict of interest. This study was performed by a grant from the Kerman Neuroscience Research Center [KNRC/93-35] for the MSc thesis of Samaneh Ghotbi.

References

[1] I. Aghaei, M. Nazeri, M. Shabani, M. Mossavinasab, F.K. Mirhosseini, M. Nayebpour, et al., Erythropoietin ameliorates the motor and cognitive function impairments in a rat model of hepatic cirrhosis, Metab. Brain Dis. 1–8 (2014).
[2] I. Aghaei, M. Shabani, N. Doustar, M. Nazeri, A. Dehpour, Peroxisome proliferator-activated receptor-γ activation attenuates motor and cognition impairments induced by bile duct ligation in a rat model of hepatic cirrhosis, Pharmacol. Biochem. Behav. 120 (2014) 133–139.
[3] R.E. Bowman, N.J. MacLusky, Y. Sarmiento, M. Frankfurt, M. Gordon, V.N. Luine, Sexually dimorphic effects of prenatal stress on cognition, hormonal responses, and central neurotransmitters, Endocrinology 145 (2004) 3778–3787.
[4] A.S. Khashan, K.M. Abel, R. McNamee, M.G. Pedersen, R.T. Webb, P.N. Baker, et al., Higher risk of offspring schizophrenia following antenatal maternal exposure to severe adverse life events, Arch. Gen. Psychiatry 65 (2008) 146–152.
[5] J.I. Koenig, G.I. Elmer, P.D. Shepard, P.R. Lee, C. Mayo, B. Joy, et al., Prenatal exposure to a repeated variable stress paradigm elicits behavioral and neuroendocrinological changes in the adult offspring: potential relevance to schizophrenia, Behav. Brain Res. 156 (2005) 251–261.
[6] O. Kofman, The role of prenatal stress in the etiology of developmental behavioural disorders, Neurosci. Biobehav. Rev. 26 (2002) 457–470.
[7] V. Lemaire, M. Koehl, M. Le Moal, D. Abrous, Prenatal stress produces learning deficits associated with an inhibition of neurogenesis in the hippocampus, Proc. Natl. Acad. Sci. 97 (2000) 11032–11037.
[8] D.J. Lodge, A.A. Grace, Developmental pathology, dopamine, stress and schizophrenia, Int. J. Dev. Neurosci. 29 (2011) 207–213.
[9] S.J. Lupien, B.S. McEwen, M.R. Gunnar, C. Heim, Effects of stress throughout the lifespan on the brain, behaviour and cognition, Nat. Rev. Neurosci. 10 (2009) 434–445.
[10] J.A. Markham, A.R. Taylor, S.B. Taylor, D.B. Bell, J.I. Koenig, Characterization of the cognitive impairments induced by prenatal exposure to stress in the rat, Front. Behav. Neurosci. 4 (2010).
[11] F. Modir, M. Elahdadi Salmani, I. Goudarzi, T. Lashkarboluki, K. Abrari, Prenatal stress decreases spatial learning and memory retrieval of the adult male offspring of rats, Physiol. Behav. 129 (2014) 104–109.
[12] B.R. Mueller, T.L. Bale, Early prenatal stress impact on coping strategies and learning performance is sex dependent, Physiol. Behav. 91 (2007) 55–65.
[13] M. Nazeri, M. Razavinasab, F. Abareghi, M. Shabani, Role of nitric oxide in altered nociception and memory following chronic stress, Physiol. Behav. 129 (2014) 214–220.
[14] C. Noorlander, G. Visser, G. Ramakers, P. Nikkels, P. De Graan, Prenatal corticosteroid exposure affects hippocampal plasticity and reduces lifespan, Dev. Neurobiol. 68 (2008) 237–246.
[15] K. Pacák, M. Palkovits, Stressor specificity of central neuroendocrine responses: implications for stress-related disorders, Endocr. Rev. 22 (2001) 502–548.
[16] K. Pacak, M. Palkovits, G. Yadid, R. Kvetnansky, I.J. Kopin, D.S. Goldstein, Heterogeneous neurochemical responses to different stressors: a test of Selye's doctrine of nonspecificity, Am J Physiol 275 (4 Pt 2) (1998 Oct) R1247–R1255.
[17] S. Parsania, M. Shabani, K. Moazzami, M. Razavinasab, M.H. Larizadeh, M. Nazeri, et al., Gender difference in motor impairments induced by chronic administration of vinblastine, Iran. J. Basic Med. Sci. 17 (2014) 433.
[18] M. Razavinasab, K. Moazzami, M. Shabani, Maternal mobile phone exposure alters intrinsic electrophysiological properties of CA1 pyramidal neurons in rat offspring, Toxicol. Ind. Health 0748233714525497 (2014).
[19] M. Shabani, M.H. Larizadeh, S. Parsania, V. Hajali, A. Shojaei, Evaluation of destructive effects of exposure to cisplatin during developmental stage: no profound evidence for sex differences in impaired motor and memory performance, Int. J. Neurosci. 122 (2012) 439–448.
[20] T.F. Szuran, V. Pliška, J. Pokorny, H. Welzl, Prenatal stress in rats: effects on plasma corticosterone, hippocampal glucocorticoid receptors, and maze performance, Physiol. Behav. 71 (2000) 353–362.
[21] E. Tavassoli, E. Saboory, M. Teshfam, Y. Rasmi, S. Roshan-Milani, B. Ilkhanizadeh, et al., Effect of prenatal stress on density of NMDA receptors in rat brain, Int. J. Dev. Neurosci. 31 (2013) 790–795.
[22] M. Vallée, S. Maccari, F. Dellu, H. Simon, M. Le Moal, W. Mayo, Long-term effects of prenatal stress and postnatal handling on age-related glucocorticoid secretion and cognitive performance: a longitudinal study in the rat, Eur. J. Neurosci. 11 (1999) 2906–2916.
[23] M. Weinstock, The long-term behavioural consequences of prenatal stress, Neurosci. Biobehav. Rev. 32 (2008) 1073–1086.
[24] J. Yang, H. Han, J. Cao, L. Li, L. Xu, Prenatal stress modifies hippocampal synaptic plasticity and spatial learning in young rat offspring, Hippocampus 16 (2006) 431–436.