



# 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 1977 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

**Bernard Weiss**

## **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,2012-11-02 A Comprehensive Guide to Toxicology in Preclinical Drug Development is designed for toxicologists who need a thorough understanding of the drug development process This multi contributed reference will provide a detailed picture of the complex and highly interrelated activities of preclinical toxicology in both small molecules and biologics

**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

A Comprehensive Guide to Toxicology in Nonclinical Drug Development Ali S. Faqi,2016-11-03 A Comprehensive Guide to Toxicology in

Nonclinical Drug Development Second Edition is a valuable reference designed to provide a complete understanding of all aspects of nonclinical toxicology in the development of small molecules and biologics This updated edition has been reorganized and expanded to include important topics such as stem cells in nonclinical toxicology inhalation and dermal toxicology pitfalls in drug development biomarkers in toxicology and more Thoroughly updated to reflect the latest scientific advances and with increased coverage of international regulatory guidelines this second edition is an essential and practical resource for all toxicologists involved in nonclinical testing in industry academic and regulatory settings Provides unique content that is not always covered together in one comprehensive resource including chapters on stem cells abuse liability biomarkers inhalation toxicology biostatistics and more Updated with 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 the expectations associated with working in nonclinical toxicology *Comprehensive Toxicology: Nervous system and behavioral toxicology* I. Glenn Sipes, 1997 This volume in the Comprehensive Toxicology series demonstrates how the use of extremely powerful molecular and cell biology techniques has stimulated the growth of toxicology as a scientific discipline The field of toxicology has evolved from its earlier days of in vivo and descriptive studies to focusing on mechanisms Frequently mechanisms require an examination at the cellular and molecular level Molecular toxicology has opened the door to comprehending the basic mechanisms of how toxicants show their effects The volume is a comprehensive integrated profile of the molecular effects of toxicants and the molecular mechanisms involved in producing cellular and tissue injury

**Environmental Health Perspectives**, 1993    **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](http://wileyonlinelibrary.com) ref gast *Reviews in Environmental Health*, 2001 ,2001 **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 *Encyclopedia of Toxicology* Philip Wexler,Bruce D. Anderson,2005 The Encyclopedia of Toxicology second edition continues its comprehensive survey of toxicology This new edition presents entries devoted to specific chemicals the international scope of organizations included has been broadened and articles describing a number of well known toxic related incidents such as Chernobyl and Three Mile Island are included 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 Midwest **Research Report** ,1996

**Principles of Toxicology** Phillip L. Williams,Robert C. James,Stephen M. Roberts,2000-03-31 PHILLIP L WILLIAMS PhD is Associate Professor of Environmental Health Science at the University of Georgia Athens ROBERT C JAMES PhD is President of TERRA Inc Tallahassee Florida and Associate Scientist at the Center for Environmental and Human Toxicology at the University of Florida Gainesville STEPHEN M ROBERTS PhD is Professor and Program Director of the Center for Environmental and Human Toxicology at the University of Florida Gainesville **OECD Papers** ,2004 A compilation of reports previously issued by the OECD **Neuroprotective Agents** William Slikker,Russell J. Andrews,Bruce Trembly,2003

The sixth in this series of Annals volumes brings together clinical and basic science researchers from many countries and disciplines in a common forum to address various approaches to neuroprotection Topics covered include the following clinical trials clinical application of neuroprotective approaches NMDA receptors as mediators of neurotoxicity and neuroprotection models mediators and mechanisms of neurotoxicity and neuroprotection dietary supplements as neuroprotectants oxidative stress and approaches to neuroprotection mitochondria as a target of neurotoxicity and neuroprotection and genomic approaches The 35 papers and 10 posters are taken from the Sixth International Conference on Neuroprotective Agents held in September 2002 in South Carolina    Veterinary and Human Toxicology ,1995    **Guidelines for the Care and Use of Mammals in Neuroscience and Behavioral Research** Committee on Guidelines for the Use of Animals in Neuroscience and Behavioral Research,2003 Provides advice for common situations in neuroscience and behavioral research that can pose difficulties It treats the development evaluation and implementation of animal use protocols as a decision making process not just a decision It encourages the use of professional judgement and careful interpretation of regulations and guidelines to develop performance standards that ensure animal well being and high quality research This book will be an indispensable resource for researchers veterinarians and institutional animal care and use committees    **Index of Conference Proceedings** British Library. Document Supply Centre,1994    **CSA Neurosciences Abstracts** ,1995    **Toxicology Abstracts** ,1985 Includes annual author and subject indexes

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web mar 6 2017 1 the chemical reaction  $2\text{H}_2\text{O} \rightarrow 2\text{H}_2 + \text{O}_2$  is a synthesis reaction decomposition reaction single displacement reaction double displacement reaction combustion reaction you can recognize a decomposition or analysis reaction by noticing a compound or molecule breaks into smaller chemical species 2 the chemical reaction

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web for each reaction in part i and part ii record your observations molecular equation total ionic equation and net ionic

equation make sure to write any evidence of any evidence of a chemical reaction with sufficient detail to help you  
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web what type of chemical reaction is shown  $\text{ab} \rightarrow \text{cd}$   $\text{ad} \rightarrow \text{bc}$  decomposition the reaction  $\text{pb no}_3 + 2\text{ki} \rightarrow \text{pbi} + 2\text{kno}$  is a double replacement reaction the reaction  $2\text{mg} + \text{o}_2 \rightarrow 2\text{mgo}$  is a synthesis

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