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Research Report

Effects of vitamin E on lead-induced impairments in hippocampal synaptic plasticity

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ABSTRACT

Lead (Pb) exposure during development is associated with impaired cognitive function and long-term potentiation (LTP). Vitamin E (VE) is an antioxidant that could have protective effects against Pb intoxication. In this study, we examined the protective effects of vitamin E against Pb-induced LTP impairments. Forty-six adult male Wistar rats were randomly divided into 6 treatment groups: (1) control; (2) Pb exposure; (3) VE; (4) Pb +VE; (5) Pb exposure followed by VE 2 months after exposure; (6) VE followed by Pb exposure 1 month after treatment. Rats were exposed to Pb through daily consumption of Pb-contaminated distilled water; VE was administered by daily gavage for 3 months. After this period, the population spike (PS) amplitudes and the slopes of excitatory postsynaptic potentials (EPSPs) were measured in the dentate gyrus (DG) area of the hippocampus in adult rats in response to electrical stimulation applied to the perforant pathway in vivo. Blood samples were also collected to evaluate malondialdehyde (MDA) levels, total antioxidant capacity (TAC), and total oxidant status (TOS). Biochemical analyses demonstrated significant increases in plasma MDA and TOS levels in the Pb-exposed group compared to the control group. VE–protected groups revealed significant increases in TAC levels. Our results demonstrate that Pb decreased EPSP slopes and PS amplitudes compared to the control group, whereas VE increased these parameters compared to the control group. Co-administration of VE with Pb exposure inhibited Pb-induced effects. These findings suggest that VE via its antioxidant activity reverses Pb-induced impairments of synaptic plasticity in the DG.

1. Introduction

Lead (Pb) is a toxic environmental agent with debilitating effects on human health (Kumawat et al., 2014). It is a heavy metal, environmental pollutant, and toxicant that causes a wide variety of long-lasting adverse effects in adults and children, particularly in the developing nervous system (Garber and Heiman, 2002; Xu and Rajanna, 2006; White et al., 2007a, 2007b; Prasanthi et al., 2010; Basha et al., 2012; Fan et al., 2013). Pb was modestly used in ancient medicines

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and cosmetics. Today, it has many industrial uses (e.g., in building materials and paints). One of the main sources of Pb exposure is gasoline smoke, especially in cities with heavy traffic (Mudipalli, 2007). Human exposure to Pb occurs via food, water, air, and soil. Pb exposure from food and water can include the use of Pb-containing ceramic dishware, metal plumbing, and food cans that contain Pb solder (White et al., 2007a, 2007b). This accounts for most of the cases of heavy metal poisoning, as Pb has been shown to interfere with nervous system development, resulting in permanent learning and behavioral disorders (Chen et al., 2007; Yuan et al., 2006; Kumawat et al., 2014). Both acute and chronic 0.2% Pb acetate exposure during development impairs the induction, magnitude, and duration of long-term potentiation (LTP) in the CA1 and dentate gyrus (DG) areas of the rat hippocampus (Chen et al., 2007; Gilbert et al., 1999; Wu et al., 2011). LTP is an electrophysiological model of activity-dependent plasticity that embodies the cellular components of information storage at the synaptic level. LTP is widely accepted as a primary mechanism of memory (Bliss and Collingridge, 1993; McNaughton, 1993; Gilbert and Lasley, 2007).

Vitamin E is a fat-soluble vitamin with numerous biological functions (Flora, 2002; Flora et al., 2012). Vitamin E represents a generic term for all tocopherols and their derivatives, including naturally occurring and biologically active stereoisomeric compounds of α-tocopherol (Traber and Packer, 1995; Papas, 1998). It is the most effective chain breaking lipid soluble antioxidant in biological membranes, and protects cellular structures against damage from oxygen free radicals and reactive products of lipid peroxidation (Liebler, 1993; Zingg, 2007; El-Shenawy et al., 2015). The antioxidant activity of vitamin E has persuaded many groups to study its ability to prevent chronic diseases, especially those believed to have an oxidative stress component, such as cardiovascular diseases, atherosclerosis, and cancer (Stampfer et al., 1993; Rimm et al., 1993; Brigelius-Flohe and Traber, 1999). Vitamin E has also been shown to play a role in immune function, DNA repair, and other metabolic processes (Packer et al., 2001; El-Shenawy et al., 2015).

