



# Translating Neurobehavioral Toxicity Across Species From Zebrafish to Rats to Humans: Implications for Risk Assessment

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There is a spectrum of approaches to neurotoxicological science from high-throughput in vitro cell-based assays, through a variety of experimental animal models to human epidemiological and clinical studies. Each level of analysis has its own advantages and limitations. Experimental animal models give essential information for neurobehavioral toxicology, providing cause-and-effect information regarding risks of neurobehavioral dysfunction caused by toxicant exposure. Human epidemiological and clinical studies give the closest information to characterizing human risk, but without randomized treatment of subjects to different toxicant doses can only give information about association between toxicant exposure and neurobehavioral impairment. In vitro methods give much needed high throughput for many chemicals and mixtures but cannot provide information about toxicant impacts on behavioral function. Crucial to the utility of experimental animal model studies is cross-species translation. This is vital for both risk assessment and mechanistic determination. Interspecies extrapolation is important to characterize from experimental animal models to humans and between different experimental animal models. This article reviews the literature concerning extrapolation of neurobehavioral toxicology from established rat models to humans and from zebrafish a newer experimental model to rats. The functions covered include locomotor activity, emotion, and cognition and the neurotoxicants covered include pesticides, metals, drugs of abuse, flame retardants and polycyclic aromatic hydrocarbons. With more complete understanding of the strengths and limitations of interspecies translation, we can better use animal models to protect humans from neurobehavioral toxicity.

**Keywords:** human neurotoxicity, rat neurotoxicity, zebrafish neurotoxicity, developmental neurotoxicity, neurobehavioral toxicity

## INTRODUCTION

The field of neurotoxicology has grown steadily over the last 50 years as demonstrated by a search on the term neurotoxicity in PubMed. In 1927 only 1 paper cited used the term neurotoxicity, in 1970 that number was 138, whereas in 2019 the number was 3,756. Much has been accomplished but much remains to be discovered. It is useful at this juncture to look at where the field is and ahead to ask how we can develop the field further.

# Neurobehavioral Toxicity Analysis And Interpretation



**Scientific Group on Methodologies for  
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Workshop**

## **Neurobehavioral Toxicity Analysis And Interpretation:**

**Neurobehavioral Toxicity** Bernard Weiss,1994-06-30 In establishing how certain chemicals can cause behavioural disorders the process of neurotoxicity risk assessment poses significant challenges to every discipline within neuroscience In this volume leaders from industrial academic and government settings share insights on behavioural measurement in neurotoxicity risk assessment and address the critical scientific issues arising from the expanding role of neurobehavioral toxicology in public policy development The authors set out to provide a comprehensive and authoritative review of current methods in the analysis and interpretation of neurobehavioural toxicology Coverage begins with a discussion of criteria for determining neurotoxic potential The next section examines neurobehavioural evaluations in developmental neurotoxicity Subsequent sections focus on activity and observational data and applications of schedule controlled operant behaviour in toxicity testing The contributors address controversies surrounding the suitability and interpretation of procedures designed for neurotoxicological assessments Some case studies are also included *Neurotoxicology* Jean Harry G,Hugh A.

Tilson,1999-07-22 This second edition of Neurotoxicology is valuable for scientists in government and industry who are responsible for public health and for the safe and efficient use of chemicals This integrated approach to neurotoxicology will aid in the understanding of the sites and mechanisms of neurotoxicity stimulate the formulation of testable hypotheses about how chemicals affect the nervous system and help improve the risk assessment process This edition focuses primarily on the neurobiological basis underlying neurotoxic sites and modes of action The contents include molecular biological and in vitro approaches potential cellular and molecular sites involving neuron glia interactions axonal transport ion channels metabolic influences on neurotoxicity role of free radical formation in neurotoxicity interaction between chemicals and trophic factors endocrine disruptors apoptosis in neurotoxicity in vivo brain imaging advances in measuring cognitive function advances in developing quantitative models for neurotoxicology risk assessment **A Comprehensive Guide to Toxicology in**

