Alzheimer’s Disease

Alzheimer’s disease (AD) is the most common form of dementia. There is no cure. AD worsens as it progresses, and eventually leads to death. Most often, AD is diagnosed in people over 65 years of age, although the less-prevalent early-onset Alzheimer’s can occur much earlier. In 2006, there were 26.6 million sufferers worldwide. AD is predicted to affect 1 in 85 people globally by 2050. The key here is that there is no cure. Medical treatments to date have been unsuccessful.

The cause and progression of Alzheimer’s disease are not well understood. Research indicates that AD is associated with plaques and tangles in the brain. Current treatments only help with the symptoms. There are no available treatments that stop or reverse the progression of AD.

Cause
The cause for most Alzheimer’s cases is still unknown (except for 1% to 5% of cases where genetic differences have been identified). There are several competing theories to explain the cause of the disease:

The oldest, on which most currently available drug therapies are based, is the cholinergic theory, which proposes that AD is caused by reduced formation of the neurotransmitter acetylcholine.

In the amyloid theory it is thought that beta-amyloid (Aβ) deposits are the fundamental cause of the disease. Large-scale accumulation of amyloid leads to widespread neuro-inflammation. This may happen because of a genetic defect. People with Down Syndrome, who have an extra gene
copy almost universally show AD by 40 years of age. An experimental vaccine was found to clear the amyloid plaques in early human trials, but it did not have any significant effect on the dementia. In 2009, this theory was updated, suggesting that a close relative of the beta-amyloid protein, and not necessarily the beta-amyloid itself, may be a major culprit in the disease. This theory holds that an amyloid-related mechanism that prunes neuronal connections in the brain in the fast-growth phase of early life may be triggered by ageing-related processes in later life to cause the neuronal withering of Alzheimer's disease. A fragment from amyloid is altered by an enzyme, which then triggers a self-destruct pathway by activating a neuronal receptor called death receptor 6 (DR6). DR6 is common in the human brain regions most affected by Alzheimer's. So, beta-amyloid may only play a complementary role, by depressing the function of nerve fiber connections.

The tau theory is the idea that tau protein abnormalities start the disease cascade. Tau protein threads pair with each other to form the neuro-fibrillary tangles classic for AD. They then collapse the involved neurons’ transport systems. This may result first in malfunctions in biochemical communication between neurons and later in the death of the cells.

There are several other theories that may help to explain A.D. Herpes simplex virus type 1 has also been proposed to cause A.D. in people carrying the susceptible versions of the apoE gene.

In another theory the disease may be caused by age-related myelin [the cover of nerve fibers] breakdown in the brain releasing iron, which itself causes further damage. Normal, natural myelin repair processes which are triggered then contribute to the development of protein deposits such as beta-amyloid and tau.

Oxidative stress and rebalancing of biometal metabolism may be significant in the formation of the disease.

AD individuals show 70% loss of local brain cells that make norepinephrine. Norepinephrine acts in this situation as an internal anti-inflammatory agent in the microenvironment around the neurons, glial cells, and blood vessels in the brain cortex and hippocampus. It has been shown that norepinephrine stimulates mouse microglia to suppress production of cytokines. The cytokines are responsible for the breakdown of amyloid.

**Prevention**
There appear to be relationships between certain modifiable factors, such as diet, cardiovascular risk, pharmaceutical products, or intellectual activities among others, and a population’s likelihood of developing AD.

Although cardiovascular risk factors, such as high blood cholesterol, hypertension, diabetes, and smoking, are associated with a higher risk of onset and course of AD. Statins, used to lower cholesterol, are not effective in preventing or improving the course of AD. The components of a Mediterranean diet, which include fruit and vegetables, bread, wheat and other cereals, olive oil,
fish, and red wine, may all individually or together reduce the risk and course of AD. The positive impact of this diet on the cardiovascular system has been proposed as the mechanism of action of the benefit seen. There is also limited evidence that light to moderate use of alcohol, particularly red wine, is associated with lower risk of AD.

