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Research Report

Effects of low-level organic selenium on lead-induced alterations in neural cell adhesion molecules

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ABSTRACT

Low-level lead (Pb) exposure has been reported to impair the formation and consolidation of learning and memory by inhibiting the expression of neural cell adhesion molecules (NCAMs) and altering the temporal profile of its polysialylation state. In this study, we investigated whether administration of low-level organic selenium (selenomethionine, Se) at different time points could affect Pb-induced changes of NCAMs in female Wistar rats. Here we reported that the exposure of Se (60 μg/kg body weight/day) at different time points significantly alleviated Pb-induced reductions in the mRNA and protein levels of NCAMs, and increases in the mRNA levels of two polysialyltransferases (*St8sia II*, *Stx*; *St8sia IV*, *Pst*) as well as the sialyltransferase activity ($p<0.05$). The concentrations of Pb in blood and hippocampi of Wistar rats treated with the combination of Se and Pb were significantly lower than those treated with Pb alone ($p<0.05$). Our results suggest that low-level organic Se can not only prevent but also reverse Pb-induced alterations in the expression and polysialylated state of NCAMs as well as the concentration of Pb in rat blood and hippocampus.

1. Introduction

Neural cell adhesion molecules (NCAMs) are involved in morphogenesis, plasticity and regeneration of the nervous system (Minana et al., 2000; Kiss et al., 2001; Ditlevsen et al., 2003). Developmental low-level Pb exposure has been reported to alter the expression of NCAMs and its polysialylation state (i.e. the expression of ST8SiaIV/PST and ST8SiaII/STX, and the activity of sialyltransferase) and therefore may induce the neurotoxicity and the impairment of learning and memory (Fox et al., 1995; Murphy and Regan, 1999; Hu et al., 2008).

Selenium (Se) has been shown to protect against lead-induced neurotoxicity by regulating the uptake and excretion of Pb (Flora et al., 1983), preventing damage from oxygen free radicals (Li et al., 2013; Liu et al., 2013), enhancing the DNA, RNA, protein content, and several enzyme activities such as succinic dehydrogenase, acetylcholinesterase, Na^+/K^+ ATPase,

Abbreviations: Pb, lead; Se, Selenium; NCAMs, neural cell adhesion molecules; PST, ST8Sia IV; STX, ST8Sia II; CNS, central nervous system; PVDF, polyvinylidene difluoride; SPF, specific pathogen free; PSA, α-2,8-polysialic acid

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and monoamine oxidase (Nehru and Iyer, 1994; Nehru and Dua, 1997; Nehru et al., 1997). However, there is no report of how the treatments of Se at different time points affect the changes of NCAMs induced by Pb, especially the effect of administration of Se after Pb exposure.

There are two kinds of Se: organic and inorganic Se. Organic Se (e.g. SeMet) is easier to get to and much slower to disappear from the central nervous system (CNS) compared to inorganic Se (e.g. sodium selenite) (Gronbaek and Thorlacius-Ussing, 1992). It seems that organic Se may be a much safer and more effective supplement for CNS compared to inorganic Se. Se at low levels is recognized as an essential dietary element for mammalian and for different classes of living organisms, but it is toxic at higher levels (Nogueira and Rocha, 2011). Thus, in this study, we try to investigate the effects of low-level organic Se on the alterations in NCAMs induced by Pb. It was found that low-level organic Se not only prevented but also reversed Pb-induced changes of NCAMs and its polysialylation state in Wistar rats.

2. Results

2.1. *Effects of Pb and Se on the expression of NCAMs in rat hippocampus*

Three isoforms of NCAMs (NCAM-180, -140 and -120) in the hippocampal homogenates after the removal of polysialic acid by neuraminidase were measured by Western blot assay (Fig. 1A). The Pb exposure alone significantly reduced the expression of NCAM-180, -140 and -120 ($p<0.05$), compared to the control group, while the Se exposure alone significantly increased the expression of NCAM-140 and NCAM-120 ($p<0.05$). The pre-, co- or post-treatment of Se significantly increased the expression of all three isoforms of NCAM ($p<0.05$), compared to the group exposed to Pb alone (Fig. 1B–D).