**Preclinical Drug Development** Ali S. Faqi,2012-10-18 A Comprehensive Guide to Toxicology in Preclinical Drug Development is a resource for toxicologists in industry and regulatory settings as well as directors working in contract resource organizations who need a thorough understanding of the drug development process Incorporating real life case studies and examples the book is a practical guide that outlines day to day activities and experiences in preclinical toxicology This multi contributed reference provides a detailed picture of the complex and highly interrelated activities of preclinical toxicology in both small molecules and biologics The book discusses discovery toxicology and the international guidelines for safety evaluation and presents traditional and nontraditional toxicology models Chapters cover development of vaccines oncology drugs botanic drugs monoclonal antibodies and more as well as study development and personnel the role of imaging in preclinical evaluation and supporting materials for IND applications By incorporating the latest research in this area and featuring practical scenarios this reference is a complete and actionable guide to all aspects of preclinical drug

testing Chapters written by world renowned contributors who are experts in their fields Includes the latest research in preclinical drug testing and international guidelines Covers preclinical toxicology in small molecules and biologics in one single source

**A Comprehensive Guide to Toxicology in Nonclinical Drug Development** Ali S. Faqi, 2024-02-11 Selected for 2025 Doody's Core Titles in Toxicology A Comprehensive Guide to Toxicology in Nonclinical Drug Development Third Edition is a valuable reference providing a complete understanding of all aspects of nonclinical toxicology in pharmaceutical research This updated edition has been expanded and re developed covering a wide range of toxicological issues in small molecules and biologics Topics include ADME in drug discovery pharmacokinetics toxicokinetics formulations and genetic toxicology testing The book has been thoroughly updated throughout to reflect the latest scientific advances and includes new information on antiviral drugs anti diabetic drugs immunotherapy and a discussion on post pandemic drug development challenges and opportunities This is an essential and practical resource for all toxicologists involved in nonclinical testing in industry academic and regulatory settings Provides updated unique content not covered in one comprehensive resource including chapters on stem cells antiviral drugs anti diabetic drugs and immunotherapy Includes the latest international guidelines for nonclinical toxicology in both small and large molecules Incorporates practical examples in order to illustrate day to day activities and expectations associated with working in nonclinical toxicology

**Toxicology in Transition** Gisela H. Degen, Jürg P. Seiler, Philip Bentley, 2012-12-06 The volume contains the main papers presented at the 1994 EUROTOX Congress Basel Switzerland August 21-24 1994 Toxicology has become a less descriptive science because more importance has been placed on the mechanisms underlying toxic effects This is reflected in symposia and workshops devoted to species differences in organ toxicity receptor mediated toxicity and stereochemical effects of xenobiotics Recent progress in the fields of immunotoxicology ecotoxicology and neurotoxicology is highlighted and documented together with the present discussion on harmonized regulatory guidelines

**Experimental Neurotoxicology Methods** Jordi Llorens, Marta Barenys, 2021-07-23 This volume explores the latest methods that seek to address the vital questions being asked in neurotoxicology research The chapters in this book cover a variety of available methods from the molecular level to the organism level and both in vitro and in vivo approaches including alternative model organisms In the Neuromethods series style chapters include the kind of detail and key advice from the specialists needed to get successful results in your laboratory Cutting edge and authoritative Experimental Neurotoxicology Methods is a valuable resource for both young and experienced researchers who are looking for guidance to implement these methods in their laboratories or for understanding the data generated through these techniques

**Environmental Health Perspectives**, 1993 *Comprehensive Toxicology*, 2017-12-01 Comprehensive Toxicology Third Edition Fifteen Volume Set discusses chemical effects on biological systems with a focus on understanding the mechanisms by which chemicals induce adverse health effects Organized by organ system this comprehensive reference work addresses the toxicological effects of chemicals on the immune system the

hematopoietic system cardiovascular system respiratory system hepatic toxicology renal toxicology gastrointestinal toxicology reproductive and endocrine toxicology neuro and behavioral toxicology developmental toxicology and carcinogenesis also including critical sections that cover the general principles of toxicology cellular and molecular toxicology biotransformation and toxicology testing and evaluation Each section is examined in state of the art chapters written by domain experts providing key information to support the investigations of researchers across the medical veterinary food environment and chemical research industries and national and international regulatory agencies Thoroughly revised and expanded to 15 volumes that include the latest advances in research and uniquely organized by organ system for ease of reference and diagnosis this new edition is an essential reference for researchers of toxicology Organized to cover both the fundamental principles of toxicology and unique aspects of major organ systems Thoroughly revised to include the latest advances in the toxicological effects of chemicals on the immune system Features additional coverage throughout and a new volume on toxicology of the hematopoietic system Presents in depth comprehensive coverage from an international author base of domain experts