Reviews on the use of supplements have not found them to be effective. Fish oil may not slow decline of mental function in the setting of A.D.

Long-term usage of non-steroidal anti-inflammatory drug (NSAIDs) is associated with a reduced likelihood of developing AD. NSAIDs can reduce inflammation related to amyloid plaques. However, research evaluating their use as “palliative” treatment have not shown positive results. No prevention trial has been completed. Hormone replacement therapy, although previously used, may increase the risk of dementia.

Curcumin has not shown benefit in people even though there is tentative evidence in animals. There is inconsistent and unconvincing evidence that ginkgo has any positive effect on cognitive impairment and dementia, and a recent study concludes that it has no effect in reducing the rate of AD incidence. There is tentative evidence that caffeine may be protective. Cannabinoids (marijuana) may show promise in improving the symptoms of AD or dementia in its early stages.

People who engage in intellectual activities such as reading, playing board games, completing crossword puzzles, playing musical instruments, or having regular social interaction show a reduced risk for Alzheimer’s disease, Learning a second language even later in life seems to delay getting Alzheimer disease. Physical activity has also been found to reduce risk of AD.

Some studies have shown an increased risk of developing AD with environmental factors such as intake of metals, particularly aluminum. Smoking is a significant AD risk factor. Systemic markers of the innate immune system are risk factors for late-onset AD.

**Disease mechanism**

Exactly how disturbances of production and accumulation of the beta-amyloid gives rise to the pathology of AD is not known. The amyloid theory traditionally points to the accumulation of beta-amyloid peptides as the central event triggering neuron degeneration. Accumulation of aggregated amyloid fibrils, which are believed to be the toxic form of the protein responsible for disrupting the cell’s calcium ion balance, induces programmed cell death (apoptosis). It is also known that amyloid selectively builds up in the mitochondria (the part of the cell that produces the power for the cell) in the cells of Alzheimer’s-affected brains, and it also inhibits certain enzyme functions and the use of glucose by neurons.

Various inflammatory processes and cytokines may also have a role in the pathology of Alzheimer’s disease. *Inflammation* is a general marker of tissue damage in any disease, and may be either secondary to tissue damage in AD or a marker of an immune response.
Changes in the distribution of different neurotrophic factors and in the expression of their receptors, such as the brain-derived neurotrophic factor (BDNF) have been described in AD.

To understand better what may be happening in the brain to explain the development of AD, the relationship between structure and function of the brain were examined. The cortical thickness, based on structural MRI, and motor cortex excitability were okay assessed with transcranial magnetic stimulation were correlated in AD and mild cognitive impairment (MCI) patients, as well as in age-matched healthy controls, different changes were seen. The nerve excitability of the part of the brain cortex involved in movement (motor cortex) was decreased with less cortical thickness in several areas of the brain. Reduced cortical thickness is suggestive of reduced brain function. Only the sensorimotor cortex was involved in MCI subjects. Other parts of the brain had significant changes both in AD and MCI subjects. In healthy controls the motor cortex excitability did not correlate with the cortical thickness. In AD subjects there seems to be a protective mechanism of hyperexcitability in the sensorimotor cortex counteracting the prominent loss of cortical volume, since the motor cortex excitability did not correlate with the cortical thickness.

In brain mapping of persons with mild Alzheimer’s disease (AD) compared to vascular dementia (VaD) or normal elderly people (Nold), there was a decline of central, parietal, temporal, and limbic alpha 1 (low alpha) sources specific for mild AD group with respect to Nold and VaD groups. Occipital alpha 1 sources showed a strong decline in mild AD compared to VaD group. Theta was largely abnormal in VaD but not in mild AD group. There was lower occipital alpha in mild AD subgroup with more severe disease.

**Role of PEMFs**
As we have noted many times before, PEMFs have general functions and actions relating to all cells, even brain cells. It is these general effects that may help people with or predisposed to AD, even though they are not addressing AD specifically. Not that any current conventional therapy addresses AD at all, except to help people adapt to their condition! The challenge is getting people to start therapy earlier in their disease process or even doing prevention in those at high risk, that is, those with strong family histories.

