A Pathway-Based Approach to Predicting Interactions between Chemical and Non-Chemical Stressors: Applications to Global Climate Change

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1. Introduction

A variety of environmental variables influenced by global climate change (GCC) can directly or indirectly affect the health of organisms. These variables may include temperature, salinity, pH, and penetration of ultraviolet radiation (UVR) in aquatic environments, and water shortages or alterations in air quality in terrestrial systems. There has been consideration of the direct effects of changes in many of these factors on biota, e.g., the potential influence of temperature on distributions of fish populations. However, far less is known concerning the indirect effects of variables affected by GCC on humans and the environment, including the potential for interactions with toxic chemicals. Recent reviews of the existing literature on the topic have shown that factors such as temperature can indeed greatly influence the toxicity of chemicals in a variety of taxa [1]. But, a critical consideration which becomes apparent when considering these types of analyses is that, other than for a very few species, chemicals and endpoints, the information collected to date concerning the effects of changes in global climate on chemical toxicity is not comprehensive enough to routinely support integrated risk assessments. Hence, there is a need to develop approaches/tools that better enable prediction of potential interactions of chemical toxicants with non-chemical stressors influenced by GCC. To achieve this requires a mechanism-based understanding of the biological pathway(s) through which chemicals exert their effects, and identification of points in these pathways that could be influenced by nonchemical stressors.

2. Materials and Methods

A major impediment to the use of mechanistic data in risk assessments has been an inability to clearly translate information collected at lower levels of biological organization (e.g., molecular, biochemical and cellular responses) into alterations in endpoints meaningful to risk assessments, namely effects on individuals and, ultimately, populations. To address this shortcoming Ankley et al. [2] described a conceptual framework based on constructs called adverse outcome pathways. Adverse outcome pathways (AOPs) depict linkages between molecular initiating events (interaction of chemicals with biological targets) and the subsequent cascade or responses that occur across biological levels of organization that culminate in impacts in individuals (or populations) that can be used for assessing risk. In the present analysis we describe how the AOP concept can be adapted to support the use of mechanistic data for assessing the effects of variables influenced by GCC on chemical toxicity. The ultimate goal of this effort is to develop assessment approaches/tools that are not based solely on the collection of empirical data for different combinations of chemical and non-chemical stressors but, rather, enable some degree of prediction of when and how significant interactions between stressors might be expected to occur.

3. Results and Discussion

Our analysis focused on documenting a number of "real world" examples illustrating how an understanding of mechanistic toxicology supports consideration of known or hypothesized interactions between chemical and non-chemical stressors relative to incorporation of GCC into chemical risk assessments. We include case studies relevant both to human and ecological health, and demonstrate how the AOP framework can be applied to either prospective or retrospective risk assessments. Specifically, we present several scenarios where—based on established or plausible interactions between chemical and GCC-related non-chemical stressors—prospective assessments of risk can be developed, e.g., for chemicals not yet present in the environment and/or for variables not yet affected by GCC. In addition we describe retrospective situations in which observed impacts can be dissected and diagnosed relative to determination of mechanistic interactions between chemical and non-chemical stressors, as a basis for developing predictive models that can be applied in a generalized manner, e.g., at sites or in situations removed from where initial observations were made.

Specific case examples include: (a) interactions between thyroid-disrupting chemicals and temperature stress on amphibian metamorphosis, (b) effects of extreme weather events on mercury toxicity to tree swallow nestlings, (c) influence of changes in salinity and temperature alterations on pesticide uptake, metabolism and toxicity in fish, (d) effects of changes in UVR intensity on the photo-toxicity of polycyclic aromatic hydrocarbons to aquatic organisms, (e) influence of GCC variables in concert with persistent organo-chlorines on polar bear health, (f) interactions between temperature or hypoxia and chemicals that affect reproductive endocrine function in fish, and (g) interactions between GCC-induced alteration in air quality (e.g., increased ozone) and contaminants on human health.

5. References

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