



Long-term memory in brain magnetite

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SUMMARY

Despite theoretical and experimental efforts to model neuronal networks, the origin of cerebral cognitive functions and memory formation are still unknown. Recently, we have proposed that in addition to chemical and electrical signals, the cellular components of the neocortex (especially neurons and astrocytes) may communicate with each other through magnetic signals generated by themselves. This magnetic communication would be the ground of short-term memory. In the present paper, we propose that brain magnetite may be a component of the mechanisms, conserved during evolution, to detect and transduce magnetic fields generated inside the cerebral neocortex. Specifically, we propose a possible role for magnetite nanoparticles, distributed through neuronal and astroglial membranes, in perception, transduction and storage of information that arrives to the neocortex.

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Introduction

It is widely accepted that neocortical functions are accomplished solely through utilization of complex networks of neuronal connections, which integrate a huge number of inputs from multiple peripheral organs at the same time. Integration of such a lot of inputs seems to be mediated by electrical and chemical signals generated by networks of neurons firing interactively and at coherent rates. However, despite theoretical efforts to model neuronal networks, the origin of neuro-cognitive functions and memory formation are still unknown. Recently, we have proposed that in addition to chemical and electrical signals, the cellular components of the neocortex (especially neurons and astrocytes) may communicate with each other through magnetic signals generated by themselves [1,2]. In this context, we propose a role of brain magnetite in long-term memory and retrieval.

Magnetite has been found in a taxonomically diverse range of organisms (from bacteria to humans) some of which are known to orient to external magnetic fields [3–5]. Magnetoreception is currently under intensive investigation, and it has been the issue of theoretical and experimental reviews [6–10]. However, the interest for magnetite in neurobiology increased exponentially, since the discovery that these nanocrystals were in the human brain [11]. Now, magnetite has been seriously implicated, even, in neurodegenerative and neoplastic diseases [12–16].

On the other hand, the assumption that magnetite is not only sensitive to magnetic fields, but also can take part in the inheri-

tance of magnetosome polarity has been raised a long time ago [17,18]. It was the first possibility to “heredity without genes”, namely, that the process of information fixation did not take place only within the DNA but in biomagnetites, and yet this fixed information could be manifested at the DNA level.

In the present paper, we propose that brain magnetite may be a component of the mechanisms, conserved during evolution, to detect and transduce magnetic fields generated inside the cerebral neocortex. Specifically, we propose a possible role for magnetite nanoparticles, distributed through neuronal and astroglial membranes, in perception, transduction and storage of information that arrives to the neocortex.

Biochemical and biophysical characteristics of biomagnetite

Magnetite crystals found in organisms (biomagnetite) have particular characteristics that distinguish them from geological magnetite. It is a ferrimagnetic iron oxide that crystallize in the prismatic or isometric system (crystallographic axes of equal length at 90° to each other), while inorganic magnetite are usually small octahedral crystals. Biomagnetite is made from alternating lattices of Fe(II) and Fe(III), which are antiferromagnetically coupled. This alternation of lattices and their corresponding differences in the number of unpaired electron spins supplies magnetite its strong magnetization [14]. Magnetite found from magnetotactic bacteria to human's brain is chemically pure and were found to be organized into magnetically interacting clusters and linear membrane-bound chains a few μm in length. Individual crystals faces are aligned along the length of the chain axes, maximizing the magnetic moment per particle with the faces of adjacent crystals

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lying perpendicular to the chain axes [14]. These chains of many crystals are structurally well-ordered and form single-domain magnetite, which means that its generation must be under precise biological control [4,11,19]. Then, most magnetite isolated from animals is in the form of single-domain crystals similar to those found in magnetotactic bacteria. Single-domain crystals are permanently magnetized and then, can twist into alignment with an external magnetic field. A magnetic pulse antiparallel to the magnetization direction causes the magnetic moment to reverse direction. Then, the controlled application of weak static magnetic fields may cause the rotation of single-domain magnetite, which may be transduced in other physiological functions as may be the opening of ionic membrane channels [5,20] resulting in the modulation of the transmembrane potential and/or generation of action potentials in neurons.

In addition, biomagnetite also exist in a form called superparamagnetic magnetite that has different magnetic properties than single-domain nanocrystals. These properties are based on the fact that kT energy is comparable to the energy pinning the magnetization to make remanent magnetization possible. Then, superparamagnetic crystals do not have a permanent magnetic moment in the absence of an external magnetic field [21], but if an external magnetic field is present, the crystal develops a magnetic moment that track the direction of the local magnetic fields, without rotation of the crystal itself. Thus, superparamagnetic magnetite tends to track the direction of an external magnetic field, whereas the magnetic axis of single-domain magnetite is fixed and stable under the same conditions. Under external magnetic fields, superparamagnetic magnetite may generate fields strong enough to attract or repel adjacent crystals providing the basis for a possible transduction mechanism [20–23]. In view of the above mentioned, it is possible that a previously suggested coupling between magnetic fields and membrane depolarization through superparamagnetic magnetite can exist [24], detecting the direction or the intensity of one magnetic field or an array of structurally organized magnetic fields.