**Is there evidence that PEMFs help AD?**
Various studies have approached the issue from different directions and used an assortment of PEMF devices.

Research includes high intensity systems, low intensity systems; high frequency systems and low frequency systems. All showed some benefit. I’m not surprised since we’re not yet sure of the final common pathway for the condition. Inflammation is the constant. Inflammation is the constant causal factor in most diseases. So, if we do nothing but address chronic inflammation we could have a substantial impact on the development and progression of AD.

**Transcranial electromagnetic treatment (TEMT)**
In AD mice, long-term TEMT prevents and reverses both cognitive impairment and brain amyloid deposition, while TEMT even improves cognitive performance in normal mice. Three disease-modifying and inter-related mechanisms of TEMT action have been identified in the brain: 1) anti-amyloid accumulation, both inside and outside the neuron; 2) mitochondrial enhancement; and 3) increased neuronal activity. TEMT's mechanisms of action provide extraordinary therapeutic potential against other neurologic disorders/injuries, such as Parkinson’s disease, traumatic brain injury, and stroke.

Even the long-term impact of adulthood cell phone level EMF exposure (GSM, pulsed/modulated, 918 MHz, 0.25-1.05 W/kg) for 6+ months daily, protects against or reverses cognitive impairment in AD mice, while even having cognitive benefit to normal mice. This study extends this work by showing that daily EMF treatment given to very old (21-27 month) AD mice over a 2-month period reverses their very advanced brain amyloid accumulation/deposition. These very old AD mice and their normal litter mates together showed an increase in general memory function. These results show that long-term EMF treatment can provide general cognitive benefit to very old AD mice and normal mice, as well as reversal of advanced amyloid neuropathology. Results further underscore the potential for EMF treatment against AD.

Brain mitochondrial function was evaluated in aged AD mice and normal littermates following 1 month of daily high frequency EMF exposure. In AD mice, EMF treatment enhanced brain mitochondrial function by 50-150% across six established measures, greatest in cognitively-important brain areas. EMF treatment also increased brain mitochondrial function in normal aged mice, although the enhancement was not as robust and less widespread compared to that of AD mice. The EMF-induced enhancement of brain mitochondrial function in AD mice was accompanied by 5-10 fold increases in soluble amyloid compared to presumed disease causing insoluble amyloid clusters within the mitochondria. EMF treatment appears to break apart amyloid clusters. So, brain mitochondrial enhancement may be a primary mechanism through which EMF treatment provides cognitive benefit to both AD and normal mice. Especially in the context that mitochondrial dysfunction is an early and prominent characteristic of Alzheimer’s pathogenesis, EMF treatment could have profound value in AD prevention and treatment through intervention at the mitochondrial level.

While there is an appropriate general concern that high-frequency electromagnetic field (EMF) exposure is a risk to human health, there is a possibility that even these PEMFs may benefit as well as possibly harm. There is evidence that long-term EMF exposure directly associated with cell phone use (918 MHz; 0.25 w/kg) provides cognitive benefits. Both cognitive-protective and cognitive-enhancing effects of EMF exposure were discovered in mice destined to develop Alzheimer’s-like cognitive impairment. In Alzheimer’s disease mice, long-term EMF exposure reduced brain amyloid deposition through amyloid breakdown mechanisms. Also other mechanisms of EMF action are possible, including increased amyloid clearance from the brains of Alzheimer’s disease mice, increased neuronal activity, and increased cerebral blood flow.
Although caution should be taken in extrapolating these mouse studies to humans, even this type of EMF exposure may be useful as a non-invasive, non-pharmacologic therapy against Alzheimer’s disease and may be an effective memory-enhancing approach in general.