**Toxic Effects of Mercury** Shabnum Nabi, 2014-07-25 Mercury is widespread in our environment Methylmercury an organic form of mercury can accumulate in the aquatic food chain and lead to high concentrations in predatory fish When consumed by humans contaminated fish represent a public health risk Toxic Effects of Mercury intends to facilitate among its readers the understanding of the importance of mercury pollution in the environment and the health consequences associated with exposure to this metal The knowledge on methylmercury MeHg toxicity collected over the years is undoubtedly robust creating an impression all that is to be learnt about this metal has already been accomplished However in large measure past knowledge has merely laid the ground for interesting questions that have yet to be fully addressed and concepts have yet to be deciphered One of my major goals was to make a valiant attempt to include state of the art information on the mechanisms of mercury toxicity describing its effects on cultured cellular systems as well as in whole living organisms starting from the lessons learned from the tragic events in Minamata Bay Japan A special focus of the book is on the neurotoxic effects of MeHg An understanding at the cellular level is necessary to gather information on the structural and functional alterations induced by MeHg and how they possibly become unmasked and evident at the behavioral level 32 chapters of the book have been organised having these considerations in mind This book will provide state of the art information to the graduate students training in toxicology risk assessors researchers and medical providers at large It is aimed to bring the readers updated information on contemporary issues associated with exposure to methylmercury from its effects on stem cells and neurons to population studies It is a valuable resource for individuals interested in the public health effects and regulation of mercury The report provides an excellent example of the implications of decisions in the risk assessment process for a larger audience and is written with the hope that the information will provide better understanding of the mercury problems which confront us

Principles of Toxicology Phillip

L. Williams, Robert C. James, Stephen M. Roberts, 2003-10-10 A fully updated and expanded edition of the bestselling guide on toxicology and its practical application The field of toxicology has grown enormously since Industrial Toxicology Safety and Health Applications in the Workplace was first published in 1985 And while the original edition was hugely popular among occupational health professionals the time is ripe to address toxic agents not only in the industrial setting but also in the environment at large Renamed Principles of Toxicology Environmental and Industrial Applications this new edition provides health protection professionals as well as environmental scientists with precise up to date practical information on how to apply the science of toxicology in both the occupational and environmental setting Through contributions from leading experts in diverse fields Principles of Toxicology Second Edition features Clear explanations of the fundamentals necessary for an understanding of the effects of chemical hazards on human health and ecosystems Coverage of occupational medicine and epidemiological issues The manifestation of toxic agents such as metals pesticides organic solvents and natural toxins Special emphasis on the evaluation and control of toxic hazards Specific case histories on applying risk assessment methods in the modern workplace Ample figures references and a comprehensive glossary of toxicological terms **Risk**

**Assessment for Neurobehavioral Toxicity** Scientific Group on Methodologies for the Safety Evaluation of Chemicals.

Workshop, 1996 **Neurotoxicology** Louis W. Chang, William Slikker Jr., 1995-04-20 Neurotoxicology Approaches and Methods provides a unique and comprehensive presentation of the current concepts and state of the art methods for the assessment of neurotoxicity The book analyzes various techniques available and discusses their strengths and weaknesses This volume will serve as an excellent desk companion and laboratory guide for all investigators researchers clinicians and students interested in neurotoxicology The internationally known group of editors divide the book into seven sections Neuromorphological and Neuropathological Approaches Neurophysiological Approaches Neurobehavioral Toxicology Neurochemical and Biomolecular Approaches In Vitro Models Clinical Neurotoxicology and Risk Assessment of Neurotoxicity Each section yields the most up to date information by experts in their fields Meticulously organized and edited Neurotoxicology Approaches and Methods is the most authoritative and well planned neurotoxicology book on the market Discusses neurobehavioral testing methods for assessment of neural dysfunctions Explains state of the art diagnostic methods such as clinico neuropsychological and neurophysiological methods for patients confronted by neurotoxic problems Discusses In Vitro methods including aggregating brain cell methods organotypic cultures and the use of human neuronal cell lines for the assessment of neurotoxicity Presents step by step procedures for many methods Provides state of the art neuromorphological and biomolecular methods and approaches for neurotoxicity investigation **Haschek and**

