Alzheimer's Disease And Attention Deficit Disorder May Share A Single Cause: Refined Vegetable Oil

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In 1990 I identified a potential cause of typical late-onset Alzheimer's disease (AD), reporting my findings (a small case/control study) in a letter to the New Zealand Medical Journal [Ref 1] in 1993 (letter: "Alzheimer's Disease And Vegetable Oils"). I found that 12 cases of diagnosed AD had all consumed refined polyunsaturated seed oils for many years, contrasting with 20 age-matched control subjects with good memories, none of whom used such oils.

The reason for seeking a dietary cause was simple and compelling: AD had been seen to sometimes affect only one of a pair of identical twins [Ref 2], a striking finding that points strongly to some toxic or dietary cause. In addition, it was very unlikely to be caused by ageing itself, since the other twin was the same age, but remained unaffected in the long term; and because most older people do not in fact get the disease. I reasoned that those who were affected were somehow getting it from their diet, but how?

My initial reading even disclosed a likely dietary suspect: Professor Scott Henderson, an Australian research psychiatrist, cites in his 1988 AD review/hypothesis paper [Ref 3] a remarkable study [Ref 4] done by Professor Denham Harman in 1976, in Nebraska. Harman had a free radical theory of ageing, and knowing that both seed oils and the brain are rich in oxidizable polyunsaturated fatty acids, he wondered whether feeding safflower oil to his rats might cause free radical damage to the brain: it certainly did, as his rats soon lost their way in a maze. Furthermore, giving vitamin E to a new group of rats, fed the same oil, prevented these cognitive deficits—a finding that suggests that his oil, and perhaps other seed oils too, were low in vitamin E.

This work made me very curious about common vegetable seed oils, which were well known to reduce cholesterol and heart disease risk, but nobody had previously suspected them of actually causing a disease, and here they were evidently oxidizing the brain!

Soon after setting out on my library search for a dietary factor in 1990, I discovered that deodorized seed oils lose about a third of their antioxidant vitamin E during refining [Ref 5]—a potentially serious deficiency not seen in the soft margarines made from the same oils,

which suffer polyunsaturate losses during hydrogenation, restoring the vitamin E/polyunsaturate balance. I realized immediately how important this deficiency would be in the brain, whose nerve cell membranes are very rich in highly oxidizable long-chain polyunsaturated fatty acids.

Since the main function of vitamin E is to protect these vulnerable essential fatty acids against oxidation, a low level of vitamin E in the nerve cell membrane would invite cerebral "lipid peroxidation". Oxidation of polyunsaturated fatty acids breaks up the fatty acid chain, and among the fragments are neurotoxic aldehyde molecules.

Oxidized Omega-6 fatty acids, in particular, release the highly reactive aldehyde 4-hydroxy nonenal (4-HNE), whose toxic effects on nerve synapses may account for the faulty memory seen in "Seed Oil Syndrome", described below. But 4-HNE does more than that: it activates a key enzyme involved in AD development, and may also—more importantly--mediate the impaired beta-amyloid clearance caused by cerebral lipid peroxidation.

Elena Tamagno, in Turin, has shown [Ref 6], in recent years, that 4-HNE indirectly activates the pivotal AD enzyme beta-secretase (BACE 1), a small rise in the activity of which causes a sharp increase in beta-amyloid formation [S Cole, Ref 7]. Beta-amyloid is a peptide—a small protein fragment--that is the molecular cause of AD, as in rare genetic cases, where a gene mutation increases the production of a more toxic form of this peptide (the longer form, with 42 aminoacids, rather than the 40 residues seen in the much less toxic and more abundant form).

Although small amounts of this important protein fragment are produced in the normal brain, it is easily cleared away by degrading enzymes, and it can also exit the brain through the blood-brain barrier. However, people consuming refined vegetable oil will be forming increased beta-amyloid in abnormal oxidizing conditions, that may damage the clearance mechanism, resulting in progressive beta-peptide accumulation and, ultimately, Alzheimer's disease.

