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Effects of subchronic methylmercury exposure on response to acute hypoxia in mice: role of HIF-1α

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INTRODUCTION

Methylmercury (MeHg) is a neurotoxic environmental pollutant. Hypoxic response is an adaptive response of organisms to cope with hypoxia, and HIF-1α is a key nuclear transcription factor in response to hypoxia. Acute MeHg exposure can decrease HIF-1α protein in vitro and in vivo, but the impact of subchronic MeHg exposure on hypoxic response has not yet been elucidated.

Theoretical Mechanism Framework of Hypoxia Preconditioning

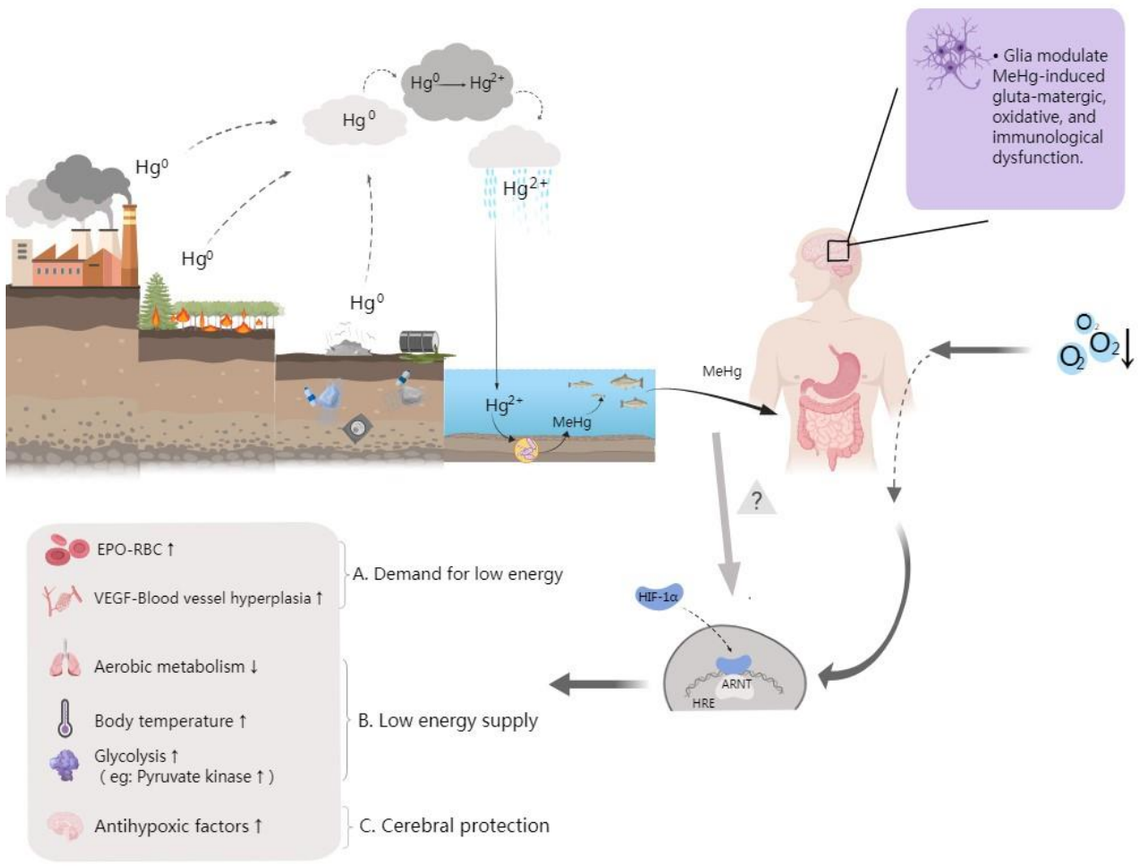

Figure 1. The accumulation of methylmercury in nature and its entry into human body. The accumulation of methylmercury in nature and its entry into human body → Hypoxic exposure → Activates specific oxygen receptors in a variety of organs and tissues → Regulate HIF synthesis → Initiate a series of protection procedures.

