

# ETHICS AND THE NEUROLOGICAL EFFECTS OF WATER CONTAMINATION BY METHYLMERCURY

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## ABSTRACT

What ethics-related discussion is present in journal articles on brain damage due to water contamination by methylmercury? As a neurotoxin, increased bioavailability of methylmercury driven by human activities can have a significant adverse impact on future generations. We categorized ethics-related content according to a framework for Environmental Neuroethics (Cabrera et al., 2016). The framework provides a systematic way of examining phenomena at the intersection of ethics, brain, and environmental change. Measures of the relative quantity of ethics-related content and sources of academic discourse were also made. The most extensive ethical discussion concerned implications for social policy and regulation. We also noted a lack of ethics-related content with regard to cross-cultural perspectives.

## INTRODUCTION

Methylmercury (MeHg) is a potent neurotoxin, especially for a fetus exposed in utero. Research into its effects in brain health evolved after the fall-out of major anthropogenic mercury pollution incidents in Japan (1956, 1965) and Iraq (1971) (Harada, 1995; Amin-Zaki et al., 1974). MeHg is mercury (Hg) in its fat soluble organic form, which readily passes through the blood brain barrier (Järup, 2003). Brain damage resulting from exposure in adulthood is focal, and primarily causes impairment of movement, vision and audition as well as cognitive impairments (Castoldi et al., 2001). Prenatal exposure impairs normal neurodevelopment and leads to widespread neuronal degradation. Expressions of such MeHg-induced neurotoxicity can take a variety of forms, including cerebral palsy and autism spectrum disorder.

MeHg is produced through methylation of inorganic Hg by aquatic micro-organisms (Clarkson, 1995). Increasing anthropogenic emissions of mercury through

industrial practices have increased the environmental availability of Hg as well as rates of conversion to its neurotoxic form MeHg (Booth and Zeller, 2005). This conversion of Hg to MeHg poses the greatest threat to brain health, because MeHg bio-accumulates through the food chain (Wang et al. 2004). This may render local waters safe to drink, while fish and marine mammals contain toxic concentrations. The size and age of the fish also contributes to its relative MeHg concentration. For example, king mackerel is significantly more toxic than smaller species of mackerel (Silbernagel et al., 2011). Increased environmental availability of MeHg and subsequent low dose exposure by human populations is implicated in what has been considered as the silent pandemic of neurodevelopmental disorders arising from subclinical neurotoxicity (Labies, 2007; Grandjean and Landrigan, 2006).

Contradictory findings from two major longitudinal studies on the neurological effects of MeHg have sparked debate concerning policy regulation for restricting the consumption of certain foods. One such ongoing study is based in a cohort of children in the Republic of Seychelles, whose pre- and postnatal MeHg exposure results primarily from consumption of ocean fish. This cohort has almost no reported adverse effects on neurodevelopment with increased MeHg exposure; and even show slight improvements on tests of cognitive ability (Davidson et al., 2011). These findings are commonly attributed to the paired increased intake of nutrients beneficial for neurological function that occur naturally in the same fish. In stark contrast, a cohort of children on the Faroe Islands exposed to MeHg primarily through consumption of both fish and whale products have reported significant and lasting cognitive deficits (Debes et al., 2016).

A major motivator for the present study was the Calder et al.'s (2016) report that 11 of 22 planned hydroelectric facilities in Canada will increase MeHg

concentrations in surrounding areas sufficiently to produce an adverse effect in local communities. Many of these are First Nations settlements. Even active efforts to reduce anthropogenic effects on the natural environment lack consideration of potential adverse effects on brain health. No review of the extent or themes present in the ethical discussion has been carried out with regard to methylmercury. To address this knowledge gap, the framework for Environmental Neuroethics (Cabrera et al., 2016) (Fig. 1) was used to investigate the ethical considerations reflected in the academic literature on brain damage due to environmental water contamination by methylmercury. Such an investigation has the potential to address directions for further academic discourse and impact policy decisions.

Framework Environmental Neuroethics	
<b>Brain science and the environment</b>	Neuroscience discovery that is aligned with the measurement and evaluation of factors that affect the way individuals, communities and society adapt and cope with real or perceived environmental threats to well-being.
<b>The relational self and the environment</b>	The interface between the environment and brain, and the mechanisms by which exposures at key points in life may mediate different brain and mental effects; relationships with different environmental stressors, individual susceptibility and resilience.
<b>Cross-cultural factors and the environment</b>	Exploration of the role of culture in the relationship between environment and brain and mental health; interactions between Traditional Ecological Knowledge and neuroscience evidence.
<b>Social policy and the environment</b>	Priorities and allocation of resources of local social organizations to deal with environmental impacts on brain and mental health.
<b>Public discourse and the environment</b>	The engagement of professional disciplines and communities in multidirectional communication and discourse about neurological, psychological, sociological and ethical dimensions of environmental change; facilitation of international, cross-disciplinary, transdisciplinary collaborations.