Brain magnetite and its possible role in neocortical memory

Magnetic sources in the brain

Various studies on iron storage, magnetic resonance imaging and biophysical effects of static or extremely low-frequency magnetic fields on humans, assumed that there was not permanent magnetized material in the human body. However, the ferromagnetic mineral magnetite was discovered in human brain in 1992 by the group of Joseph Kirschvink [11]. Although the total amount of magnetite in adult human brain is small (a few micrograms) there are several million crystals per gram, distributed diffusely over all the brain. Likewise, magnetite in human brain tissue occurs mostly in the brain surface and regions associated with memory, such as hippocampus and cerebellum [11,14,25–27]. Indeed, some reports have proposed that biomagnetite is homogeneously distributed in cell membranes of neurons and glial cells, playing a role in the biophysical or biochemical mechanisms of membrane ion channels [20,24].

Although there are grounds for thinking that magnetite may be a toxic substance in the brain, having in account that magnetite has been found throughout the brain [3,11,12,14,25] and specifically in regions associated with memory, it is not surprising that magnetite were found in senile plaques as consequence of neuroglial degeneration [14].

Posterior studies have demonstrated that the brain generates magnetic fields that belong from different components. Using various magnetic methods it was found that brain cells contribute to

the strongest magnetic signal, followed by the iron in the blood of the brain, the ferritin (an iron-carrying protein found in nanoparticle form) and a fourth component composed by either the iron-oxygen magnetite (Fe_3O_4)/maghemite ($\gamma\text{Fe}_2\text{O}_3$) [25].

Background hypothesis

In an attempt to understand superior cerebral functions such as memory and other cognitive functions, we have proposed a new hypothesis that connects recent neurobiological data with classical physic (electromagnetic forces) and modern nonlinear science (self-organization, attractors). Based on neuroanatomical and biophysical data, we have suggested that besides electrical, molecular and synaptic communications into the neocortex, there is a magnetic interplay between neuronal and astroglial networks [1,2], which is consistent with the statistical mechanics of neocortical interactions [28,29] for explain memory and cerebral computation. This hypothesis suggests that neural activity-associated magnetic fields (NAAMFs) generated into neocortical minicolumns, can determine, over time, the intensity and orientation of the static magnetic fields in neighboring astrocytes (Fig. 1a). This would result in the generation of complex but specific 3-D magnetic structures supported by the astroglial network, which in combination with columnar attractor states would constitute the basis of short-term memory (Fig. 1b) and other cognitive functions [1,2].

Cells can be defined by an electromagnetic field supported by the complex distribution of ions, molecules, macromolecules and other biochemical structures, which generate distribution of charge density and current density. Every living cell carries these two sources that ensure an associated bioelectromagnetic field [30]. Neurons generate alternating (time-varying) magnetic fields, while astrocytes have associated static magnetic fields [31–33]. Thus, we have proposed that magnetic storage of information can be accomplished through astrocytic parcellation of the cortical neuropil into small cellular domains [1,2]. These cellular domains can work in a similar way than those drawn from other physical systems, such as artificial magnetic memory storage devices. These systems work by reorienting permanent magnetic domains (dipoles), which are stuck to the tape substrate. In the same way, cellular magnets formed by astrocytic domains can be modified in response to adjacent alternating neuronal magnetic fields. Since astrocytic magnetic fields would be stuck to the astroglial network, the potential change in the polarization of these magnetic fields in the space around neuronal minicolumns and layers may result in specific 3-D magnetic structures that would support many complex physical representations into the neocortex and, then, short-term memory (Fig. 1b). These 3-D physical constructs may result from astroglial magnetic fields self-assembly, since magnetic interactions are insensitive to the surrounding medium and to the details of surface chemistry, they have a wide range of distances over which they can act and, finally, magnetic dipoles tend to form stable constructs following specific physical laws [34].

Present hypothesis

Traditionally, electromagnetic fields (EMFs) bioeffects have been explained as a consequence of biophysical interactions between EMFs and membranes, leading to changes in cell behavior. Recently, it has been proposed a neural transduction hypothesis for explain EMFs effects in cells [20]. This hypothesis suggests that EMFs exposure will result in the modulation of the membrane conductance of ion channels, through interactions with extracellular or membrane-bound proteins.

