

Impacts of Passive Smoking on Learning and Memory Ability of Mouse Offsprings and Intervention by Antioxidants

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Objective To determine the impact of passive smoking and the protective effect of antioxidants such as vitamin E and quercetin on learning and memory ability of mouse offsprings. **Methods** A passive smoking model of pregnant mice was established. Learning and memory ability was evaluated by the water maze test and long term potentiation (LTP). Nitric oxide (NO), content, nitric oxide synthase (NOS), acetylcholinesterase (Ache) activity in brain, vitamin E concentration, and reactive oxygen species (ROS) in serum were determined. The latency period (the time during which the mice swim from the starting position to the ending position) and errors (the number of mice entering the blind end) in control and antioxidant intervention groups were compared with those in the smoke exposure group after 6 days. **Results** The latency period as well as errors in the air, control diet, tobacco smoke (TS), and vitamin E diet groups were decreased significantly as compared with the TS and control diet groups ($P < 0.05$). LTP was restrained in the TS and control diet groups. LTP in all the antioxidant diet groups was significantly increased compared with the TS and control diet groups. In addition, NOS and acetylcholinesterase (Ache) activity was significantly higher in the TS and control diet groups than in the air and control diet group. NO content was not significantly different among the different groups, and significantly lower in the TS and vitamin E diet groups than in the TS group, control diet group, quercetin diet group, and mixture diet group ($P < 0.05$). Vitamin E concentration and ROS activity in serum were correlated with the outcome of water maze and LTP. **Conclusion** Passive smoking reduces LTP formation by disturbing the hippocampus function of mice, by decreasing NOS and Ache activity and increasing NO content. Antioxidants (especially vitamin E) partially improve the learning and memory ability of offsprings whose mothers are exposed to tobacco smoke during pregnancy.

Key Word: Passive smoking; Mice offspring; Learning and memory ability; Long term potentiation; Antioxidant intervention

REFERENCES

1. Perera F P, Jedrychowski W, Rauh V, *et al.* (1999). Molecular epidemiologic research on the effects of environmental pollutants on the fetus. *Environ Health Perspect* **107**, 451-460.
2. Roy T S, Seidler F J, Slotkin T A (2002). Prenatal Nicotine Exposure Evokes Alterations of Cell Structure in Hippocampus and Somatosensory Cortex. *JPET* **300**, 124-133.
3. WHO. Global tobacco treaty enters into force with 57 countries already committed. 2005, GENEVA. <http://www.who.int/tobacco>, 2005-2-24.
4. Yang G H, Ma J M, Liu N, *et al.* (2005). Smoking and passive smoking in Chinese, 2002. *Chin J Epidemiol* **26**, 77-83. (In Chinese)
5. Yang W R, Wang Z Z (2003). The relationship of infant respiration infection and family smoke in Wu Han China. *Maternal and Child Health Care of China* **18**, 108-110. (In Chinese)
6. Cui G C, Ye G L (2002). Recent advances in the study of long-term potentiation (Part I). *Nervous Diseases and Mental Hygiene* **2**, 179-182.
7. Brenda M, Larry R S, Eric P K (1998). Cognitive neuroscience and the study of memory. *Neuron* **20**, 445-468.
8. Geddes D M, LaPlaca M C, Cargill R S (2003). Susceptibility of hippocampal neurons to mechanically induced injury. *Experimental Neurology* **184**, 420-427.
9. Squire L R (1992). Memory and the hippocampus: a synthesis from findings with rats, monkeys and humans. *Psychol Rev* **99**, 195-231.
10. Siwinska E, Mielzynska D, Bubak A, *et al.* (1999). The effect of coal stoves and environmental tobacco smoke on the level of urinary 1-hydroxypyrene. *Mutat Res* **445**, 147-153.
11. Coyle J T, Puttfarcken P (1993). Oxidative stress, glutamate, and neurodegenerative disorders. *Science* **262**, 689-695.
12. Xie Z, Sastry B R (1995). Impairment of long-term potentiation in rats fed with vitamin E deficient diet. *Brain Res* **681**, 193-196.
13. WANG X R (2003). Experimental method and technology of Toxicology. People's Medicine Publishing House, Beijing, pp.

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14. Li Y K (1991). The methodology of Chinese traditional medicine pharmacology experiment. Shanghai: Shanghai Scientific and Technical Publishers, pp.170-182.
15. Namgung U K, Valcourt E, Routtenberg A (1995). Long-term potentiation in vivo in the intact mouse hippocampus. *Brain Research* **689**, 85-92.
16. Sofikitis N, Miyagama I, Dimitriadis D, *et al.* (1995). Effects of smoking on testicular function semen quality and sperm fertilizing capacity. *J Urol* **154**, 1030-1034.
17. Chen J, Zhang S, Zuo P, *et al.* (1997). Memory-related changes of nitric oxide synthase activity and nitrite level in rat brain. *Neuroreport* **7**, 1771-1774.
18. Luine V, Villegas M, Martinez C, *et al.* (1994). Repeated stress causes reversible impairments on spatial memory performance. *Brain Res* **639**, 167-170.
19. Behl C (1999). Vitamin E and other antioxidants in Neuroprotection. *Int J Vitam Nutr Res* **69**, 213-219.
20. Kaneko T, Baba N (1999). Protective effect of flavonoids on endothelial cells against linoleic acid hydroperoxide induced toxicity. *Biosci Biotechnol Biochem* **63**, 323-328.
21. Xie Z, Bhagavatula R (1995). Impairment of long-term potentiation in rats fed with vitamin E-deficient diet. *Brain Res* **681**, 193-196.

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