One possibility is that lipid peroxidation products, like the same 4-HNE, might inhibit a key clearance enzyme, called Insulin-Degrading Enzyme (which also degrades beta-amyloid). In fact, an amyloid clearance problem is all that is required to cause AD, since even a mild over-production of beta-amyloid—as I postulate above—may still be successfully cleared.

So my theory does require a clearance defect, whether or not amyloid production is increased. And now, in 2009, Dr Y Nishida in Japan has shown [Ref 8] that by blocking vitamin E transport to mouse brain, lipid membrane peroxidation ensues, which impairs beta-amyloid clearance, by somehow reducing the expression of the gene coding for the above Insulin-Degrading Enzyme. Vitamin E-depleted seed oils, likewise, lower vitamin E levels in most tissues, causing lipid peroxidation [Y H Wang, Ref 9], which must include the brain, as shown by the early cognitive deficits seen in Harman's pioneering work (above), and their notable prevention with vitamin E.

Common Omega-6 seed oils, which are usually steam-deodorized, have been linked to cognitive decline in Holland [S Kalmijn, Ref 10], and also in Greece [D Psaltopoulou, Ref 11]), and to over double the risk of incident dementia (70% being AD) in the prospective "Three Cities Study" in France [P Barberger-Gateau, Ref 12]. Processed safflower oil, as discussed above, was shown many years ago (1976!) to cause memory faults in rats, which could be prevented with vitamin E. For some reason, Dr Harman did not alert the US food safety authorities to this alarming discovery.

Low vitamin E levels in corn, soya and safflower oils were first demonstrated by Dr David Herting in Rochester, New York State (Ref 5--see "herting d and 1963" on www.pubmed.gov, to find and down-load his free Journal of Nutrition paper). He concluded that widespread vitamin E deficiency would occur in populations consuming processed polyunsaturated seed oils. However, he did not realize the extreme peroxidation vulnerability of the brain and retina, where reduced vitamin E levels mean rapid lipid peroxidation of long-chain Omega-3 and Omega-6 fatty acids, in synapses and in retinal rod cell disc membranes. Had he known this, he could have predicted a new disease of the brain, with the further possibility of a new childhood brain disorder, arising in the fetal brain during pregnancy.

It was precisely these most vulnerable tissues that were tragically ignored in the landmark nutritional study, completed in 1960 in Illinois, on which current recommended daily intake of vitamin E is based [Ref 13]. Although lead investigator Dr Max Horwitt should have been aware of the brain's rich concentration of polyunsaturated fatty acids (mentioned, for example, in 1950s biochemistry texts), he judged vitamin E requirement exclusively by testing the fragility of red blood cell membranes in vitamin E-deprived human subjects, finding even greater fragility when the subjects were given vitamin E-stripped

corn oil.

It did not occur to Horwitt to ask his vitamin E-deprived subjects about higher mental functions like memory or mood. Memory difficulties (and glare sensitivity and night-blindness from retinal damage) are likely to occur long before the red cell test becomes positive in response to gradual dietary vitamin E depletion, because the oxidizable polyunsaturated fatty acids are much less concentrated in the red cell membrane, than in retina and brain. Lipid peroxidation is a very rapid chain-reaction, that proceeds much faster in a vitamin E-depleted cell membrane containing a high concentration of polyunsaturated fatty acids, especially when those fatty acids—as in brain and retina—are of the long-chain variety, full of oxidizable double bonds.

To his credit, Horwitt did realize that the main function of vitamin E is to protect polyunsaturated fatty acids, so he based the recommended daily intake on the ratio of vitamin E to the intake of these fatty acids. He assumed that higher polyunsaturate intake, for example seed oil, would automatically mean higher vitamin E intake, but neglected the possibility that processed seed oils might lose some of this vitamin E during refining, and so cause some new disease specifically involving tissues prone to lipid peroxidation.