Figure 1. Framework for Environmental Neuroethics (Cabrera et al., 2016). Reprinted with permission.

## Methods

### MeSH search terms and PubMed search

As a first step in this scoping review, the research question was formulated into a PubMed search query based on Medical Subject Headings (MeSH). A MeSH search includes both articles indexed according to this system, and other papers under the same keywords in the larger PubMed database. Prior to finalizing the query, different search terms were tested to ensure that the result reflected the research question.

Search terms were extracted from three categor-

ies; terms relating to environmental sources of pollution in water environments, terms relating to brain health, and terms relating to methylmercury. The MeSH terms used under the umbrella of environment were: 'environment', 'industry', 'water', 'chemical water pollution' and 'environmental pollution'. Terms related to brain health were; 'neurology', 'neurotoxins', 'chronic brain damage' and 'neurodevelopmental disorders'. The only relevant search term for the compound name was 'methylmercury compounds' (Fig. 2). Terms under an umbrella category were joined by disjunction, and these content categories were then joined by conjunction. This enforced that some subset of terms from each of the three umbrella categories had to appear as search terms for every query return.

ENVIRONMENT	BRAIN	COMPOUND
Environment	Neurology	Methylmercury Compounds
Industry	Neurotoxins	
Water	Chronic Brain Damage	
Chemical Water Pollution	Neurodevelopmental Disorders	
Environmental Pollution		

Figure 2: MeSH search terms for the PubMed query. Column terms were joined by disjunction; and rows by conjunction such that at least one element from each column category must have been a search term used to index a given article.

The search was conducted in March 2017. All returns were manually curated and reviewed by the first author. Articles were excluded if they did not concern impacts on human health (e.g., focused on another species), or were written in a language other than English or French. There was a sharp decline in the indexed coverage of the debate published prior to 1995, so articles prior to January 1995 were also excluded. An additional five articles were excluded because they could not be accessed.

### Framework Operationalization

In order to categorize articles consistently according to the framework, each category was operationalized as follows:

- *Brain science and the Environment (BSE)*: Discussion relating to measurements of neurotoxicity, prevention methods, physical and/or psychological methodology for detecting, evaluating, preventing, and/or treating neurotoxic effects.

- *Relational Self and the Environment (RSE)*: Discussion concerning mental health and the vulnerability to MeHg neurotoxicity at different life stages, comparing pre-/peri- and postnatal effect sizes to that of adult populations, as well as the long-term effects of exposure during neurodevelopment.

- *Cross-Cultural Factors and the Environment (CCFE)*: Discussion on how exposure to MeHg differ in populations resulting from a community's cultural practices, such as traditional sources of food and ways of living, as well as differing approaches to neurotoxicity and the knowledge thereof. An article containing mention of differential exposure due to location rather than culture would not fall under this category.

- *Public Discourse and the Environment (PDE)*: Discussion of the spread of knowledge and communication concerning neurotoxicity and environmental sources of methylmercury, as well as the effectiveness and implementation of intervention methods. Strongly ties in with education.

- *Social Policy and the Environment (SPE)*: Discussion of regulation, legislation and policy-making, and utility calculations that often are based in economic considerations.

### Additional Categorizations

In addition to categorizations according to the framework, the extent of ethical discussion was recorded in three broad categories; none, minimal/some, and extensive. An article would fall under 'extensive' if the main purpose of the paper was related to ethics-based discussion; under 'minimal/some' if some content was related to ethics but not the main aim of the paper. While many articles contained ethics-related words such as vulnerability, a quantitative measure of the number of such words did not necessarily correspond to the extent of the ethical discussion. An article would fall under 'none', therefore, if no ethics-related implications were discussed, or an ethics-related content word (such as vulnerable) appeared without more elaborate discussion.

The type of literary source was also recorded; primary research, reviews and other types of sources such as letters were represented in the sample.

### Controls

As a measure of consistency, 20% randomly chosen articles were double-coded by an independent researcher in the same lab. The reviewer was supplied with categories and corresponding operationalizations, exclusion criteria, and the code for evaluating the extent of the ethical discussion. After a first pass, the results and implications on the broader search were discussed, and categorizations were re-evaluated until consensus was reached. The remaining articles were subject to a second pass after this review.

