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The Role of HIF-1 in manganese-induced premature aging and nerve damage in C. elegans

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INTRODUCTION & AIM

Chronic manganese exposure has been associated with multiple health consequences,including neurological,behavioral,and cognitive impairments.However,the precise mechanism of manganese toxicity remains unclear.The nematode Caenorhabditis elegans,a model organism in environmental toxicology,offers an excellent platform to investigate the role of HIF-1 in manganese-induced toxicity.

HIF-1 is a transcription factor that becomes activated under hypoxic conditions and regulates genes related to cell survival,energy metabolism,and angiogenesis.In this study,we aimed to explore the involvement of HIF-1 in manganese-induced toxicity and its potential mechanism.

METHOD

We used wild-type Caenorhabditis elegans (N2), HIF-1 mutant nematodes (ZG31), and DAF-16::GFP nematodes as models for manganese exposure. Low-, medium-, and high-dose groups (10, 20, 50 mM MnCl2) were set up to observe the regulatory effects of manganese exposure on nematode lifespan and behavior. Quantitative real-time PCR (qPCR) was used to measure the expression levels of genes such as Daf-16 and HIF-1 to explore the relationship between HIF-1 and manganese-induced nematode toxicity.

RESULTS & DISCUSSION

Toxic damage of C. elegans induced by exposure to manganese chloride

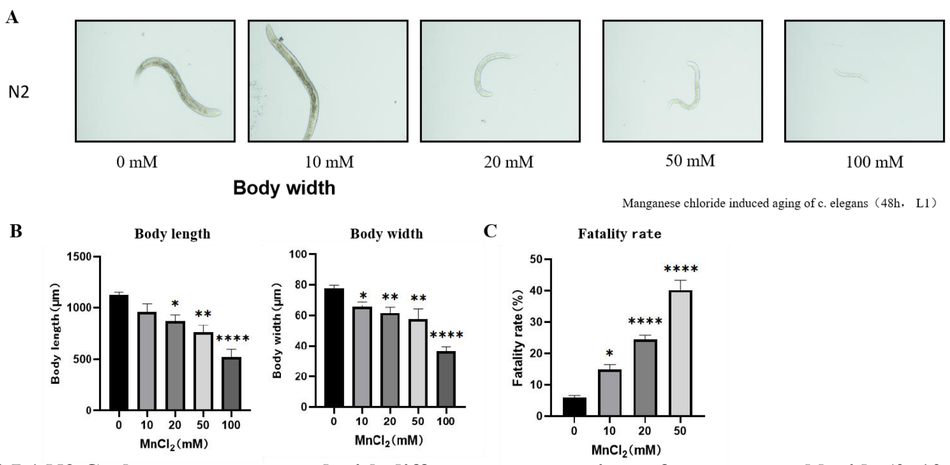

Figure 1.L1 N2 C. elegans were treated with different concentrations of manganese chloride (0, 10, 20, 50, 100 mM) for 48h. (A) morphogram; (B) Length and width; (C) Fatality rate.

Nerve damage in C. elegans induced by exposure to manganese chloride

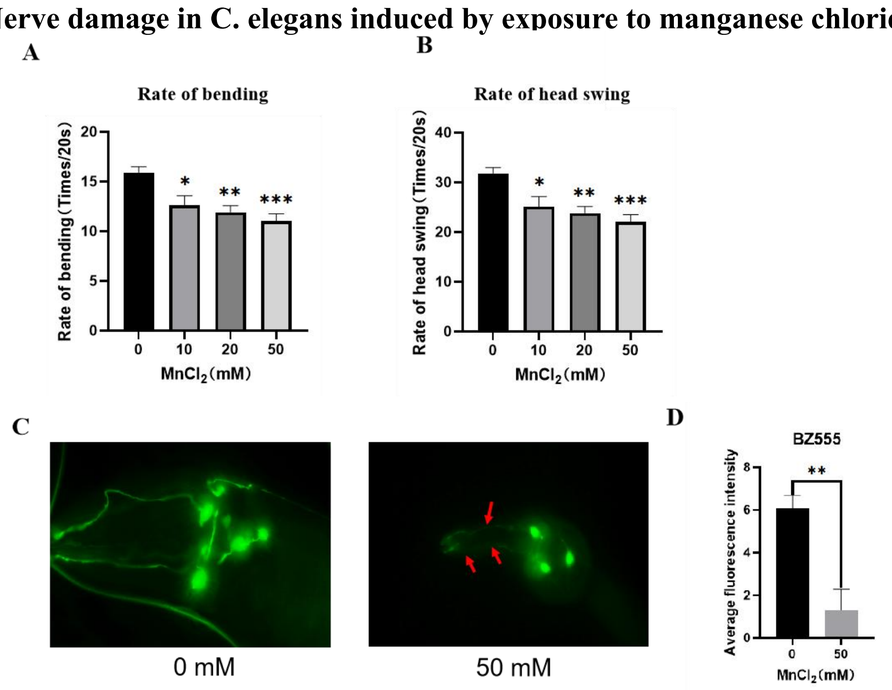

Figure 2.Nerve damage in C. elegans induced by exposure to manganese chloride. (A) Rate of bending; (B)Rate of head swing; (C) Manganese exposure induced BZ555 dopaminergic neuronal morphology; (D) GFP fluorescence intensity in dopaminergic neurons