Indeed, he failed to pursue this possibility, even when he found that some members of staff at the Elgin Mental Hospital, who were not on the vitamin E deficient test diet, also had an abnormal red cell test. He did not ask himself how that could have happened, but could have taken a dietary history, and might have discovered that they were consumers of common vegetable oils, which could therefore have had something in common with his experimental stripped corn oil: low content of vitamin E. He may then have gone on to investigate the vitamin E content of such oils, and found it to be low—as David Herting found three years later, in 1963. Had Horwitt detected mild memory faults in consumers of refined seed oils, and set himself to do a little thinking, he could have nipped Alzheimer's in the bud, in 1960.

Any child, young person or adult consuming refined seed oils will report, if asked, memory problems, poor dark adaptation and glare sensitivity (photophobia--which is irreversible). I discovered this syndrome in general practice, and I call it Seed Oil Syndrome, and it probably reflects 4-HNE neurotoxicity in the synapses. Lipid peroxidation, which in the long term causes impaired beta-amyloid clearance, has early clinical effects due to synaptic damage: 4-HNE impairs neuronal glucose uptake, among other effects.

I have seen this hitherto undescribed syndrome in 100s of oil-using patients in family practice, over many years. The memory responds well to vitamin E (I sometimes add fish oil, for a faster response), except after the age of 50 or so, when subjects report long-term stability of memory, without actual improvement.

I am hoping that these cases, who, after some 20-30 years of refined oil exposure, may have a significant brain amyloid load, will not progress to AD, once off seed oils, and using olive oil, vitamin E and fish oil supplement. I also have some of them on Inositol, a seed sugar known to neutralize toxic Abeta oligomers [Ref 14] and improve language and orientation in established AD [Ref 15].

This simple glucose isomer, which is easily obtained in the diet (from grains, nuts, legumes, soymilk, cantaloupe and citrus), may prove to be a powerful weapon—along with cessation of refined-oil exposure--in preventing Seed Oil Syndrome progressing slowly to Mild Cognitive Impairment and, ultimately, diagnosed AD. Given the extensive neuronal damage already evident in these two later stages, ultra-early prevention is now thought to be the only way to stop this disease, and nutrition—if it can do the job—is far preferable to preventive drugs.

From the public health angle, all cases of Seed Oil Syndrome—which is easily identified by symptoms and diet history—should change to olive oil (or any cold-pressed oil), eat a high–Inositol diet (even citrus juice is very rich in Inositol), and preferably take fish-oil capsules as well.

Saturated fat intake from butter, cream, cheese, fatty meat, pastries etc., must also be reduced, for it commonly causes co-morbid vascular dementia in the Alzheimer victim.

Inositol, given as a higher dose (5 gm/day) via supplement, also reverses anxiety disorder and depression [Ref 16], which affect perhaps 40% of AD cases. Anxiety alone doubles the risk of progressing from Mild Cognitive Impairment to AD [Ref 17], possibly because of cortisol-induced hippocampal damage, low Brain-Derived Neurotrophic Factor levels and poor hippocampal neurogenesis. Depression, often resulting from anxiety plus fatty diet, may increase inflammation—pro-inflammatory cytokines like Interleukin 1-beta may aggravate neuronal damage and increase stress axis activation even further. Anti-anxiety doses of Inositol also have a place here, by greatly decreasing stress-induced comfort-eating of fatty foods like chocolate, cheese, cakes and pastries [author’s clinical observations].

One extra benefit from Inositol in brain disease is its unexpected anti-ageing effect [Ref 18], a possible example of which is the NIH 31 grain-rich mouse diet, that prolongs the median lifespan of female mice by 25% [Ref 19]. By altering the same genes that are altered by caloric restriction—including the key mitochondrial biogenesis gene PGC 1 alpha—Inositol is clearly a caloric restriction mimetic, with the same potential as dietary restriction to provide neurotrophic, antioxidant and energizing benefits in brain, as described by nutritional neuroscientist Mark Mattson [Ref 20]. Already, a multiple sclerosis animal model has been found to respond well to caloric restriction [Ref 21]: Inositol is a more practical intervention.