## RESULTS

The search returned 108 papers, of which 91 met inclusion criteria. Among the 91 articles, 44 (48%) had no ethics-related content, 27 (30%) had minimal/some discussion, and 20 (22%) contained extensive ethical discussion (Fig. 3). Among the 47 articles with ethics-related content, 19 (40.5%) originated in primary research and 25 (53%) in reviews. Three articles (6.5%) were letters and elaborations on previous research.

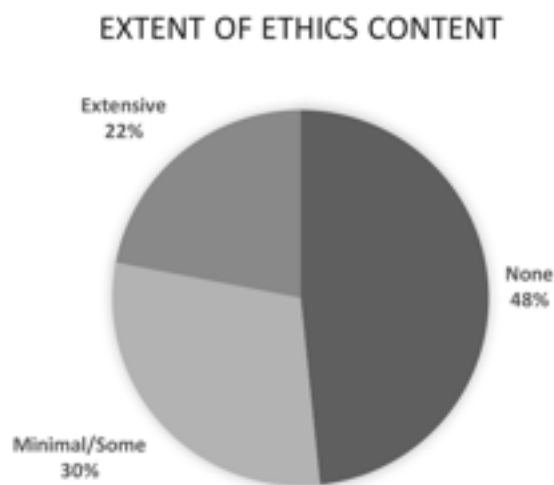


Figure 3. Proportion of articles containing extensive, minimal/some, and no ethical discussion (N=91).

Among articles with ethics-related discussion, 15 were categorized under BSE, 6 under RSE, 2 under CCFF, 8 under PDE and 16 under SPE (Fig. 4). Categorizations reflect the primary theme in the article's ethics-related content. Articles with no ethical content were not categorized.

The extent of ethics-related discourse in the analyzed papers varied significantly across framework

categories. The highest proportion of extensive discussion (10 extensive, 6 minimal/some) was found in SPE, while the highest proportion of minimal/some ethical discussion (12 minimal/some, 3 extensive) was found in BSE. Both PDE and CCFE had an equal split, while RSE had extensive ethical discussion in 2 among its total of 6 papers.

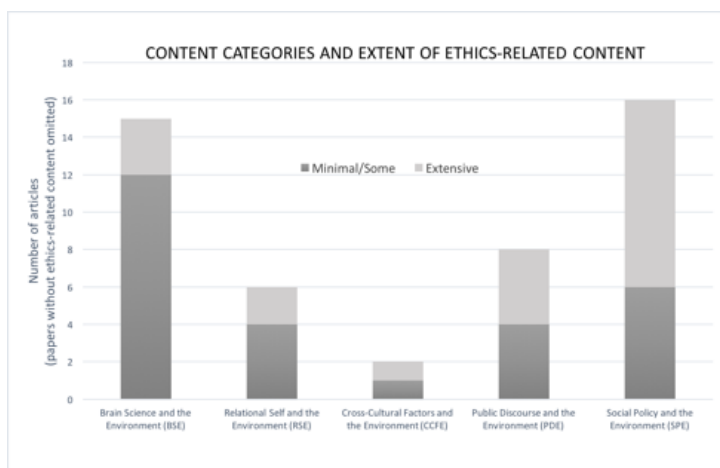


Figure 4. Number of articles among those with ethics-related content separated according to framework category and extent of discussion.

In terms of category distribution between types of literature, there was a roughly equal split between primary research and reviews overall. The most significant difference was under PDE, where a majority of articles were reviews. The distribution of primary among the total number of articles (primary / total), were; BSE: 7/15, RSE: 3/6, CCFE: 1/2, PDE: 2/8 (one letter included in total), and SPE: 6/16 total (two letters included in total) (Fig. 5). Among review articles containing some ethics-based discourse, 14 out of 25 discussed the topic extensively. In papers originating from the primary literature, this proportion shifted dramatically to 3 out of the total 19. Two out of the three letters and elaborations to previous research contained extensive ethics-based discussion.

## DISCUSSION

The categorizations offered by the framework for Environmental Neuroethics provided insight into ethics-related contributions to the academic discussion about brain and methylmercury (MeHg). The category Social Policy and the Environment (SPE) contained the greatest proportion of articles with any ethics content

overall. These articles were also the most likely to contain extensive ethical discussion. SPE and Public Discourse and the Environment (PDE) included the greatest proportion of review articles relative to primary research articles. Since methylmercury has long been known for its neurotoxic effects, the results seen for SPE and PDE reflect the contemporary debate concerning evaluation of reference dosages, suggestions for health and safety policies, and the impact on society from education and implementation of regulatory practices.