Senescence of C. elegans induced by exposure to manganese chloride

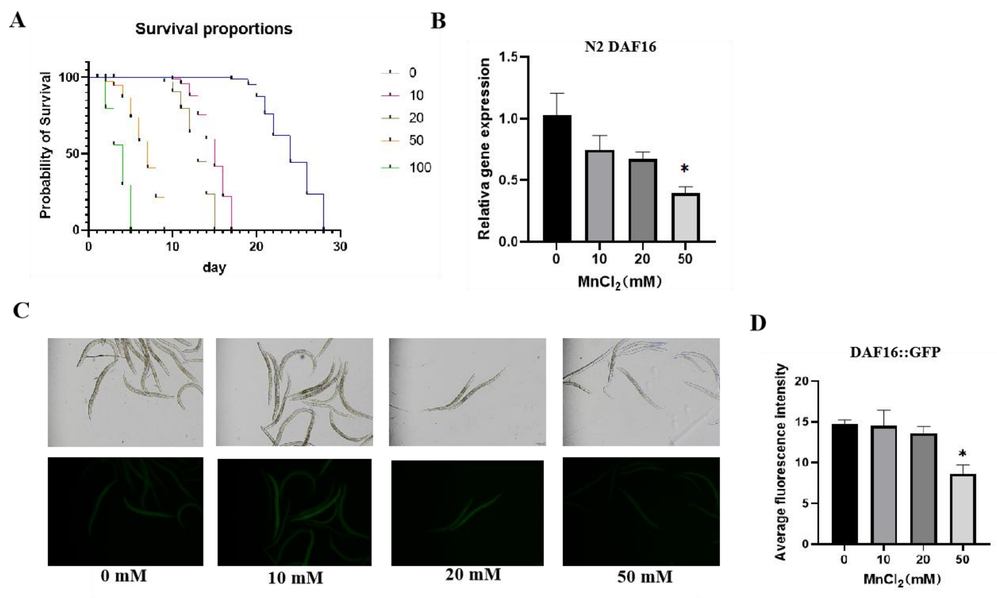

Figure 3.Senescence of C. elegans induced by exposure to manganese chloride. (A) Life test; (B)Anti-aging related gene *DAF16* in C. elegans; (C) Morphology of C. elegans (DAF16: : GFP) under fluorescence microscope; (D) GFP fluorescence intensity of *DAF16*.

Role of *HIF-1* gene in manganese-exposed Caenorhabditis elegans model

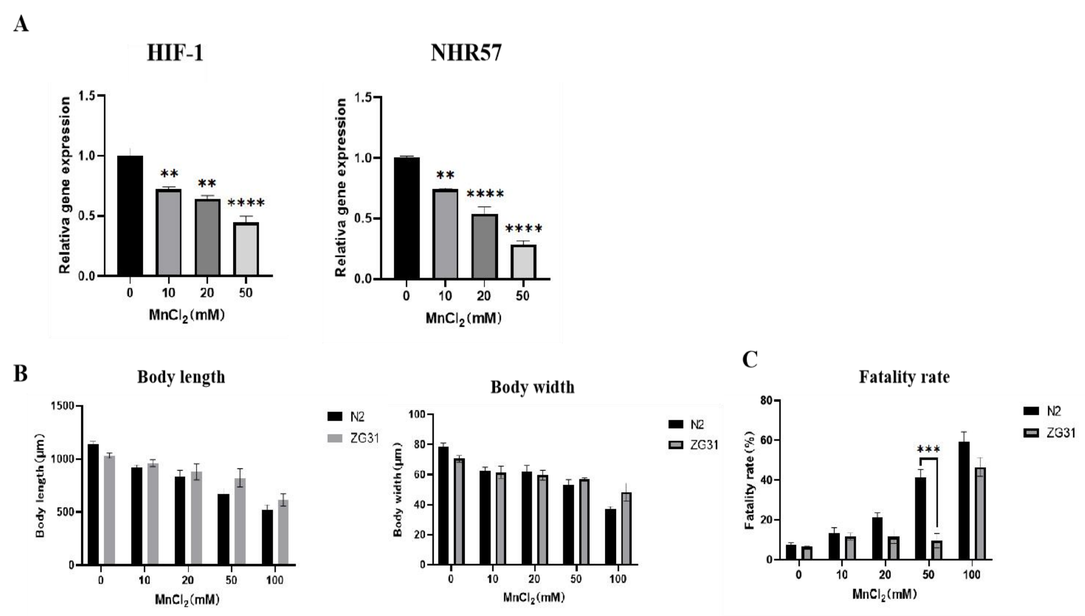

Figure 4.Role of HIF-1 gene in manganese-exposed Caenorhabditis elegans model. (A) *HIF-1* and HIF-1-dependent gene *NHR57* in C. elegans; (B)Body length and width of N2 and HiF1-deficient caenorhabditis elegans (ZG31); (C) Fatality rate.

Manganese exposure significantly inhibited the growth of L1-stage nematodes, leading to increased mortality and decreased bending frequency. As manganese concentration increased, the nematodes' curvature rate decreased. Lifespan experiments demonstrated that manganese exposure shortened the nematodes' lifespan and decreased the expression of the DAF-16 gene, which is associated with lifespan and aging. Notably, manganese exposure downregulated the expression of HIF-1 and its downstream genes. However, knockout of HIF-1 genes alleviated the toxic effects of manganese exposure on the nematodes.

CONCLUSION

Manganese exposure induces premature aging and nerve damage in C. elegans, in which the downregulation of HIF-1 gene may play an important role. The deficiency of HIF-1 gene has a certain tendency to protect the development and mortality of manganese-induced nematodes. The role and regulation of HIF-1 in manganese-induced toxicity need further study.

FUTURE WORK

Next, we will increase the sample size to make the experiment more persuasive. The role and mechanism of HIF-1 gene in manganese-induced aging and nerve injury were investigated in specific nerve cells.

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