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Perspective

Is there a Connection between Alzheimer's Disease, Magnetite and Prions?

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Abstract

Magnetite and prions are obviously connected to Alzheimer's disease (AD). An increase in the amount of magnetite has been observed in the brain of AD patients and prions are involved in the formation of amyloid plaques. It has been postulated that these two compounds together are involved in storage of memory in the brain. It is not surprising that the two most stable compounds in the brain have "found each other". In this system several things could go wrong. For example there could be disturbances in the connection between magnetite and the protein resulting in memory problems. Several other diseases like type 2 diabetes and schizophrenia are linked to AD.

Keywords: Alzheimer's disease; Magnetite; Prions; Memory

Abbreviations

Alzheimer's Disease

Introduction

AD is a complex multifactorial disorder associated with protein aggregation. Amyloids are highly ordered protein aggregates associated with many diseases including AD. Common cellular prion proteins, not the beta amyloid plaques themselves are needed to produce the cognitive impairments associated with AD [1]. In plaque core material magnetite has been detected as the dominant iron compound [2]. Disrupted closed compartments inside neurons releasing nanocrystals of magnetite to the surrounding cytoplasm are one possible trigger for the development of several neurodegenerative disorders [Størmer-2009].

It has recently been suggested that strings of magnetite together with prions are involved in memory storage in the brain [3]. The magnetite chains behave like paramagnets which display a response to incident signals but its magnetism drops to zero after each signal. Incident impulses could be received and reshaped by the nanocrystalline magnetite to a form that is accepted by the proteins where the information is possibly stored. Both magnetite and prions are well suited for being involved in memory storage. Prions are highly expressed in neurons and the sequence patterns are conserved in evolution. They may play an important role in the cellular function in the central nervous system. It could be a connection between the release of prions from the neurons and the formation of amyloid plaques.

Magnetite is a ferromagnetic compound

Magnetite (Fe_3O_4) exhibits permanent magnetization. It is magnetic at room temperature. These nanocrystals are synthesized de novo and they are perfect crystals without impurities.

All cells in the body contain ferritin. It is a large multifunctional multisubunit protein that produces magnetite from ferrous iron and oxygen. Ferritin is a spherical protein shell with a 8 nm core diameter. The magnetite produced in ferritin must have a maximum this diameter in order to be released. The crystals observed in the brain are in the range of 10-70nm [4]. Therefore they must grow to the appropriate size outside the ferritin molecule by an unknown mechanism.

Magnetite in human brain

In the human brain it is 5 million nanocrystals per g tissue [4] and it is also described from heart, spleen and liver [5].

Biogenic magnetite is associated with neurogenerative diseases like Alzheimer and Parkinson. It has been shown that the amount of magnetite present is generally high in the Alzheimer brain [6,7]. In some cases the values are as much as 15 times greater than in the controls. Magnetite is present in human hippocampus [8,9].

Are prions involved in memory storage?

Prions, mostly known for causing several degenerative diseases, can also play an important role in healthy cells. Prions are obviously candidates to be involved in memory storage. Proteins play a role in the formation of long term memory in fruit flies (*Drosophila)* [10]. The prion-forming protein Orb2 is necessary for memory to persist. Orb2 exists in two forms, Orb2A and Orb2B where Orb2B is the most common. Orb2A has a half life of only about one hour but it can be stabilized by a protein called TOB. The specific proteins involved in long term memory have also been identified in the neurons of mice, human and a sea snail *(Aplysia)* indicating that a basic mechanism appears to be conserved across species. It has been a popular belief that long term memories are stored in the synapses. Newer findings indicate that this is not the case but that the memory is stored in the neurons [11].

Are magnetite and prions involved in the storage of memory?

Nanocrystalline magnetite has been suggested to be involved in memory storage [12,13] The magnetite crystals have been observed to be organized into linear chains in humans [4,14] with up to 80 crystals in the chain [15]. For example magnetotactic bacteria contain biogenic magnetite in chains and such chains have also been described in salmon [16,17]. The behavior of magnetite nanoparticles

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can be attributed to their size. When the size gets small enough they are in the paramagnetic state i.e. that it loses its magnetization when the external magnetite source is removed. Many such crystals in a string will behave like a paramagnet.

The incoming electromagnetic signals could possibly be transformed by the magnetite chain to a signal that can be accepted and permanently stored in the protein counterpart in the information storage center. Therefore magnetite is unlikely to be the substance in which the information is permanently stored. This could also explain the role of magnetite in animal's navigation using the Earth's magnetic field where it increases the strength of the weak incoming signals.

