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Review

Why does Finland have the highest dementia mortality rate? Environmental factors may be generalizable

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ABSTRACT

Finland has the highest death rate from dementia in the world and its environmental features can be instructive in understanding hidden causes of dementia. Environmental factors there include: 1) a climate that is both very cold and humid resulting in housing frequently harboring molds that are capable of producing a neurotoxic mycotoxin 2) the Gulf of Finland as well as Finnish lakes harbor cyanobacteria that produce the neurotoxin, beta-N-methyl amino-L-alanine, known to cause dementia and related disorders 3) the aforementioned toxins can be potentiated by the presence of mercury and methyl mercury which can be found in Finnish waters 4) soil in Finland is naturally low in selenium and selenium deficiency may reduce the quantity and effectiveness of glutathione's ability to protect against neurotoxins. A high rate of fatal dementia could be the consequence of these environmental factors. Studies that can support or disprove this hypothesis are suggested. Such environmental toxins are likely to promote Alzheimer's disease elsewhere in the world where such a combination of neurotoxins may also occur.

Contents

1. Introduction

Increasingly dementia researchers are finding increasing evidence that microbes are involved in the development of dementia disorders (Holmes and Cottrell, 2009). Evidence that beta-amyloid has anti-microbial activity (Kumar et al., 2016) has lent credence to this concept. Studies have demonstrated a role for microorganisms in the development of Alzheimer' disease (AD) include oral spirochetes, viruses, and fungi (Olsen and Singrhao, 2015) as well as chlamydia (Balin et al., 1998). Entry to brain tissue may gained via ingestion, inhalation, direct oral-brain route, and blood borne with an impaired blood-brain barrier. The development of a chronic inflammatory response appears to underlie neuronal destruction and beta-amyloid deposition (Miklossy, 2011) and the development of AD.

Finland has the highest death rate for dementia in the world (World Health Rankiings, 2016) exceeding those of the USA and Canada and the other Nordic countries who also have high rates. This small advanced nation provides a unique opportunity to develop testable hypotheses concerning the causes of AD so that

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research and preventive efforts can be developed efficaciously. Dementia mortality in Finland has risen nearly eightfold in the past half century (Statistics Finland, 2017) so there is a compelling need to address the causes. The aforementioned other countries also have major public health concerns regarding a high incidence and prevalence of dementia as well, and what is the case with Finland may likely apply in varying degrees to them as well. Death rates and prevalence rates are related to one another although somewhat imprecisely because not all recorders of causes of death follow the international guidelines and severity of dementia may also vary depending on the type of dementia (Bredesen, 2015) and the causative factors.

This review examines the somewhat unique environmental, climatological, and geological features of Finland that may be promoting the high rate of dementia mortality there. Described herein are neurotoxins in the environment that exposure to which may promote AD as well as soil and water qualities that contribute to the high dementia rate.

2. Empirical data: fungal toxins

Of note, Finland has a somewhat unusual climate, being both very cold and very humid with humidity averaging over 80% over the winter months (Average Humidity in Helsinki, 2017). The extreme cold promotes effective insulation of homes and businesses while the humidity is permissive to fungi to growth. The net effect is that many homes and other buildings have problem with mold growth. One study found 80% of residences had current or previous moisture faults (Nevalainen et al., 1998) and another recent survey found visible mold in 38% of homes (Karvonen et al., 2015). Studies detailing the type of mold found in the homes include several species of Aspergillus, Stachybotrys, and Pencillium (Täubel et al., 2016). These molds are known to produce ochratoxin A as well as other toxins which has been shown to produce apoptosis in neuronal cells in cell culture in a dose dependent fashion (Zhang et al., 2009).

Bredesen, an experienced AD researcher, reported that mycotoxins can induce a chronic inflammatory response that can be manifested as AD and the exposure is frequently inhalational in nature (Bredersen, 2016). Pencillium, Stachybotrys, and Aspergillus molds were identified in homes of several of the patients described in this series (and these molds correspond to those found in Finnish homes). The inflammatory response described by Bredersen in these patients suffering from dementia was characterized by elevation of complement component, C4a, transforming growth factor beta1 (TGF-beta) as well as several cytokines. Bredesen also reports that this syndrome occurred mostly in patients with certain HLA DR/DQ haplotypes (11-3-52B and 4-3-53) and such a genetic predisposition may be a prerequisite to developing the syndrome following exposure and may explain its sporadic incidence.