We propose that biomagnetite may have a key role in the transduction of the magnetic signals produced inside the neocortex itself (Fig. 1). In virtue of their physico-chemical properties, it is

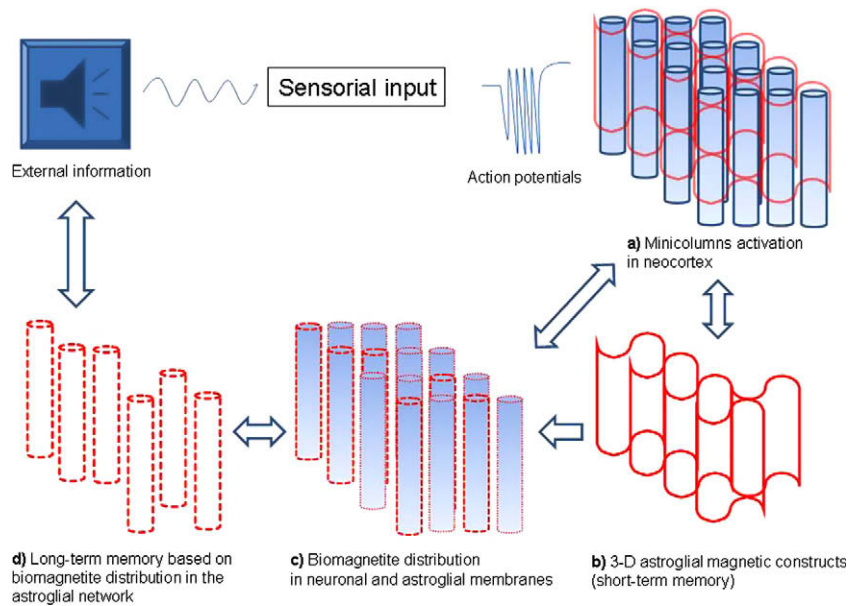


Fig. 1. Long-term memory based on the magnetite nanoparticles distributed in neuronal and astroglial membranes (see text): (a) cylinders represent neuronal minicolumns in the neocortex; (b) network that represent 3-D magnetic structures generated by self-organization of multiple astroglial magnetic fields; (c) biomagnetite distribution on neuronal and astroglial cells; (d) long-term memory based on single-domain magnetite distribution in the astroglial network.

plausible that magnetite crystals were synthesized and distributed in the human brain in a specific and controlled form. Having in account that neurons and astrocytes generate the strongest magnetic fields into the brain [25] and that magnetite seems to be homogeneously distributed in neuronal and astroglial membranes, we suggest that: (a) NAAMFs may drive the distribution and organization of biomagnetite nanoparticles (single domain and/or superparamagnetic) in neuronal membranes, which would result in a non-random distribution of these crystals in neuronal surfaces; (b) if alternating magnetic fields associated with each neuron activity drive magnetite distribution on their own membranes, this would mean that each neurons might have a specific biomagnetite hallmark, depending on their activity and connectivity; these magnetite signatures would change depending on long-time activity of each specific neuronal circuit and would constitute a dynamic process; (c) this non-random but specific distribution of magnetite on neuronal surfaces might have an important role in the induction of static 3-D magnetic constructs in neocortical astrocytes (Fig. 1b and c); (d) this organization of static (dc) astroglial magnetic fields generated around neuronal minicolumns would influence magnetite nanoparticles distribution in astroglial membranes; (e) this biomagnetite distribution in neocortical astroglial network would store long-term information (Fig. 1d).

Predictions of the model

The controlled distribution of biomagnetite in neuronal and astroglial membranes would have a fundamental role in the transduction mechanisms of magnetic signals generated inside the brain. The model proposes that biomagnetite distribution in astroglial network support long-term memory and would generate 3-D magnetic construct of sufficient intensity to affect magnetite nanoparticles localized in adjacent neuronal membranes. This predicts that each neuron might have a specific response to the effects of adjacent astroglial magnetic fields depending on the distribution of magnetite biocrystals in its own membranes. This bidirectional (Fig. 1) magnetic cross-talk would be the basis of long-term memory and retrieval, and would explain basic processes known as memory plasticity and learning. Besides, self-organization of

astroglial magnetic fields in 3-D magnetic constructs can work as complex and dynamic physical attractors, driving and modulating spontaneous neuronal activity in the neocortex [35–37]. This could explain some “spontaneous” cognitive functions as the result of magnetic physical properties that arise naturally as consequence of the cytoarchitectonic organization of biomagnetite in the neocortex. Consequently, creativity, imagination, thinking and dreams would arise “spontaneously” when magnetically memorised items of information in the astroglial biomagnetite network drive feed-forward coherent and synchronised neuronal activities in specific minicolumns and layers. In this model, dreams may be constructed from starting magnetic physical states that give diverse partial information previously stored in the astroglial biomagnetite network. Then, the model predicts that the integration and self-organization of multiple astroglial magnetic fields may store external information for long time, which would be retrieved by specific neuronal responses. These responses would depend on the specific distribution of single-domain and superparamagnetic magnetite nanoparticles in neuronal membranes and the controlled manipulation of their magnetic moments according to neighboring astroglial magnetite network.

Summary

Here we proposed a new role of magnetite nanoparticles in the human brain. Biomagnetite may be a component of the mechanisms, conserved during evolution, to detect the magnetic signals generated into the neocortex itself. Specifically, magnetite might be implicated in the magnetic communication between neuronal and astroglial networks, playing a key role in neocortical memory.

Conflict of interest statement

None declared.

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