

Review

Interrelationships of undernutrition and neurotoxicity: Food for thought and research attention

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ABSTRACT

The neurotoxic actions of chemical agents on humans and animals are usually studied with little consideration of the subject's nutritional status. States of protein-calorie, vitamin and/or mineral undernutrition are associated with a range of neurodevelopmental, neurological and psychiatric disorders, commonly with involvement of both the central and the peripheral nervous system. Undernutrition can modify risk for certain chemical-induced neurologic diseases, and in some cases undernutrition may be a prerequisite for neurotoxicity to surface. In addition, neurologic disease associated with undernutrition or neurotoxicity may show similarities in clinical and neuropathological expression, especially in the peripheral nervous system. The combined effects of undernutrition and chemical neurotoxicity are most relevant to people with low incomes who experience chronic hunger, parasitism and infectious disease, monotonous diets of plants with neurotoxic potential (notably cassava), environmental pollution from rapid industrial development, chronic alcohol abuse, or prolonged treatment with certain therapeutic drugs. Undernutrition alone or in combination with chemical exposure is also important in high-income societies in the setting of drug and alcohol abuse, old age, food faddism, post-bariatric surgery, and drug treatment for certain medical conditions, including cancer and tuberculosis. The nutritional demands of pregnancy and lactation increase the risk of fetal and infant undernutrition and chemical interactions therewith.

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1. Introduction

Neurotoxicity in the present context refers to the adverse effects of chemicals of all types, including those of natural origin. Undernutrition is a form of malnutrition resulting from insufficient intake of food, or the vitamin and mineral components thereof, or from the inability to digest, assimilate, and use required nutrients. Undernourishment exists when caloric intake is below the minimum dietary energy requirement: this is the amount of energy needed for light activity and a minimum acceptable weight for attained height, and it varies by country and from year to year depending on the gender and age structure of the population. Those affected by undernutrition are often of low weight for age, thin for height and have impaired immunological function (Hughes and Kelly, 2006).

The risk of undernutrition is increased during pregnancy and lactation because of augmented nutritional requirements, and the elderly have an enhanced risk because of inadequate self-care or neglect. Severe chronic infections, especially those associated with chronic diarrhea (notably HIV-AIDS), represent an additional major cause of protein-energy undernutrition.

How an undernourished physiological state modulates human and animal responses to chemicals with neurotoxic potential is a subject of great relevance to a significant portion of the human population. This includes the rural poor, who represent a majority of undernourished people, especially those living in rain-fed areas of low-income countries where food insecurity arising from environmental extremes is a constant threat; and the urban poor, who frequently lack the means to purchase food, and victims of civil disturbance, war and environmental catastrophes that set the stage for acute or chronic hunger.

The World Food Program cites data reporting the presence of 925 million hungry people in the world of which 98% live in developing countries (<http://www.wfp.org/hunger/who-are>). This includes 578 million in Asia and the Pacific, 239 million in sub-Saharan Africa, 53 million in Latin America and the Caribbean, 37 million in the Near East and North Africa, and 19 million in

developed countries. Three-quarters of all hungry people live in rural areas, mainly in the villages of Asia and Africa. Around 50% of pregnant women in developing countries are iron-deficient, and some 17 million children are born underweight annually, the result of undernutrition before and during pregnancy. Acute and chronic hunger accounts for an estimated 146 million hungry children worldwide. The prevalence of undernourishment is shown in Fig. 1, and the effects of undernutrition on brain development have been reviewed by Holden (2008). Additional information on the global geographic distribution of hunger and undernutrition is available (e.g. http://gamapserver.who.int/gho/interactive_charts/mdg1/atlas.html). Animal studies suggest that undernutrition can adversely impact brain function both of the affected generation (F0) and also the brain weight and learning behavior of future generations (F2) (Bresler et al., 1975); this suggests the operation of epigenetic factors, a subject of considerable debate and relevance to public health (Martins et al., 2011).

The neural effects of undernutrition have been recorded both as an isolated pathophysiological phenomenon and in combination with food dependency on plant components with neurotoxic potential. Neurological disease, sometimes in the form of sizeable epidemics (lathyrism, cassavism), may result from nutritional dependence on single plant foods (grass pea, cassava, respectively), or on widespread but poorly defined dietary deficiency. Food spoilage exposes impoverished humans to high levels of tremorgenic and other mycotoxins (Ludolph and Spencer, 2000) of which some 300–400 are known (Sulyok et al., 2007). The clinical effects of a contaminated or inadequate diet on the developing and adult nervous system may be reversible, persistent, or progressive. Relative to a healthy newborn, undernutrition during pregnancy may result in a low birth weight, smaller head circumference and reduced brain weight. Cognitive development is at special risk up to the age of 3 years. States of general and specific undernutrition during development have been linked with poorer cognitive function in adult life and susceptibility to neuropsychiatric disorders (Kejantie, 2008; Eyles et al., 2009). Neurological deficits in adults may arise from restrictive diets (veganism), food

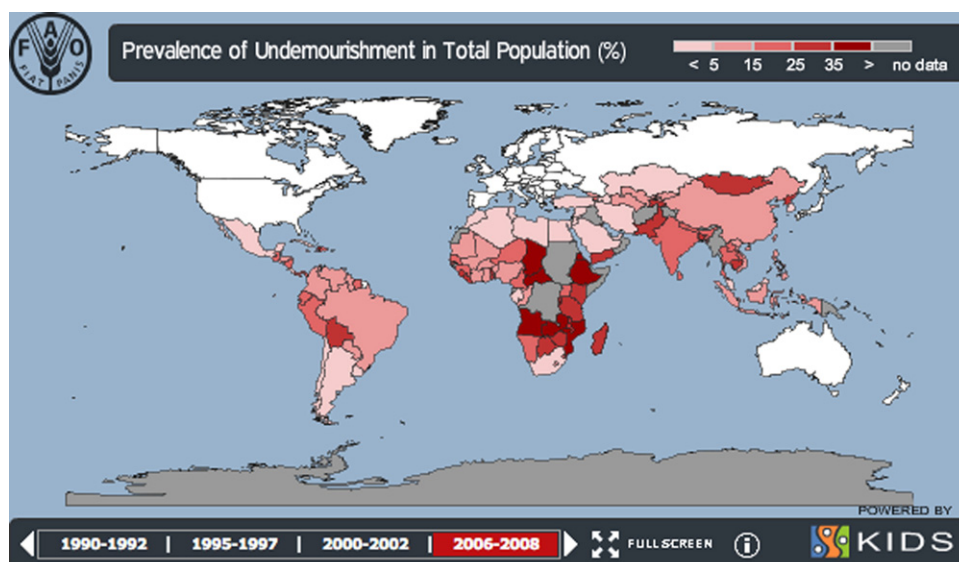


Fig. 1. Food and Agriculture Organization Hunger Map 2010. Prevalence of undernourishment by country. <http://www.fao.org/hunger/en/>.

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