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Effects of Handling-Injection Stress with Noise Stress on Learning and Memory in the Early Life of Male Rats

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ABSTRACT

Effects of stress on learning and memory in the early life have been one of the hot topics in neuroscience. The aim of this study was to investigate the combined effects of handling-injection stress with noise stress in the passive avoidance task in rats. The performance of rats was evaluated in the retention test 24 h after a single acquisition trial. Male Wistar rats were divided into 4 groups of 6 animals for 4 weeks: subcutaneous injection ofss sodium chloride 0.9% and handling stress (I+H), subcutaneous injection of sodium chloride 0.9% and handling with noise exposure (I+N), noise exposure (N) and control (C). After 4 weeks, we studied passive avoidance conditioning test in a shuttle box. The step-through latency after training animals significantly increased in (I + H) group as compared with (I+N) and (N) groups ($p<0.01$). But using noise stress with handling-injection stress significantly attenuated learning and memory in the (I+N) group than other 3 groups ($p<0.05$). The data suggested that moderate stress (handling-injection) increased learning and memory in the early life of animals but using moderate stress with sound stress impaired them.

Key words: handling-injection stress, early life, learning and memory, passive avoidance, rat.

INTRODUCTION

The effect of chronic stress on learning and memory functions has been one of the hot topics in neuroscience. Different stress stimulation has different effects on learning and memory (1). However, studies in animals and people have reported divergent findings, with stress producing an enhancement, impairment, or no effect on learning and memory (2). With the growing competition in the world, people usually live in a circumstance with different kinds of chronic stressors. Many studies showed that chronic stress was harmful to health, even led to diseases. Meanwhile it impacts the brain cognitive functions and leads to learning and memory impairment (3).

The early postnatal environment is seen as providing the potential for altering vulnerability to psychiatric disorders such as addiction, posttraumatic stress disorders (PTSD) and depression. The rat is an appropriate animal model to study early life psychiatric disorders (4, 5). Neonatal handling decreased the aging impairment on performance in a spatial learning task, including T-maze and radial arm maze (6). Environmental manipulations during the early postnatal period induced a decreased anxiety-like behavior in adulthood (7, 8 and 9). Stressful events in early life are involved in behavioral alterations in adulthood. Meany and colleagues showed that neonatal handling of rat pups during the first 3 weeks of life was able to improve the spatial learning ability of aged animals in a water-maze task (9). Early postnatal handling induces a decrease in corticosterone secretion in response to stress (9, 10 and 11) and an increase in the number of hippocampal receptors in adult rats (12). Exposure to stress early in life can induce an increased vulnerability to mood disorders later in life. Indeed, the origin of many adult diseases such as depression, anxiety, or impulse control disorders, can be found in infancy (14). There is growing evidence that stress during prenatal and postnatal periods of life can modify adaptive capacities in adulthoods. Postnatal handling protected from the age-related neuroendocrine and behavioral alterations. Handling in the early life, has been reported to prevent the change in behavioral reactivity observed in adult rats previously submitted to a prenatal stress (15).

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Postnatal handling has no effect on the performance of adult animals in a spatial memory task (the water maze) but improves performance during senescence (9).

Among the factors inducing stress, Environmental noise is a known stressful condition that induces alterations of various physiological responses in the exposed individuals. The extent of noise disturbance depends on intensity, frequency, individual sensitivity, age, and sex. Noise not only affects the nervous system of man, but also causes some psychological and psychosomatic problems. Noise has always been an important environmental problem for mankind. Among the cognitive effects, reading, attention, problem solving and memory are most strongly affected by noise. (3, 16)

The combined effects of noise stress with a moderate stress hasn't considered in literature. Therefore in this study we attend to examine the Simultaneous effect of noise stress with moderate stress (handling and injection stress) on learning and memory in the early life of male Wistar rats.

MATERIALS AND METHODS

Animals and experimental design

Twenty two days old male Wistar rats, 55 g weight were housed in a room that was maintained on 12-h light/dark cycle and kept at 24° C. All rats were maintained on Standard rat food and water ad libitum. After 4 days of acclimatization to these conditions, the animals were divided into four experimental groups of 12 rats as follows: subcutaneous injection of sodium chloride 0.9% and handling stress (I+H), subcutaneous injection of sodium chloride 0.9% and handling with noise exposure (I+N), noise exposure (N) and control (C) for 4 weeks.

Handling stress

The animals of group 1 were handled daily for 15 min. when the rats were handling, they were picked up from the home cage and held in the hands for 15 min.