METHOD

Healthy ICR mice were intraperitoneally infected with 0.25, 0.5, and 1.0 mg/kg methylmercury, treated with hypoxia in a 250 ml hypoxia bottle for 15 min, and then recorded the time of death and collected blood, heart tissue, and brain tissue for detection by Western blotting. Analyzing the contents of lactic acid (LA), pyruvate kinase (PK), malondialdehyde (MDA), glutathione (GSH), and Hypoxia-inducible factor-1α (HIF-1α).

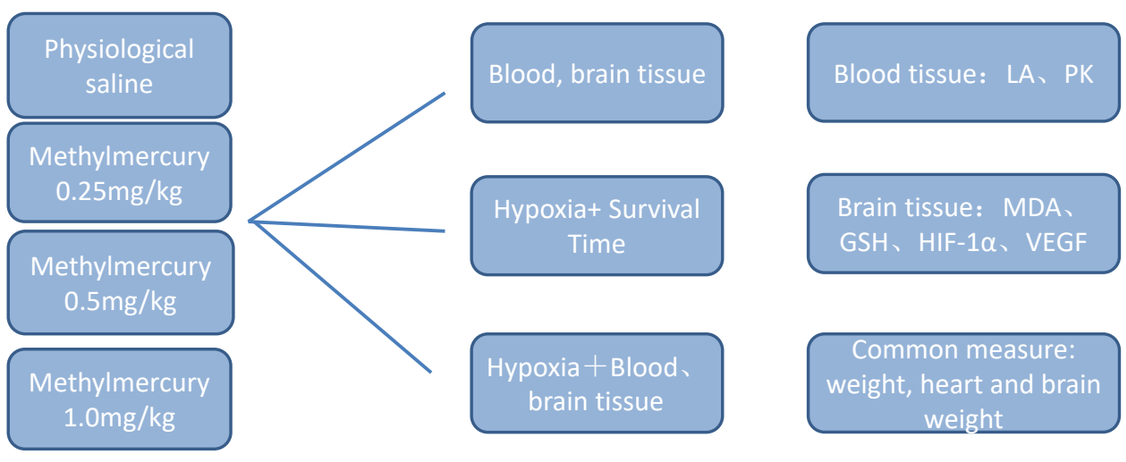

Figure 2. Experimental grouping and determination of biochemical indexes

RESULTS & DISCUSSION

Km survival curve of mice under atmospheric pressure and closed hypoxia

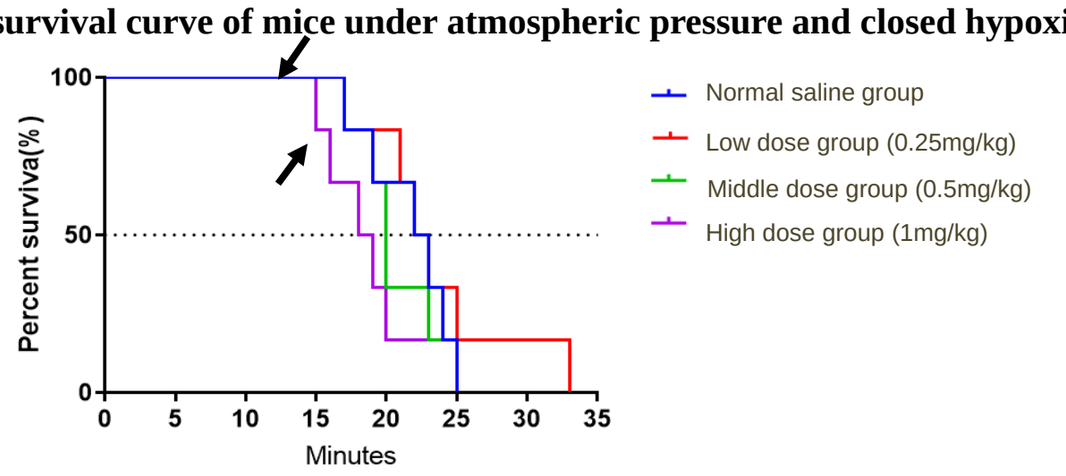

Figure 3. According to the mouse survival curve, after methylmercury exposure, the hypoxic survival time of mice in the medium and high dose groups was significantly shorter than that of the normal saline group. The survival rates of mice in the medium- and high-dose groups were 33.3% and 16.7%, which were significantly lower than those in the normal saline group.