To my knowledge the prions are the most insoluble and stable organic compounds in the brain. Prions are characterized by an unusual resistance to thermal or chemical treatment and all known prions can induce the formation of an amyloid form.

It is well known that amyloid peptides are a key player in the pathogenesis of Alzheimer's disease and they accumulate in the spaces between the brain cells. The released prions could contribute to the formation of amyloid plaques. Dysfunction in neuronal communication is almost certainly the underlying cause of many neurologic diseases such as AD [18]. Similar problems could arise when the connection point between magnetite and prions were out of balance. All the steps leading from incoming electromagnetic signals to the neuron and to the release to other neurons could be disturbed, resulting in memory loss.

The removal of beta amyloid plaques in a mouse model has recently been reported where it accumulates in the spaces between neurons and interferes with the communication between them. After ultrasound exposure 75% of cleared plaques were observed and they restored memory function to the levels observed in healthy mice [19]. "It is obvious that the basic memory system is intact but that the signals leaving the neurons are disturbed. Therefore it should be possible to restore memory in AD patients if the amyloid plaques could be removed. In addition, it should be possible for the patients to store incoming information without being able to use it" [20].

The cryptochrome and magnetite connection to dementia

Cryptochromes are mediating a response of blue light falling on the retina, triggering a cascade of reactions like the formation of free radicals. They are also involved in circadian clock rhythms. One of these intermediates has magnetic properties and is expected to be sensitive to a magnetic field. It could be the link to the magnetite in the brain that could possibly lead to dementia [21].

Place cells, which are neurons in hippocampus, are involved in the planning of the route that rats are going to perform [22]. The grid cells in the rats participate in spatial localization. Such neurons have also been localized in human which indicate that we navigate by the same system [23]. The "end station" for the possible effect of blue light could well be these cells since many demented persons have navigation problems.

AD linked to circadian rhythms and memory dysfunction

It has been suggested a connection between circadian rhythms and memory dysfunction in schizophrenia patients and elderly patients often also suffer from Alzheimer's disease or other forms of dementia. In addition the same regions of the brain were affected [24]. Possibly there are links between circadian rhythms, cryptochrome and magnetite and this could be disturbed in schizophrenia patients [25].

Why one neurodegenerating disease or schizophrenia is developed, may be due to genetical and or environmental factors. For example cryptochrome mutations have been reported for mice resulting in altered circadian rhythms [26].

Type 2 diabetes arises as consequence of interactions between genetic predisposition and environmental triggers like disturbances of circadian rhythms and it has been shown that disruption of circadian rhythms accelerates development of the disease in rats [27]. Experiments with mice indicate a link between diabetes and memory [28]. Type 2 diabetes has been suggested to be an early stage of Alzheimer because it can damage the blood vessels by reducing or blocking the blood flow to the brain and lead to mild cognitive impairment memory problems that are usually present in normally ageing. It could leave the neurons more exposed to damaging influences and possibly lead to AD [29]. There may therefore be links between diabetes, memory and magnetite in the brain [30].

Conclusion

Magnetite and prions are the most insoluble compounds in the brain, both are involved in the development of AD and they are suggested to be involved in memory storage. In iron-rich plaque core material, magnetite was found to be the dominant iron compound. It was indicated that abnormal iron biomineralization processes are likely occurring within the plaques or the surrounding diseased tissue and may play a role in aberant peptide aggregation [2]. Could it be a connection between the magnetite-prion storage system and AD? For example in the link between the magnetite chain and the prions?. It has been speculated if the magnetite formation in the ferritin core associated with ageing become abnormal and uncontrolled in AD brain [31].

When blue light hits retina, a cascade of chemical reactions occur that results in a magnetic intermediate. Disturbances in this system can influence on the development of diseases like schizophrenia and type 2 diabetes which also are linked to AD. Common for these diseases are that they are influenced by the circadian rhythms which in turn are linked to the blue light and cryptochrome system in retina.

If this magnetite-prion model is correct, much could possibly go wrong. Disturbance of the incoming electromagnetic signals. Defects in the magnetic chain. Problems with the signal transmission from the chain to the prions and altered protein configuration. The transfers of signals to other neurons are not working properly. These questions open a new avenue in studying AD and other memory related diseases and how further studies should be directed.

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