2.2. *Effects of Pb and Se on the mRNA levels of Ncam, Pst and Stx in rat hippocampus*

The results of fluorescent real-time quantitative RT-PCR showed that the exposure of Pb alone significantly reduced the mRNA levels of *Ncam*, while increased the mRNA levels of *Pst* and *Stx* compared to the control group ($p<0.05$), whereas the exposure of Se alone did not significantly affect their expressions ($p>0.05$). The pre-, co- or post-treatment of Se significantly increased the mRNA levels of *Ncam*; while the pre- or co-treatment of Se significantly reduced the mRNA levels of *Pst* and *Stx* ($p<0.05$) compared to the group exposed to Pb alone (Table 2).

2.3. *Effects of Pb and Se on the activity of sialyltransferase in rat hippocampus*

The results showed that Pb exposure alone significantly increased the activity of sialyltransferase in rat hippocampus by 45.7% ($p<0.05$) compared to the control group, whereas Se exposure alone did not affect its activity significantly ($p>0.05$). The pre- or co-treatment of Se significantly reduced the activity of sialyltransferase by 11.1% or 15.4% compared to the group exposed to Pb alone ($p<0.05$), however, the post-treatment of Se could not reduce the activity of sialyltransferase induced by the exposure of Pb ($p>0.05$) (Fig. 2).

2.4. *Concentrations of Pb and Se in the blood and hippocampi of rats*

Compared with the control group, blood and hippocampal Pb increased significantly in the group of rats treated with Pb ($p<0.05$), while blood and hippocampal Se increased significantly in the group treated with Se ($p<0.05$). The pre- or co-treatment of Se significantly reduced the concentration of Pb in blood and hippocampus by 31.2% and 33.1% ($p<0.05$), and 32.7% and 36.8% ($p<0.05$), respectively, compared to the

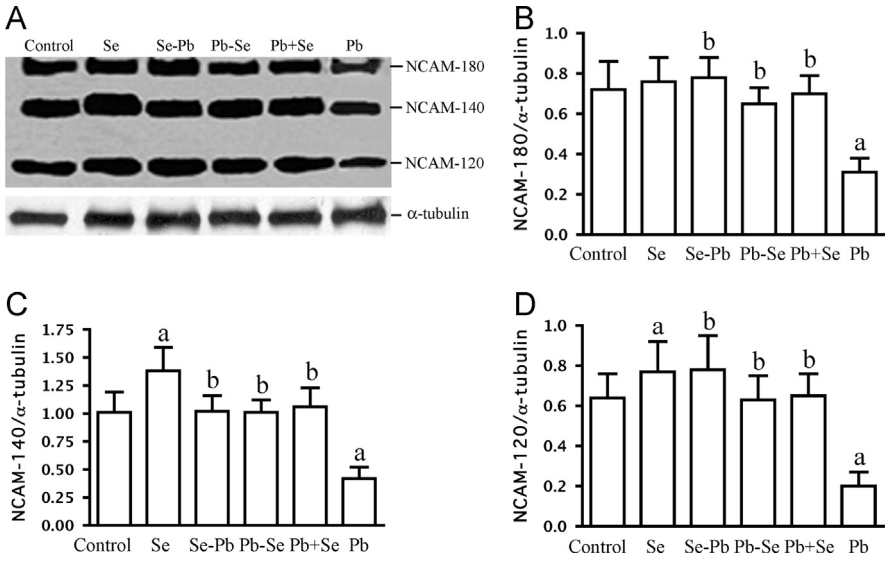

Fig. 1 – Effects of Pb and Se on the expression of three isoforms of NCAM in rat hippocampus. The expression of NCAM isoforms in rat hippocampus following different exposures was measured by Western blot assay (A–D). The α-tubulin was used as a loading control. The data, expressed as NCAMs/α-tubulin, represent the means ± S.D. of 8 samples in each group; [a]$p<0.05$, versus control; [b]$p<0.05$, versus the group treated with Pb alone (one-way ANOVA and Bonferroni test).