Exposure to mycotoxins may also occur through food consumption including plant food supplements that may harbor ochratoxin (Piemontese, 2017).

Also regarding fungi and dementia, Spanish researchers recently detected Candida species in the brains of AD patients but not in the brains of control subjects (Pisa, 2015). As noted, amyloid-beta itself has anti-fungal activity (Kumar and Cho, 2016). In a similar regard the antimicrobial peptide, beta-1-defensin, is upregulated in the hippocampus of AD sufferers (Williams et al.).

Curcumin which appears in several studies to have preventive properties with regard to AD (Mitra, 2008) also has anti-fungal potency (Martins et al., 2009). Of historical note Oskar Fischer, a colleague of Alzheimer, first proposed a role for fungus in the development of AD in 1909 when he observed the histologic appearance of brain plaques the resembling actinomycosis (Godert, 2009).

Other agents also share this combination of properties. Rutin, a multifunctional natural flavonoid glycoside, quercetin 3,0 rutinoside, has properties that make it a candidate to protect against neurodegenerative disorders (Habtemariam, 2016) and it too has substantial anti-fungal activity (Lupascu, 2017).

3. BMAA neurotoxin and heavy metals

Another neurotoxin that the Finnish people may come into contact with is beta-N-Methylamino-L-alanine (BMAA), a product of cyanobacteria, also known as blue green algae. Although the neurotoxicity of BMAA was worked out on the other side the world (Guam) by Cox and colleagues (Cox et al., 2003), it has also been found in the mollusks and fish in the Baltic Sea (Jonasson et al., 2010) and the risk is increased in the western parts of the Gulf of Finland, possibly related to differences in salinity (Jiang and Rosen, 2014). Moreover methylmercury potentiates the toxicity of BMAA rendering non-toxic levels toxic by synergistically depleting the antioxidant glutathione (Rush et al., 2012). The Nordic countries have high atmospheric mercury for various reasons and this has also raised the mercury level in fish in lakes in the region (Mercury, 2016). The Finnish diet averages over 72 pounds of fish in a year (National Marines Fishery Service, 2017) (quite high comparatively but not the highest). Methyl mercury levels tended to be higher there than elsewhere (Porvari, 2003). Other Nordic countries with similar ecosystems make up 4 of the top eight countries with the highest rate of dementia death (Food and Agricultural Organization of the United Nations, 2017). Iceland which has the highest rate of fish consumption (Chandler, 2017) has the second highest rate of AD (Mykkanen et al. (1986)) suggesting that fish consumption from certain bodies of water may contribute to the development of AD. Other dietary products such as cereals potatoes, and milk has also been found in Finland to contain cadmium and arsenic as well as mercury (Lahermo et al., 1998), and all heavy metals that could contribute to neurotoxicity.

Several other factors including genetic susceptibility may have bearing as well.

4. Geological considerations

The geological conditions in Finland indicate a low concentration of selenium in soil and ground water (Mäkelä, 1993). Low selenium levels in the soil in Finland could conceivably also contribute to the pathogenesis of AD. Selenium is a vital part of glutathione peroxidase, the anti-oxidant enzyme that is essential to protect human neuronal cells from toxic injury. However selenium enriched fertilizer was used in Finland from 1985 but has been reduced since 1991 (Tyler and Allan, 2014). Arsenic levels in ground water may be high there as well. This too could contribute to the development of AD (Hooper, 2009) and warrants addition measurements.

Hence the high incidence of fatal dementia in Finland appears to be the consequence of a series of environmental factors that promote neuronal cell death by neurotoxins, both biologic and metallic, and the reduction of the protective capacity against such neurotoxins.

5. Suggested evaluation of the hypothesis

There are several ways to assess this hypothesis: