



Zinc supplement reverses short-term memory deficit in sodium benzoate-induced neurotoxicity in male Wistar rats by enhancing anti-oxidative capacity via Nrf 2 up-regulation

O.O. Akintoye^a  , A.J. Ajibare^a, M.A. Folawiyo^a, H.O. Jimoh-Abdulghaffaar^b, A. Asuku^d, G.A. Owolabi^a, K.T. Babalola^c

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Abstract

Sodium benzoate (SB) is a commonly-used food preservative, with a controversial report to its neurological benefit and toxicity. Zinc (Zn) is a trace element that plays a crucial role in memory, inflammation and oxidative stress. This study was to investigate the effect of SB on rat cognition and memory and the possible modulatory effect of Zn supplement. Twenty four male Wistar rats were divided into four groups of six animals each. Animals in groups 1–4 were treated with normal saline 1 ml/kg, SB 200 mg/kg, zinc sulphate 10 ml/kg and SB 200 mg/kg + zinc sulphate 10 ml/kg/day daily respectively for three weeks. After treatment, the animals were subjected to different behavioural tests, and then sacrificed. Their blood samples were collected for catalase(CAT), superoxide dismutase(SOD) and interleukin-1B(IL-1B) assay. Brain samples were also collected for nuclear factor-erythroid-related factor 2(Nrf2), and acetylcholinesterase (AChE) mRNA gene expression. The serum levels of CAT and SOD were ($p < 0.0001$; $p < 0.0001$) reduced in the SB only-treated group compared to the other groups. Nrf2 gene expression was totally shut down in the SB only-treated group but, up-regulated in the Zn-treated groups ($p < 0.0001$). The serum level of IL-1B was higher in the SB only-treated group compared to the other groups. SB-treated group spent longer time in the close arm ($p = <0.0001$), shorter time in the open arm ($p = <0.0001$) and had higher anxiety index ($p = 0.0045$) than the Zn-treated groups. Conclusively, Zinc improves memory deficit, has anxiolytic, anti-oxidant and anti-inflammatory properties.

Introduction

The brain plays a central role in bodily functions including but, not limited to memory, speech, thought and movement. However, exposure of the nervous system to neurotoxicants, either naturally or artificially, can initiate or potentiate neural pathology, leading to significant alterations in the normal functioning of the nervous system [1] presenting as cognition deficits, memory loss, and various locomotion disorders. Various reports as suggested the role of side effect of chemotherapy, drug therapies, and vulnerability to heavy metals such as mercury and lead, certain foods preservative substances, pesticides, industrial products, and pharmaceutical products [1] in the pathogenesis of various neural disorders. An example of industrial products commonly used as food preservative due to its high safety profile is sodium benzoate (SB). Although some studies have shown that it is useful in the treatment of conditions such as depression, pain, schizophrenia, autism spectrum disorders, and neuro-degenerative diseases [2], other studies reveal that it impairs memory and motor co-ordination [3], generates oxidative stress, increases anxiety-like, depressive-like and antisocial behaviors [2] and causes tissue damage which is evident by an increase in inflammatory cytokines (TNF- α , IL-6, IL-1b) [4]. Accumulating evidence also suggest that essential mineral elements like Selenium and Zinc can restore tissue damage caused by xenobiotics [5]. Zinc (Zn) is an essential trace mineral required in the human body for numerous biological processes, including cellular apoptosis, immune function, brain maturation and development, taste and smell regulation, skin and mucosal integrity, and metabolic function [6]. The human body contains about two grams of Zn, mostly in the testis, muscle, liver, and brain tissues. In the brain, the highest concentration of Zn is found in the hippocampus, amygdala, cerebral cortex, thalamus, and olfactory cortex [7]. Recent studies have suggested that released Zn²⁺ plays crucial roles in information processing, synaptic plasticity, learning, and memory. Indeed, Zn²⁺ has been shown to be essential in the hippocampus for the induction of long-term potentiation, a form of synaptic information storage that has become a well-known paradigm for the mechanisms underlying memory formation [8]. However, research reveals that Zn plays substantial roles in suppression of inflammation, reduction of oxidative stress and correct functioning of lipid and glucose metabolism [9], especially in the brain. Nuclear factor erythroid 2–related factor 2 (Nrf-2) which has been established scientifically to place a pivot role in redox balance mechanism was investigated to understudy its possible involvement in the pathophysiology of SB induced neurotoxicity and the protective role of Zinc supplement.

Section snippets

Chemicals

Sodium benzoate salt was purchased from May and Baker Ltd. Dagenham, England. Other chemicals were sourced from Sigma Chemical Company, St Louis, USA....

Animals

Twenty-four mature, male, Wistar rats weighing between 160 &180 g were procured from Ekiti State University, Ado –Ekiti, Ekiti-State, Nigeria. The rats were housed and kept in plastic cages with good aeration in the animal house of the Department of Physiology, Ekiti State University, Ado-Ekiti, Ekiti-State, Nigeria, under standard light, feeding, ...

Zinc supplement ameliorates anxiety-like effect of SB neurobehavioral toxicity in male Wistar rat

As shown in Table 1, rats in SB group spent significantly longer time in the close arm compared to the time spent by other animals in the other groups ($p = <0.0001$; <0.0001 ; <0.0001 respectively), and relatively lower time in the open arm during the test period. Even though, our results showed no significant statistical difference between the number of open and close arm entries among the rats in SB and SB+Zn groups. The SB-treated animals demonstrated a statistically high anxiety index which...

Discussion

Modern lifestyle which is associated with processed food and exposure to a wide range of chemically prepared cosmetic, in which sodium benzoate (SB) sits at the center, plays an important role in the disruption of the body's normal redox balance. Causing increased reactive oxygen species (ROS) generation and reduction in anti-oxidants generation leading to induction of oxidative stress [15]. Anti-oxidants (enzymatic or non-enzymatic) are substances that prevent the formation of free radicals...

Conclusion

This study showed that Zn supplement caused a remarkable improvement in memory reversed anxiety-like behaviour in SB induced neurotoxicity by attenuating the redox imbalance via increased Nrf2 mRNA gene expression....

CRedit authorship contribution statement

O.O Akintoye and A.J. Ajibare are responsible for the conceptualization, design of the work, and the experiment, while all other authors (M.A Folawiyo, H.O Jimoh-Abdulhaffaar, A. Asuku, G.A Owolabi, K.T. Babalola) carried out the data collection, analysis and interpretation. The writing of the research was done by all authors.

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Ethical approval

Ethical approval was obtained from the Ekiti State University (Reference number - EKSU/P100/2022/06/016) and the date of approval being 16th of June, 2022....

Declaration of competing interest

The authors report no conflict of interest....

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