



OPEN Maternal suboptimal selenium intake and low-level lead exposure affect offspring's microglial immune profile and its reactivity to a subsequent inflammatory hit

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Micronutrients such as selenium (Se) are essentials since prenatal life to support brain and cognitive development. Se deficiency, which affects up to 1 billion people worldwide, can interact with common adverse environmental challenges including (Pb), exacerbating their toxic effects. Exploiting our recently validated rat model of maternal Se restriction and developmental low Pb exposure, our aims were to investigate: (i) the early consequences of suboptimal Se intake and low-Pb exposure on neuroinflammation in neonates' whole brains; (ii) the potential priming effect of suboptimal Se and low-Pb exposure on offspring's glial reactivity to a further inflammatory hit. To these aims female rats were fed with suboptimal (0.04 mg/kg; Subopt) and optimal (0.15 mg/kg; Opt) Se dietary levels throughout pregnancy and lactation and exposed or not to environmentally relevant Pb dose in drinking water (12.5 µg/mL) since 4 weeks pre-mating. We found an overall higher basal expression of inflammatory markers in neonatal brains, as well as in purified microglia and organotypic hippocampal slice cultures, from the Subopt Se offspring. Subopt/Pb cultures were highly activated than Subopt cultures and showed a higher susceptibility to the inflammatory challenge lipopolysaccharide than cultures from the Opt groups. We demonstrate that even a mild Se deficiency and low-Pb exposure during brain development can influence the neuroinflammatory tone of microglia, exacerbate the toxic effects of Pb and prime microglial reactivity to subsequent inflammatory stimuli. These neuroinflammatory changes may be responsible, at least in part, for adverse neurodevelopmental outcomes.

Abbreviations

Se	Selenium
Opt	Optimal
Subopt	Suboptimal
Pb	Lead
Veh	Vehicle
LPS	Lipopolysaccharide
CNS	Central nervous system
PND	Postnatal day
OHSC	Organotypic hippocampal slice cultures
IL-1β	Interleukin-1β
IL-6	Interleukin-6
IL-10	Interleukin-10
CD11b	Cluster of differentiation 11b
MRC-1	Mannose Receptor C-Type 1

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Low Level Lead Exposure The Clinical Implications Of Current Research

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Table of Contents Low Level Lead Exposure The Clinical Implications Of Current Research

1. Understanding the eBook Low Level Lead Exposure The Clinical Implications Of Current Research
 - The Rise of Digital Reading Low Level Lead Exposure The Clinical Implications Of Current Research
 - Advantages of eBooks Over Traditional Books
2. Identifying Low Level Lead Exposure The Clinical Implications Of Current Research
 - Exploring Different Genres
 - Considering Fiction vs. Non-Fiction
 - Determining Your Reading Goals
3. Choosing the Right eBook Platform
 - Popular eBook Platforms
 - Features to Look for in an Low Level Lead Exposure The Clinical Implications Of Current Research
 - User-Friendly Interface
4. Exploring eBook Recommendations from Low Level Lead Exposure The Clinical Implications Of Current Research
 - Personalized Recommendations
 - Low Level Lead Exposure The Clinical Implications Of Current Research User Reviews and Ratings
 - Low Level Lead Exposure The Clinical Implications Of Current Research and Bestseller Lists

5. Accessing Low Level Lead Exposure The Clinical Implications Of Current Research Free and Paid eBooks
 - Low Level Lead Exposure The Clinical Implications Of Current Research Public Domain eBooks
 - Low Level Lead Exposure The Clinical Implications Of Current Research eBook Subscription Services
 - Low Level Lead Exposure The Clinical Implications Of Current Research Budget-Friendly Options
6. Navigating Low Level Lead Exposure The Clinical Implications Of Current Research eBook Formats
 - ePub, PDF, MOBI, and More
 - Low Level Lead Exposure The Clinical Implications Of Current Research Compatibility with Devices
 - Low Level Lead Exposure The Clinical Implications Of Current Research Enhanced eBook Features
7. Enhancing Your Reading Experience
 - Adjustable Fonts and Text Sizes of Low Level Lead Exposure The Clinical Implications Of Current Research
 - Highlighting and Note-Taking Low Level Lead Exposure The Clinical Implications Of Current Research
 - Interactive Elements Low Level Lead Exposure The Clinical Implications Of Current Research
8. Staying Engaged with Low Level Lead Exposure The Clinical Implications Of Current Research
 - Joining Online Reading Communities
 - Participating in Virtual Book Clubs
 - Following Authors and Publishers Low Level Lead Exposure The Clinical Implications Of Current Research
9. Balancing eBooks and Physical Books Low Level Lead Exposure The Clinical Implications Of Current Research
 - Benefits of a Digital Library
 - Creating a Diverse Reading Collection Low Level Lead Exposure The Clinical Implications Of Current Research
10. Overcoming Reading Challenges
 - Dealing with Digital Eye Strain
 - Minimizing Distractions
 - Managing Screen Time
11. Cultivating a Reading Routine Low Level Lead Exposure The Clinical Implications Of Current Research
 - Setting Reading Goals Low Level Lead Exposure The Clinical Implications Of Current Research
 - Carving Out Dedicated Reading Time
12. Sourcing Reliable Information of Low Level Lead Exposure The Clinical Implications Of Current Research
 - Fact-Checking eBook Content of Low Level Lead Exposure The Clinical Implications Of Current Research
 - Distinguishing Credible Sources
13. Promoting Lifelong Learning

- Utilizing eBooks for Skill Development
- Exploring Educational eBooks

14. Embracing eBook Trends

- Integration of Multimedia Elements
- Interactive and Gamified eBooks

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