Title: Lead exposure inhibits expression of SV2C through NRSF

Authors: Meiyuan Yang, Yaobin Li, Lei Hu, Dan Luo, Yi Zhang, Xue Xiao, Guilin Li, Lixia Zhang, Gaochun Zhu

PII: S0300-483X(18)30031-3
DOI: https://doi.org/10.1016/j.tox.2018.02.009
Reference: TOX 52011

To appear in: *Toxicology*

Received date: 7-12-2017
Revised date: 11-2-2018
Accepted date: 27-2-2018

Please cite this article as: Yang, Meiyuan, Li, Yaobin, Hu, Lei, Luo, Dan, Zhang, Yi, Xiao, Xue, Li, Guilin, Zhang, Lixia, Zhu, Gaochun, Lead exposure inhibits expression of SV2C through NRSF.Toxicology https://doi.org/10.1016/j.tox.2018.02.009

Lead exposure inhibits expression of SV2C through NRSF

Meiyuan Yang[a], Yaobin Li[a], Lei Hu[a], Dan Luo[a], Yi Zhang[b], Xue Xiao[c], Guilin Li[d], Lixia Zhang[e], Gaochun Zhu[a*]

[a] Department of Anatomy, School of Medicine, Nanchang University, BaYi Road 461, Nanchang 330006, PR China

[b] Queen Marry College, School of Medicine, Nanchang University, BaYi Road 461, Nanchang 330006, PR China

[c] Anesthesiology of the Second Clinical Medical College, Nanchang University, BaYi Road 461, Nanchang 330006, PR China

[d] Department of Physiology, School of Basic Medicine, Nanchang University, BaYi Road 461, Nanchang 330006, PR China

[e] Maternity and Child Care Hospital in Jiaxing, Zhejiang 314051, PR China

[*] Corresponding author
E-mail: zhugaochun@ncu.edu.cn (G.Zhu).

A B S T R A C T

Lead (Pb) exposure has been shown to affect presynaptic neurotransmitter release in the animal and cell models. The mechanism by which Pb exposure impairs neurotransmitter release remains unknown. In this study, we aimed to investigate the effect of Pb exposure on synaptic vesicle protein 2C (SV2C) and its molecular mechanism. SV2C promoter region contains a neuron-restrictive silencer element (NRSE) binding motif. Neuron-restrictive silencer factor (NRSF) is a transcription repressor that regulates gene expression by binding to NRSE. We also observed whether Pb exposure regulates the transcriptional level of SV2C by influencing the expression of NRSF. Pregnant female rats were exposed to 0, 0.5 and 2.0 g/L lead acetate (PbAc) via drinking water from the first day of gestation until postnatal week 3. Neuro-2a (N2a) cells were divided into 3 groups: 0 μM (control group), 1 μM and 100 μM PbAc. Our data revealed that the ability of learning and memory in Pb-exposed rats were decreased, Pb exposure decreased SV2C expression and increased NRSF expression in the rat hippocampus and N2a cell. Silencing NRSF can reverse the down-regulation of Pb exposure on SV2C. These results indicate that Pb exposure can inhibit the transcription level of SV2C by up regulating the expression of NRSF. Decreased expression of SV2C can affect neurotransmitter release and synaptic transmission, which affect synaptic plasticity and then result in impairment of learning and memory.

Key words: lead; neuron-restrictive silencer element; neuron-restrictive silencer factor; synaptic vesicle protein 2C

1. Introduction

Lead (Pb) intoxication in children is found to affect learning and memorizing, with devastating effects on cognitive function and intellectual development (Hon et al. 2017; Pan et al. 2017). It is well known that the developing brain is highly susceptible to Pb exposure (Sobin et al. 2017; Wagner et al. 2017). Whole blood Pb concentrations, even those below 10 μg/dL, are resulted in a greater rate of intelligence quotient (IQ) loss than at higher exposures (Lanphear et al. 2005). More recently, studies showed that the dose-response of Pb on IQ loss is non-linear, as in fact any concentration of Pb in the organism results in the impairment of biochemical processes in the