**Rousseaux's Handbook of Toxicologic Pathology** Wanda M. Haschek, Colin G. Rousseaux, Matthew A. Wallig, Brad Bolon, Ricardo Ochoa, 2001-10-16 A comprehensive understanding of toxicologic pathology is essential for those in industry academia and government who make decisions concerning the safety and efficacy of drugs and chemicals Toxicologic

pathology relies heavily on the fields of both toxicology and pathology which are well covered individually in various texts and references however there are few texts that address the field of toxicologic pathology The Handbook of Toxicologic Pathology fills this void and is thus essential for all health professionals within or interacting with the field of toxicologic pathology This two volume set provides the reader with a single reference for toxicologic pathology In volume I the book covers toxicologic pathology in its basic aspects including its definition the basic biochemical and morphologic mechanisms underlying the discipline the basic practice of toxicologic pathology including special techniques and issues essential to the understanding of toxicologic pathology such as risk assessment experimental design and statistical analysis Next the book moves to specific issues affecting the practice toxicologic pathology including issues such as knowledge management regulatory affairs and writing pathology reports Finally Volume I closes with several chapters that deal with specific classes of environmental toxicants such as endocrine disruptors and heavy metals Volume II addresses the toxicologic pathology in a thoroughly standardized systems manner addressing the basic structure and function of a particular organ system its response to toxic injury mechanisms of injury and methods of evaluation of such injury Key Features Easy to find up to date reference information Graphic and photographic plates Current hot topics and anticipated changes in toxicologic pathology Standardized chapter format Topics that are addressed in both a broad and deep manner resulting in a stand alone text Added coverage of important environmental toxicants Chapters authored by internationally recognized experts and peer reviewed Methods and Welfare Considerations in Behavioral Research with Animals, 2002 **Handbook of**

**Developmental Neurotoxicology** William Slikker Jr., Merle G. Paule, Cheng Wang, 2018-01-04 Handbook of Developmental Neurotoxicology Second Edition provides a comprehensive view of the fundamental aspects of neurodevelopment the pathways and agents that affect them relevant clinical syndromes and risk assessment procedures for developmental neurotoxicants The editors and chapter authors are internationally recognized experts whose collaboration heralds a remarkable advance in the field bridging developmental neuroscience with the principles of neurotoxicology The book features eight new chapters with newly recruited authors making it an essential text for students and professionals in toxicology neurotoxicology developmental biology pharmacology and neuroscience Presents a comprehensive up to date resource on developmental neurotoxicology with updated chapters from the first edition Contains new chapters that focus on subjects recent to the field Includes well illustrated material with diagrams charts and tables Contains compelling case studies and chapters written by world experts **Safe Use of Chemicals** T.S.S. Dikshith, 2008-08-21 Occupational workers frequently use store and dispose of toxic chemicals without knowing the possible consequences both for the workplace and the environment Improper use or misuse of chemical substances can result in health disorders fatalities or chemical disasters Safe Use of Chemicals A Practical Guide presents quick and comprehensive i **General and Applied Toxicology, 6 Volume Set** Bryan Ballantyne, Timothy C. Marrs, Tore Syversen, 2009-12-02 Encompassing 150 articles written by leading