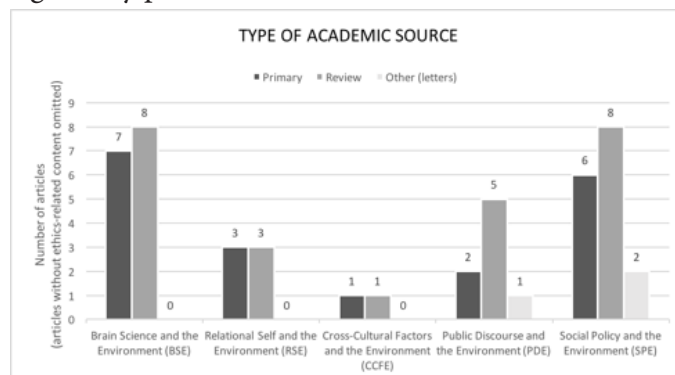


Figure 5. Number of articles among those with ethics-related content according to category and type of literary source.

The longitudinal studies in the Republic of Seychelles and Faroe Islands highlight the importance in making policy decisions and public advisories that both reduce the risk of MeHg neurotoxicity and maintain intake of beneficial nutrients from seafood. This is an especially important issue among vulnerable populations such as women of childbearing age and young children, as well as within indigenous communities where alternative sources of food may be neither readily accessible nor desired. Attempts to achieve a balanced advisory for fish consumption are reflected in articles categorized under SPE. These articles contained evidence of economic estimates as a proxy for neurological damage, through for example a drop in IQ, resulting from adherence to different regulatory practices. (See for example Bartlett and Trasande, 2014). The focus in Relational Self and the Environment (RSE) on consequences of exposure during different stages of neurodevelopment suggest a strong link to RSE and how regulation influence these effects.

It is perhaps not surprising that the greatest proportion of primary studies as well as articles cont-



aining only minimal/some ethics-related content were reported in the category Brain Science and Environment (BSE). Even though ethical considerations fell outside the primary focus of these papers, they were often present to warrant the relevance of presented research, or to stress the importance of findings. Many articles in this category focused on the neurological basis for neurotoxicity due to methylmercury exposure, as well as determinations of the effect size of confounding variables in epidemiological studies.

Given the characteristics of the neurotoxic effects from methylmercury exposure, it was not uncommon for articles to contain ethics-related discussion suitable for coding into multiple categories. In such cases, the ethics-related content was categorized according to the primary theme in the discussion. This may however have contributed to what appears to be a restricted discussion in the categories Relational Self (RSE), Public Discourse (PDE) and Crosscultural Factors (CCFE). An example of such a paper is "Maternal Fish Consumption and Prenatal Methylmercury Exposure: A Review" (Al-Ardhi and Al-Ani, 2008). This paper was categorized under BSE, owing to a focus on how properties of fish and consumption patterns contribute to producing neurotoxic effects of MeHg. However, the same paper also uses its findings to extensively engage in discussion concerning policy and regulation for public advisories, especially with regards to the unique vulnerability of the child in-utero. The relevance to themes in PDE, SPE and RSE ought also to be reflected in the classification of such articles. For future studies using the same framework, adding the dimension of relative content between categories would enrich the findings and possible conclusions.

Categorizing articles according to the framework permitted an insight into where contribution to the debate is lacking. In this study, this was most evident with regards to crosscultural perspectives. Only two out of 47 papers contained ethical discussion focused on themes under CCFE: both case studies of populations highly exposed to methylmercury through traditional ways of living. Communities that rely predominantly on wild caught fish as a source of dietary protein are especially vulnerable to methylmercury exposure. Such communities, like the Canadian First Nations, often differ in their cultural practices compared to the country's mainstream culture, and live in areas with high risk of undergoing changes due to industrial expansion. These topics are present in the academic literature, as exemplified by the

debate surrounding Canadian prospective hydroelectric power plants, but are underrepresented in this search.

PubMed provides access to the extensive MEDLINE database of biomedical research. We carefully curated returns to provide precise search results. PubMed is, however, limited papers published in life science journals. In the future, extended analyses that include papers from other search engines such as Google Scholar will provide further foundational content for related academic and regulatory pursuits in environmental neuroethics.

## ACKNOWLEDGEMENTS

This research was carried out as part of a research course in the Cognitive Systems undergraduate program at the University of British Columbia. Judy Illes, CM, PHD, is Canada Research Chair in Neuroethics. The authors would like to thank the anonymous reviewer for helpful comments, and Cody Lo for assistance with data analysis.

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