Studies have shown motor cortex involvement in Alzheimer’s disease (AD), even in its early stages, despite the lack of clinically evident motor deficit. In addition, research shows that other neurotransmitters, such as gamma-amino-butyric acid (GABA), glutamate and dopamine, also play a role. There is a potential therapeutic effect of repetitive TMS in restoring or compensating damaged cognitive functions in the rehabilitation of AD patients. Based on different patterns of cortical excitability, TMS may be useful to varying degrees in physiological brain aging, mild cognitive impairment, AD and other dementing disorders.

Patients with mild AD received ongoing medication treatment and continuous deep brain electrical stimulation (DBS) for 12 months. DBS drives neural activity in the memory circuit, activating the brain’s default mode network. PET scans found reversal of the baseline impaired glucose utilization in the temporal and parietal lobes that was maintained after 12 months of continuous stimulation. Cognitive examinations found improvements and/or slowing in the rate of cognitive decline at 6 and 12 months in some patients. While DBS is electrical vs magnetic stimulation, it is expected that PEMF stimulation, which induces currents even deep in the brain, would create similar results, but without the invasiveness of DBS.

Patients with cerebrovascular disease and mild executive dysfunction were studied in a randomised, controlled, blinded study. High intensity magnetic stimulation (rTMS) was applied either over the left forehead area (DLPFC) or over the left motor cortex (MC; a control stimulation site) in one session. Stimulation was on days 1 and 4 and the order of stimulation sites (DLPFC or MC) was randomized. Neuropsychological tests included psychomotor speed, executive function, and memory. Mild but significant stimulation results were seen in executive functioning with DLPFC but not in the MC in digit symbols testing. There was no measurable effect of rTMS in any other neuropsychological test.

Brain action benefits are possible even with low intensity PEMFs. Patients who had sustained traumatic brain injuries and who exhibited mild to moderate brain impairment according to standardized tests received 30 min. of weak (1 microT) burst-firing magnetic fields across the temporal lobes once per week for 5 weeks. There was a significant improvement of depression and reduction of phobias while physical symptoms and other complaints were not changed. Since AD patients have multiple neurological issues happening simultaneously, including depression and other psychological issues, this study is important in showing that even very weak PEMFs may help with depression and phobias and perhaps other brain functions.

Visual memory and visuoconstructive function abnormalities commonly occur in patients with Alzheimer’s disease (AD). Electromagnetic fields (EMF) of extremely low intensity (in the picotesla range) and low frequency (in the range of 5Hz-8Hz) improved visual memory and visuoperceptive
functions in patients with Parkinson’s disease. A subgroup of Parkinsonian patients with dementia, have been treated with extremely weak EMFs to the brain. Treatment with EMF resulted in a dramatic improvement in visual memory and enhancement of visuoconstructive performance as well as improvement in other cognitive functions, such as short term memory, calculations, spatial orientation, judgment and reasoning as well as level of energy, social interactions, and mood. The rapid improvement in cognitive functions in response to EMF suggests that some of the mental deficits of AD are reversible, being caused by a functional (i.e., synaptic transmission) rather than a structural (i.e., neuronal plaque) disruption of neuronal communication in the central nervous system. Again, this study with very low frequency and very low intensity PEMFs shows many improvements in functioning of patients with Parkinson’s disease accompanied by AD.

While there is always room and need for much more research in this deadly and currently untreatable condition, PEMFs of various kinds, high intensity/low intensity and/or high frequency/low frequency show potential for dramatic benefits without toxic or invasive treatments. The risk benefit ratio clearly favors benefit. Generally, the cost of treatments, that are available to be applied in the home setting on a regular basis, would amount to pennies per day. This would decrease the burden not only on the patient with AD but also on their caregivers. Longer-term human trials are clearly necessary to establish what the potential for long-term benefits would be and also whether they could be used for prevention, in the setting of familial risk or the beginning stages of mild memory impairment. Considering that this is a progressive condition, usually leading to death, for which there is no currently known therapy, involving millions of people, PEMFs certainly appear worth trying. Needless to say, the more advanced the condition is already, the less favorable the results are going to be.

References


