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

R. De Simone Latt, M. A. Ajmone-Catt, A. M. Tartaglione, G. Calamandrei & L. Minghetti

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

Selenium See Chort. Optimal Subsectimal Subsect P% Lead Web. Websiele 1.48% Lipopolysaccharide of the St. Central nervous system POSEN. Postmatali day OHISC Organotypic hippocampal slice cultures III.- BEST Interleukin-18 III.-6 Interlegikin-6 IIL-10 Interleukin-10 Cluster of differentiation 11b CHARLES AND MIRKCHI. Mannose Receptor C-Type I

"National Center for Drug Research and Evaluation, Istituto Superiore di Sanità, 00161 Rome, Italy. "Center for Behavioral Sciences and Mental Health, Istituto Superiore di Sanità, 00161 Rome, Italy. "Research Coordination and Support Service, Istituto Superiore di Sanità, 00161 Rome, Italy. "These authors contributed equally: R. De Simone and M. A. Aimone-Cat." email: roberta desimone@iss.it

Low Level Lead Exposure The Clinical Implications Of Current Research

J. Stephen Kroll-Smith, Philip M. Brown, Valerie Gunter

Low Level Lead Exposure The Clinical Implications Of Current Research:

Low Level Lead Exposure Herbert L. Needleman, 1980 **Human Lead Exposure** Herbert L. Needleman, 1991-12-07 Human Lead Exposure consists of scientific reviews and important contributions intended to increase the understanding of the legal social and economic forces that have delayed effective prevention of lead toxicity Chapters discuss the history both ancient and recent of lead explore its neurobiology and toxicology review the sources and routes to humans and examine evidence that indicates that lead may affect humans at levels previously thought to be harmless Neurobiologists epidemiologists public health officials and others concerned about the effects of lead on the human population will find a tremendous amount of useful information in this timely volume **Environmental Health Perspectives** ,1993 **Exposure and Child Development** M. Smith, L. Grant, A.I. Sors, 2012-12-06 This book arises out of a workshop on lead exposure and child development which was held at the University of Edinburgh on 8th 12th September 1986 It was organized jointly by the Commission of the European Communities CEC and the US Environmental Protection Agency EPA in association with the UK Department of the Environment and the Scottish Home and Health Department It brought together most of the internationally recognized groups working on the effects of lead exposure on child development including child psychologists psychiatrists neurologists epidemiologists toxicologists stati sticians and medical practitioners One of the unique features of the meeting was that it included workers from initially separate fields of lead research in particular those undertaking studies in infants and in older children and those carrying out behavioural research in animals as well as those undertaking biochemical studies on mechanisms of lead effect The structure of this book reflects the main elements of the meeting As such it includes three main sections The first consists of two major state of the art reviews and two invited introductory papers The reviews were prepared for the organizers of the conference by two of the Editors The objectives were to assess critically the state of current knowledge in this field and to provide a scientific basis both for policy decisions and for further research The review prepared by Marjorie Smith for the Commission of the European Communities focusses on methodological and design issues and summarizes our present scientific knowledge in this area **Reproductive and Developmental Toxicity of Metals** Tom Clarkson, 2012-12-06 The Permanent Commission and International Association on Occupational Health PCIAOH established in 1969 a Subcommittee on the Toxicology of Metals under the chairmanship of Lars Friberg This committee which later was named the Scientific Committee on the Toxicology of Metals has organized a number of previous meetings that have led to publications in three major areas of metal toxicology a preliminary meeting in Slanchev Bryag Bulgaria in 1971 followed by a meeting in 1972 in Buenos Aires Argentina which produced two reports Dukes and Friberg 1971 Task Group on Metal Accumulation 1973 that discussed the metabolism of metals with special reference to absorption excretion and biological half times The effects and dose response relationships of toxic metals including a discussion of general principles was the second major topic addressed by the Scientific Committee at a meeting in Tokyo in