Effect of methylmercury on serum LA and PK in mice

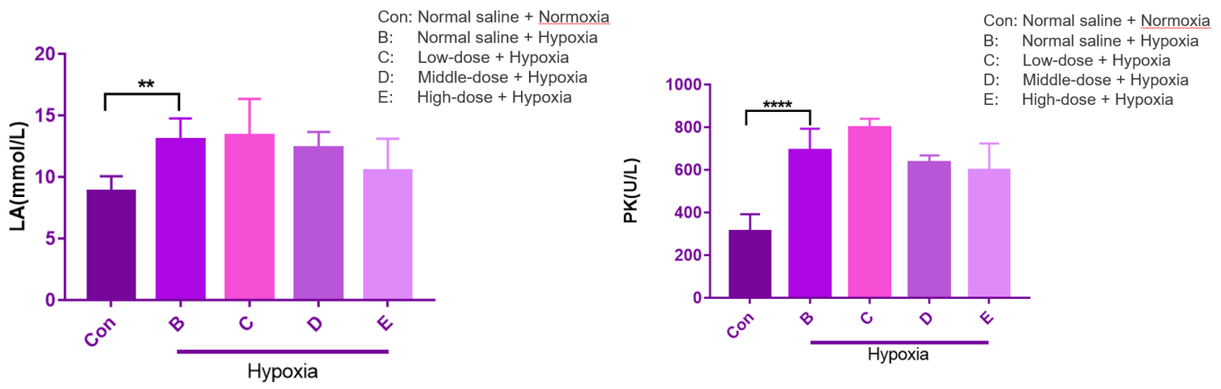

Figure 4. The detection results of lactic acid and pyruvate kinase showed that the effect of subchronic MeHg exposure on the hypoxic adaptation ability of mice was promoted by low doses and inhibited by medium and high doses.

Effects of methylmercury on oxidative and antioxidant indexes of mouse brain tissue

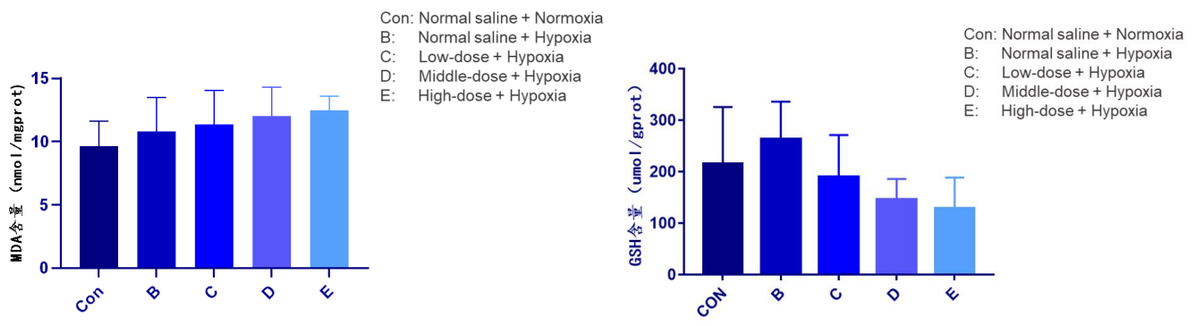

Figure 5. Malondialdehyde content increased and glutathione content decreased with MeHg treatment in a dose-dependent manner.It showed that the degree of cell damage increased and the antioxidant capacity decreased.

CONCLUSION

Subchronic exposure to methylmercury can aggravate the oxidative damage caused by hypoxia and inhibit the hypoxic response in mice by affecting the expression of HIF-1α. However, cute hypoxia will overexpress HIF-1α protein in the brain tissue of mice with subchronic methylmercury poisoning.

FUTURE WORK

We will further explore the impact and mechanisms of heavy metal toxicity on the adaptability of neural cells to hypoxia, optimize our experimental protocols, and further validate through cellular and animal experiments.

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