Previous findings suggest that oxidative stress may contribute to learning and memory deficits following oxidative stress-induced brain damage in animal models (Fukui et al., 2001; Tuzcu and Baydas 2006). Exposure to Pb has been reported to enhance oxidative stress and cause neurotoxicity (Barkur and Bairy, 2015). Vitamin E may prevent oxidative damage and cognitive deficits in the rat brain that are due to oxidative stress (Takatsu et al., 2009). Vitamin E also can prevent the oxidative damage and cognitive deficits caused by oxidative stress in the brains of aging rats (Fukui et al., 2005; Owada et al., 2008). In particular, vitamin E supplementation protects cultured hippocampal neurons against the neurotoxic effects of oxidative damage (Pazdro and Burgess, 2012; Deng et al., 2015). In recent years, vitamin E supplements have become popular as antioxidants (Bjelakovi et al., 2014). Simultaneous administration of vitamin E and Pb was effective in preventing most Pb toxic effects in experimental models (An and Zhang, 2014; Deng et al., 2015). Therefore, vitamin E may be recommended for protection against Pb intoxication (Patra et al., 2001; Al-Attar 2011).

The aim of this study was to evaluate whether vitamin E supplementation can prevent Pb-induced LTP impairments in the rat hippocampus. To test this, we used long-term administration of Pb and vitamin E and in vivo field potential recording methods to analyze the hippocampal synaptic plasticity in the rat DG. The DG is a region of the hippocampus thought to contribute to learning and memory mechanisms via the activity of dentate granule cells (Jedlicka et al., 2011). This area is one of the few sites in the adult rodent brain at which synaptic plasticity can be induced (Jedlicka et al., 2015).

2. Results

2.1. Effects of Pb, vitamin E and Pb+vitamin E on body weight

Body weight in all groups was monitored throughout the period of the study. Primary weight, and final weight are shown in following table (Table 1). Body weights at the beginning of the treatment period were not significantly different among the six groups. Analysis of the body weight over the three months demonstrated a significant difference between the groups. Rats in vitamin E and Pb groups were not significantly different compared to the control group. In contrast, post-hoc analysis demonstrated that rats in vitamin E gained higher body weight compared with the Pb group.

2.2. Effect of lead and vitamin E on TAC, TOS, and MDA

The mean concentration (±SEM) of TAC in the plasma of the Pb group (0.06650±0.0031 mmol/L) was significantly lower than the control (0.2127±0.0110 mmol/L) [F (5,40)=32.09, $P<0.001$] and vitamin E treatment (0.3297±0.0073 mmol/L) [F (5,40)=39.57, $P<0.001$] groups. Moreover, MDA levels in the plasma of the Pb group (0.1057±0.0057 nmol/mL) were significantly higher than the control group (0.05875±0.0217 nmol/mL) [F (5,40)=11.25, $P<0.01$]) and the vitamin E treatment group (0.0147±0.0013 nmol/mL) [F (5,40)=27.17, $P<0.001$]. In addition, the TOS plasma concentration was significantly higher in the Pb group (4.705±0.1433 μmol/L) when compared to the control group (1.375±0.0542 μmol/L) [F (5,40)=42.36, $P<0.001$] and the vitamin E treatment group

Table 1 – Effects of Pb, vitamin E and Pb+vitamin E on body weight of rats. Data are mean±SEM.

Groups	Control	Pb	Vit E	Pb+Vit E	Pb then Vit E	Vit E then Pb
Body weight (g) (Primary)	186±22.3	192±25.6	187±19.2	194±23.8	185±27.1	196±18.2
Body weight (g) (Last)	352±33.6	303±29.4	371±32.8*	353±35.8	329±28.4	349±32.9

* $P<0.05$ compared to Pb group. The mean difference is significant at the 0.05 level.