scientists in the field the third edition of General and Applied Toxicology provides a comprehensive and in depth review of the basic science of toxicology its specializations and the application of toxicological knowledge This new edition reflects developments within the field that have taken place since the second edition was published in 1999 These include New information developed in the areas of both the fundamental and applied aspects of toxicology Considerable increase in the development of fundamental information and its applications refinement of technical methods advances in mechanistic toxicology and greater interest in areas of toxicology previously regarded as of limited scope Changing approaches to methodological interpretative regulatory and ethical aspects of basic and applied toxicology General and Applied Toxicology 3rd Edition is the first port of call for academic researchers industrial researchers regulatory professionals and advanced students looking for timely and authoritative information in the field Due to the increase in public and media interest in exposure to toxic substances this provides an indispensable general reference source for general physicians lawyers law enforcement agencies information resource facilities and members of the general public New online resource available now In 2011 the content from the third edition of General and Applied Toxicology merged with the two volume Handbook of Systems Toxicology The result General Applied and Systems Toxicology a new online resource combining traditional toxicology with the latest developments to present the ultimate reference in toxicology For full details visit [wileyonlinelibrary.com ref gast](http://wileyonlinelibrary.com/ref/gast)

**Information Resources in Toxicology** P.J. Bert Hakkinen, Gerald Kennedy, Frederick W. Stoss, 2000-01-10 Information Resources in Toxicology Third Edition is a sourcebook for anyone who needs to know where to find toxicology information It provides an up to date selective guide to a large variety of sources books journals organizations audiovisuals internet and electronic sources and more For the Third Edition the editors have selected organized and updated the most relevant information available New information on grants and other funding opportunities physical hazards patent literature and technical reports have also been added This comprehensive time saving tool is ideal for toxicologists pharmacologists drug companies testing labs libraries poison control centers physicians legal and regulatory professionals and chemists Serves as an all in one resource for toxicology information New edition includes information on publishers grants and other funding opportunities physical hazards patent literature and technical reports Updated to include the latest internet and electronic sources e mail addresses etc Provides valuable data about the new fields that have emerged within toxicological research namely the biochemical cellular molecular and genetic aspects Methods for Developing Spacecraft Water Exposure Guidelines National Research Council, Commission on Life Sciences, Board on Environmental Studies and Toxicology, Committee on Toxicology, Subcommittee on Spacecraft Water Exposure Guidelines, 2000-11-18 The National Aeronautics and Space Administration NASA maintains an active interest in the environmental conditions associated with living and working in spacecraft and identifying hazards that might adversely affect the health and well being of crew members Despite major engineering advances in controlling the spacecraft environment some water and air contamination



appears to be inevitable Several hundred chemical species are likely to be found in the closed environment of the spacecraft and as the frequency complexity and duration of human space flight increase identifying and understanding significant health hazards will become more complicated and more critical for the success of the missions NASA asked the National Research Council NRC Committee on Toxicology to develop guidelines similar to those developed by the NRC in 1992 for airborne substances for examining the likelihood of adverse effects from water contaminants on the health and performance of spacecraft crews In this report the Subcommittee on Spacecraft Water Exposure Guidelines SWEGs examines what is known about water contaminants in spacecraft the adequacy of current risk assessment methods and the toxicologic issues of greatest concern

*Encyclopedia of Toxicology* Bruce Anderson, Ann de Peyster, Shayne C. Gad, P.J. Bert Hakkinen, Michael Kamrin, Betty Locey, Harihara M. Mehendale, Carey Pope, Lee Shugart, 2005-05-31 The second edition of the Encyclopedia of Toxicology continues its comprehensive survey of toxicology This new edition continues to present entries devoted to key concepts and specific chemicals There has been an increase in entries devoted to international organizations and well known toxic related incidents such as Love Canal and Chernobyl Along with the traditional scientifically based entries new articles focus on the societal implications of toxicological knowledge including environmental crimes chemical and biological warfare in ancient times and a history of the U S environmental movement With more than 1150 entries this second edition has been expanded in length breadth and depth and provides an extensive overview of the many facets of toxicology Also available online via ScienceDirect featuring extensive browsing searching and internal cross referencing between articles in the work plus dynamic linking to journal articles and abstract databases making navigation flexible and easy For more information pricing options and availability visit [www.info.sciencedirect.com](http://www.info.sciencedirect.com) Second edition has been expanded to 4 volumes

Encyclopedic A Z arrangement of chemicals and all core areas of the science of toxicology Covers related areas such as organizations toxic accidents historical and social issues and laws New topics covered include computational toxicology cancer potency factors chemical accidents non lethal chemical weapons drugs of abuse and consumer products and many more

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