Variations in AD incidence around the world (low in West Africa, very high in Wadi Ara Arabs in Israel, 4 times higher in Pittsburgh than in Ballabgarh, Northern India) probably reflect local patterns of refined seed oil consumption. In Northern India, unrefined traditional oils are still very popular (eg. pungent mustard oil, crude peanut oil), and in the South there is mostly coconut oil and crude peanut oil—and possibly an even lower AD rate.

Refined oils are, however, encroaching on these traditional markets. Palm oil is the main cooking oil in Malaysia and Indonesia, where AD rates may be low, but in the US and Europe—and the Middle East too--refined oils are the rule, apart from those people lucky enough to still use mainly olive oil. A study in Bari, Italy, some years ago, showed cognitive decline in older subjects not using olive oil [Ref 22]; they were apparently using common refined supermarket seed oils, which are widely used in Italy for frying.

An oil that causes a serious brain disease in adult life might also be expected to affect the fetal brain: when asking many oil-using patients about symptoms of Seed Oil Syndrome, I have noticed—as a family doctor—that young adults with the syndrome frequently have children with Attention Deficit Hyperactivity Disorder (ADHD). I proceeded to do a pilot case/control study on retrospective pregnancy diet, in 80 cases versus 80 controls.

Almost all (78) of the mothers of ADHD cases gave a history of regular consumption of refined seed oils during all or part of the pregnancy, often from fried takeaway food. All of these mothers had permanent glare sensitivity (most carried sunglasses, usually perched conveniently on their head), and those who still consumed these oils

had ongoing memory difficulties and impaired night vision.

Similarly, I have met young adults with residual ADHD, who report that their mother, if still using such oils, and now in her mid- to late-forties, has an obvious memory problem. The Scottish breath-analysis scientist Brian Ross has found evidence of lipid peroxidation (increased breath ethane gas) in some children with ADHD [Ref 23], probably due to ongoing childhood exposure to the same refined seed oils that caused their condition during gestation.

In my child patients, such further exposure significantly worsens the ADHD, by increasing cognitive problems, mood issues, aggression and impulsivity—all of which improve rapidly by stopping the exposure and recommending fish oil, to assist synaptic recovery and plasticity. Not only does fish oil work faster when refined oils are first excluded from the diet (to prevent peroxidative destruction of the fish oil fatty acids in vitamin E-depleted synapses), but the synaptic benefits of fish oil may be greatly enhanced by adding two more "synaptic building blocks"—uridine and choline—as proposed for Alzheimer's, by nutritional neuroscientist Dr Richard Wurtman, at the Massachusets Institute of Technology [Ref 24]. Uridine sources include brewer's yeast, broccoli and beetroot, while choline is found in egg, chicken, lecithin and wheat germ. Wurtman's "Souvenaid" synapse-restoring mixture, which increases synaptic density and cognitive function in gerbil rats, does improve Alzheimer symptoms, and may work even better in the developing ADHD brain of a young child, to the extent that usual medications for the latter disorder may become obsolete, due to advances in brain nutrition.

I believe there is enough evidence available to conclude that deodorized seed oils are a major public health hazard, being directly responsible for ADHD, widespread Seed Oil Syndrome, and Alzheimer's disease. I notice in my clinic that Seed Oil Syndrome causes depression and irritability in anxious subjects, and aggravates ADHD in children and adolescents, promoting delinquency, serious aggression, antisocial behaviour, and substance abuse. These problems are now endemic in Western cities, and increasing world-wide.

Correction of all such brain peroxidation problems is very simple: to protect their citizens, while at the same time keeping these heart-friendly oils available, governments must be persuaded to pass laws requiring that all deodorized seed oils be rendered safe, with respect to their vitamin E content, before being sold. Natural vitamin E can

easily be recovered from the steam distillate at the food oil refinery, and replaced in the deodorized oil: or synthetic vitamin E could be used instead. Urgent action is required.

The highly desirable result of fixing this seed oil catastrophe would be to eliminate the twin epidemics of Alzheimer's and ADHD, along with the alarming antisocial effects of refined seed oils, as specified above.

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