Sound stress:

Noise group were subjected to 100 dB SPL broadband white noise, 3 min daily for 4 weeks. The noise was produced by one loudspeakers (15W), driven by a white-noise generator (350 Hz), and installed 30 cm above the cage.

Measurement of learning and memory in the passive avoidance paradigm.

Apparatus

A shuttle-cage consisting of two compartments of equal size (26×26 cm) separated by a sliding door (8×8 cm) was used. One compartment is lighted by an overhead stimulus light and the other is black so as to remain dark. Illumination inside the lighted chamber was provided by a 40-W lamp. The two compartments are separated by an automatic guillotine door and each has a grid floor placed through which a foot shock can be delivered.

Training and testing were performed between 8.00 and 13.00 h.

Habituation

Habituation is performed by placing the mouse in the lighted part for 30 seconds while it could not be able to enter in dark area. Having finished the 30 seconds by raising the separator door the mouse is allowed to look at around freely but every time as soon as the mouse enters the dark chamber the door is closed and the mouse returned to its home cage. This training process was repeated after 30 minutes.

Training

After habituation, the training process was started. First of all the mouse was placed in lighted chamber and the same as habituation time it was not able to enter in dark part by the separator door for 30 seconds, then the guillotine door was opened after these seconds. Entering to dark compartment with four paws caused the door be closed and after 3 seconds the mouse faced to a foot shock (0.4 mA, 3 seconds duration) and after 30 seconds it is returned to its home cage. Training was terminated when the rat remained in the light chamber for 120 consecutive seconds.

Remaining in the light compartment for 120 consecutive seconds by the mouse, made the training processes was terminated.

Testing

The test is performed 24 hours after training. The mouse is placed in light chamber while it is facing away from the dark part and after 5 seconds the separator door is lifted and the test is begun. Entering to dark compartment with four paws by the mouse caused the door be closed and the mouse removed to its home cage. The latency time from opening the door till entering in dark part is recorded. In test time there is not any electric shock.

Statistical analysis

All continuous data with normal distribution were expressed as mean ± standard deviation (mean ± SD) for each group. The data were analyzed using the SPSS software (15th version) and assessed by one-way analysis of variance (ANOVA) and student t-test. The level of significance was presented at $p<0.05$.

RESULTS

Learning and memory in the passive avoidance test

-Number of correct response:

Fig.1 shows the correct responses number after passive avoidance conditioning. The percentage of correct responses after training animals with conditioned reflex significantly increased in the group was exposed to handling and injection stress(90%), when compared to other 3 groups($p<0.05$). also it was significantly lower in (I+N) group: 60% as compared with (I+H), (N), and (C) group.($p<0.05$)

-Latency period

After performing passive avoidance conditioning test, the animals of (I+H) group displayed longer latencies of transition in the dark compartment (275 seconds) as compared with (I+ N), (N), and (C) groups: 153, 183, 233 seconds respectively($p<0.05$). Adversary the (I+N) group had shorter latencies period than that of other 3 groups ($p<0.05$). (Fig.2)

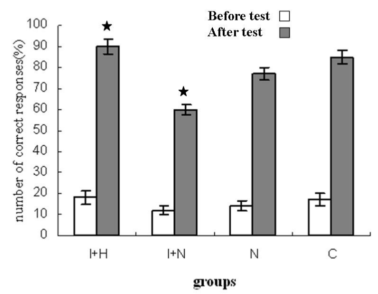

Fig. 1: effect of different kinds of stressors on passive avoidance conditioning (the percentage of correct responses). Groups: (I+H) handling and injection stress, (I+N) injection with noise stress, (N) noise stress,(C) control.* $p<0.01$, between I+H as compared with I+N, N and C groups.

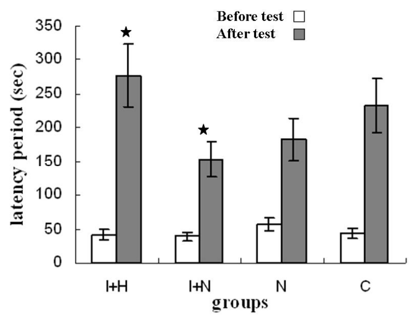

Fig. 2: effect of different kinds of stressors on passive avoidance conditioning (latency period). Groups: (I+H) handling and injection stress, (I+N) injection with noise stress, (N) noise stress,(C) control. * $p<0.01$, between I+H as compared with I+N, N and C groups.

DISCUSSION

In this study we examined the combined effects of handling and injection stress with sound stress in the early life of male Wistar rats. Our results showed that moderate stress (handling- injection) increased learning and memory in animals. But using moderate stress with sound stress impaired it. Passive avoidance procedure represents a model of learning where the effects of different stressors can be studied. We weren't able to find any publication regarding the combined effects of moderate and harsh stressors on learning and memory in the early life. However some animal studies have shown different stressors effects on learning and memory in the early life. For example Meaney et al. showed that early life handling permanently alters CNS systems that regulate hypothalamic-pituitary-adrenal (HPA) function, although the effect may depend on the gender of the animal. In both males and females, however, handling appears to prevent (or minimize) increased adrenal secretion in later life and to attenuate hippocampal cell loss and spatial memory impairments (17). The study performed by Nunez et al. and Pryce et al. showed that neonatal handling enhanced active avoidance learning (18). In this present study we found that exposed to mild stress (handling- injection) caused to high percentage of conservation of skill to avoid punishment even slightly higher than that of control group. These findings are similar to those of positive effects of chronic stress (17, 18). Valee et al. found that postnatal handling can prevent the age-induced impairment in HPA axis function. At 4 months old, handled animals secreted lower levels of corticosterone during their stress recovery response than that of control group (15).

The study by kosten et al. demonstrated that early life manipulations (neonatal isolation, neonatal handling and maternal separation) impaired fear conditioning in adult rats. (19). In another study they considered the effects of neonatal handling on inhibitory avoidance, circular maze, and object recognition performance. It was found that neonatal handling impaired inhibitory avoidance, circular maze and object recognition performance. Another prior study by Wenberg and Levin showed no effect of handling in this task. Our results are different from studies showed the impairment of learning and memory in the early life by postnatal handling stress. Therefore this experiment will extend the research to examine the effects of different stressors on inhibitory learning (19).

We found some studies about noise stress impairment effects on cognitive, reading, attention, problem solving, learning and memory (3, 16). On the other hand, based on these findings that the positive effects of moderate stress and negative effect of sound stress on learning and memory in the early life, we had predicted that companionship of moderate stress with sound stress would attenuate impairment of learning and memory by the noise. Yet we found handling-injection with sound stress impaired learning and memory in neonatal rats.

Early-life events, including stress, exert long-lasting influence on neuronal function. Stress impacts the structure and function of hippocampal neurons.(20). Increasing levels of corticosteroids, stress causes atrophy of CA3 pyramidal cell dendrites, inhibits adult neurogenesis in the dentate gyrus, and impairs hippocampus-dependent learning (21).

In adult mouse there is some change about 5-HT (1A) receptor function in medial prefrontal cortex which is related to early postnatal stress.

The risk of appearing mental diseases in adult is obviously associated with traumatic events in childhood. About the etiology of stress-related disorders the 5-hydroxytryptamine (5-HT) (1A) receptors are known as the most important parts that effect the 5-HTergic mechanisms which are associated with mental diseases. Weakness of 5-HT (1A) function in medial prefrontal cortex in adult is related with hated and aversive stress in the third week of the postnatal period and produces feedback inhibition of the raphe nuclei via postsynaptic 5-HT(1A) receptors.(22)

The present study has some limitations. We did an animal study so we can't attribute all of these findings to human absolutely. Because maybe the results of human study about early life stress effect would differ to animal study. It is needed to do more experiments about this subject for concluding exact reasons. In addition we didn't consider serotonergic system changes and HPA axis function in our study. Therefore the exact mechanism should be clarified in the future studies.

REFERENCES

1) Xiao-heng L, Neng-bao L, Min-hai Z, Yan-ling Z, Jia-wan Z, Xiang-qian L, Hong-wei C. Effects of chronic multiple stress on learning and memory and the expression of Fyn, BDNF, TrkB in the hippocampus of rats. Chinese Medical Journal 2007; 120 (8): 669-674.

2) Yang Y, Cao J, Xiong W, Zhang J, Zhou Q, Wei1 H, Liang1 C,

Den J, Li T, Yang S, Xu L. Both stress experience and age determine the impairment or Enhancement effect of stress on spatial memory retrieval. Journal of Endocrinology 2003; 178, 45–54.

3) Bo CUI, Mingquan WU, Xiaojun SHE. Effects of Chronic Noise Exposure on Spatial Learning and Memory of Rats in Relation to Neurotransmitters and NMDAR2B Alteration in the Hippocampus. Occup Health 2009; 51: 152–158.

4) Heim C, Nemeroff C.B. The role of childhood trauma in the neurobiology of mood and anxiety disorders: preclinical and clinical studies. Biol. Psychiatry 2001; 49: 1023–1039.

5) Kendler K.S, Bulik C.M, Silberg J, Hettema J.M, Myers J,Prescott C.A. Childhood sexual abuse and adult psychiatric and substance use disorders in women. Arch. Gen.Psychiatry 2000;57: 953–959.

6) Unis A.S. Developmental molecular psychopharmacology in early-onset psychiatric disorder: from models to mechanisms. Child Adolesc. Psychiatr. Clin1995; 4: 41–57.

7) Levine S, Haltmeyer G, Karas G, Denenberg V.H. Physiological and behavioral effects of infantile stimulation. Physiol. Behav1967; 2: 55-59.

8) Fernandez-Teruel, A, Escorihuela, R.M. Early stimulation effects on novelty-induced behavior in two psychogenetically-selected rat lines divergent emotionality profiles. Neurosci. Lett 1992;137:185-188

9) Vallee M, Mayo W, Dellu F, Le Moal M, Simon H, Maccari S. Prenatal stress induces high anxiety and postnatal handling induces low anxiety in adult offspring: correlation with stress induced-corticosterone. The journal of neuroscience 1997; 17:2626-2636.

10) Levine S. Plasma-free corticosterone response to electric shock in rats stimulated in infancy. Science 1962; 135: 795-796.

11) Ogawa T, Mikuni M, Kuroda Y, Muneoka K, Mori M.J, Takahashi K. Periodic maternal deprivation alters stress response in adult offspring: potentiates the negative feedback regulation of restraint stressinduced adrenocortical response and reduces the frequencies of open field induced behavior. Pharmacol. Biochem. Behav 1994; 49: 961-967.

12) Meaney M.J, Aitken D.H, Sharma S, Viau V, Sarrieau A.

Neonatal handling alters adrenocortical negative feedback sensitivity and hippocampal type II glucocorticoid receptor binding in the rat.

Neuroendocrinology 1989; 50: 597-604.

13) Meaney M.J, Aitken D.H. The effects of early postnatal handling on hippocampal glucocorticoid receptor concentrations: temporal

parameters. Dev. Brain Res 1985; 22:301-304.

14) Todeschin A, Winkelmann-Duarte E, Jacob M, Aranda B, Jacobs S, Fernandes M, Ribeiro M, Sanvitto G, Lucion A. Effects of neonatal handling on social memory, social interaction, and number of oxytocin and vasopressin neurons in rats B2009 Hormones and Behavior 2009; 56:93–100.

15) Vallee M, Maccari S, Dellu F, Simon H, Moal M, Mayo W. Long-term effects of prenatal stress and postnatal handling on age-related glucocorticoid secretion and cognitive performance: a longitudinal study in the rat. 3European Journal of Neuroscience 19993(; 11(8): 2906 – 2916.

16) Sarkaki A, Karami K.Impaired Learning Due to Noise Stress during Pregnancy in Rats Offspring. Journal of Research in Medical Sciences 2004; 6: 275-279

17) Meaney MJ, Aitken DH, Bhatnagar S, Sapolsky RM. Postnatal handling attenuates certain neuroendocrine, anatomical, and cognitive dysfunctions associated with aging in female rats. Neurobiol Aging. 1991; 12(1):31-8.

18) Nunez J.F, Ferre P,Garcia E, Escorihuela R.M, Fernandez-Teruel A, Tobena A.1995. Postnatal handling reduces emotionality ratings and accelerates two-way active. Physiology & behavior 1995; 1995; 57: 831-835.

19) Kosten TA, Lee HJ, Kim J. Neonatal handling alters learning in adult male and female rats in a task-specific manner. Brain Res. 2007 18;1154:144-53.

20) Fenoglio KA, Brunson KL, Baram TZ. Hippocampal neuroplasticity induced by early-life stress: functional and molecular aspects. Front Neuroendocrinol. 2006; 27(2):180-92.

21) Karten YJ, Olariu A, Cameron HA. Stress in early life inhibits neurogenesis in adulthood. Trends Neurosci. 2005; 28(4):171-2.

22) Matsuzaki H, Izumi T, Matsumoto M, Togashi H, Yamaguchi T, Yoshida T, Watanabe M, Yoshioka M. Early postnatal stress affects 5-HT (1A) receptor function in the medial prefrontal cortex in adult rats. Neuropharmacology and Analgesia 2008;618: 76-82.