1974 Nordberg 1976 The philosophy of this conference as well as the previous one in Buenos Aires was based on the concept of a threshold dose for the occurrence of adverse effects In a conference held in Atlanta USA in 1980 the scope of discussion on metal effects was broadened to include the role of metals in carcinogenesis Thus for the first time the Scientific Committee took under consideration the possibility of non threshold relationships Belman and Nordberg 1981 In addition the Scientific Committee on the Toxicology of Metals organized a workshop on metal interactions in Stockholm 1977 Nordberg et Illness and the Environment J. Stephen Kroll-Smith, Philip M. Brown, Valerie Gunter, 2000-08 In 25 papers academics and a few environmental scientists activists discuss profound social policy and competing paradigm issues concerning the contested environment disease link in a postnatural world Include discussion questions Kroll Smith is a professor of sociology at the U of New Orleans Annotation copyrighted by Book News Inc Portland OR **Advances in Behavioral Pharmacology** N. Krasnegor, D. B. Gray, T. Thompson, 2014-06-03 First published in 1986 This monograph is based on a conference sponsored by the Human Learning and Behavior Branch of the National Institute of Child Health and Human Development NIH The meeting that was held at the Xerox Center in Leesburg Virginia in August 1983 brought together a group of leading researchers for the purpose of providing an overview of the emerging field of developmental behavioral pharmacology More specifically as is evidenced by the chapters in this volume the intent was to put the field into historical perspective render a working definition and outline strategies and tactics for conducting behavioral pharmacological The Developmental Neurotoxicity of Lead C. Winder, 2012-12-06 Over the past research in the developing organism two millennia environmental lead levels have risen dramatically Patterson 1980 Most of this increase has occurred since the beginning of the present century Murozami et 01 1969 and taken into perspective a typical individual living in the industrialized world sustains a lead burden 500 times that of his prehistoric ancestors Patterson 1983 Lead is unique in being an environmental pollutant where the levels deemed clinically toxic are less than an order of magnitude from those that are normally encountered in the population The clinical limit for lead exposure 70 JLg Pb tOO ml blood is about three times the normal value in the range 15 30 JLg Pb 100ml blood This small difference is remarkable from the toxicological standpoint The key concept here is control of dis persal The industrial actions of man bring contact with a wide variety of substances some of which are poisonous or dangerous In such cases pro tective measures are taken to keep hazardous exposure to a minimum In the of lead compounds stringent regulations are production and distribution enforced. The exception to this is in the dispersal of lead from vehicle exhausts following purchase from the petrol pump Perhaps man's long standing acquaintance with lead in home and industry is responsible for a complacency which until only recently has been unquestioned Beginning in the late 1960s evidence began to accumulate suggesting that lead at relatively low levels of exposure might be causing negative effects on neurobiological function Scientific Studies in Mental Retardation John Dobbing, A. D. B. Clarke, 1984-06-18 Cost Increases on Four Watershed Projects of the Soil Conservation Service

United States. Congress. Senate. Committee on Environment and Public Works. Subcommittee on Water Resources, 1984 Morbidity and Mortality Weekly Report ,1990-07 **MMWR.** ,1990 Changing Metal Cycles and Human Health J.O. Nriagu, 2012-12-06 of metal interactions with subcellular biochemical systems usually either are metabolites of the system affected porphyrinurias or represent some specific function of a cellular system being impaired proteinurias One typically finds a continuum of symptoms from the subtle or so called no effect bio chemical and physiological indicators of exposure to severe clinical disease and death This continuum is the basis of much of the controversy since many health officials follow the traditional practice of applying the threshold health effect concept in evaluating the problems of environmental exposure to metals The past decade or so however has seen a vast increase in our understanding of the effects of elevated concentrations of toxic metals in local populations and ecosystems At the same time there is a growing awareness that the effects of the metals which occur naturally in the environment must be distinguished from those imposed by the pollutant fraction This point was amply document ed in a recent study of cadmium intake and cadmium in a number of human tissues in Sweden Japan and the United States which showed fairly conclu sively that the background exposure in Japan was about threefold higher than in the other two countries 2 One immediate implication is that any health of fect studies of cadmium in Japan using control groups within that country are liable to underestimate the difference between the exposed and the control groups simply because of the high background intake Lead Contamination United States. Congress. House. Committee on Energy and Commerce. Subcommittee on Health and the Environment, 1988 Neurotoxicology Kenneth Blum, L. Manzo, 1985-07-30 Lead Pollution From Motor Vehicles 1974-1986 P. Farmer, 2003-09-02 This bibliography brings together a wide range of material on the problem of environmental lead pollution from motor vehicles published during 1974 1986 It includes research and surveys from a number of countries and covers the effects of exhaust gas lead on humans including children Neurotoxicity: identifying and controlling poisons of the nervous system: new developments in neuroscience. The Nature and Extent of Lead Poisoning in Children in the United Hazardous Waste Contamination of Water Resources United States. Congress. House. Committee on Public **States** ,1988 Works and Transportation. Subcommittee on Investigations and Oversight, 1984 Environmental and Chemical Toxins and Psychiatric Illness James S. Brown, 2008-08-13 During the past 60 years the number of chemical disasters worldwide from military occupational and environmental sources has risen at an alarming rate The profound controversy surrounding many chemicals makes objective analysis nearly impossible Yet now more than ever with the daily exposure to a wide range of chemicals and the increased threat of chemical terrorism it is critical that we understand the role of chemicals in causing psychiatric illness Unlike related books this remarkable reference is intended specifically for psychiatric applications and is thus the definitive sourcebook for the many professionals called on to respond to these events. This work stands alone as the first on this topic to be written by a psychiatrist and the first to bring together the military occupational and environmental

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