Alzheimer's disease / Vascular dementia & PEMF

Background

The two most common types of dementia are Alzheimer's disease (AD), which constitutes around 60% of dementia cases and vascular dementia (VaD) with around 20%. Although both main types of dementia are associated with similar symptoms, the pathological mechanisms are very different. While VaD is caused by a reduced blood supply to the brain due to deteriorating blood vessels, AD is characterized by synapse loss, neuronal atrophy, and an abnormal accumulation of amyloid beta (Aβ) protein resulting in senile plaques, which can disrupt signals between neurons and cause inflammation. Furthermore, tau proteins inside the neurons form neurofibrillary tangles causing unstable microtubules and eventually neuronal death. Additionally, dementia often show more than one underlying pathology, which is known as mixed dementia (MD). The most common form being a combination of AD pathology with vascular components from VaD.

Dementia is often associated with numerous comorbidities, defined as diseases that co-occur on top of a primary disease. Dementia patients with comorbidities present with a higher rate of cognitive decline; hence modification of lifestyle and treatment of comorbidities have beneficial effects on cognition and could delay or even prevent the onset of dementia.

Formation model and therapies

Currently, there is no effective treatment against AD, and its pathogenesis remains unclear. A possible involvement of genetic, immunological, environmental causes, and a virus infection are discussed. Age, family history, inheritance, oxidative stress, disruption of calcium homeostasis, hormonal factors, inflammation, and vascular and cell cycle dysregulations can influence the disease. And growing evidence supports the concept, that AD possibly is a metabolic disease, due to insulin and IGF (insulin-like growth factor) resistance [1],[2],[3],[4]. For instance: IGF-1 has a major role in regulation tau phosphorylation in brain [5] or can control Beta-Amyloid clearance from brain [6]

PEMF in AD - fundamental aspects

There are emerging evidence to support the biological effect of **PEMF** in the treatment of various neurological disorders including dementia [7],[8]. Throughout life, adult neurogenesis generates new neurons in the hippocampus that have a critical role in memory formation. Strategies able to stimulate this endogenous process have raised considerable interest because of their potential use to treat neurological disorders entailing cognitive impairment. And there has been previously reported that mice exposed to extremely **low-frequency electromagnetic fields** showed increased hippocampal neurogenesis [9]. And even a chronic exposure to **ELF magnetic fields** exerts a positive effect on the acquisition and maintenance of spatial memory [10].

And behavioral studies have shown the **PEMF** could affect human cognitive function [11] and protect from the cognitive impairment or impact the memory and behaviour in mice [12]. On rats, **PEMF** exposure showed a reduction in escape latency and improved long-term memory in rats [13]. Just as a **PEMF** (1 mT / 2 hours over 9 days) significantly saved the short-term memory and suggested that it ameliorated

cognition memory in rats [14] And a special PEMF called rTMS (repetitive transcranial magnetic stimulation) is clinically used to re-establish cognitive performance in stroke patients [15] and in patients suffering from neurodegenerative diseases [16] like AD-related cognitive dysfunction [17] But as you know: rTMS do not have much in common with PEMF.

By now, first results by real **PEMF** have be released. In a recent study, **PEMF** were able to modulate the cytoskeleton function (the cytoskeleton is a structure within a cell, that helps cells maintain their shape and internal organization) and to promote the neuronal differentiation of the bone marrow mesenchymal stem cells. In particular, **PEMF** also promote the neuronal differentiation in vitro [18],[19],[20],[21] and the hippocampal neurogenesis (hippocampus = brain structure that has a major role in learning and memory) in vivo [22].

This should come as little surprise, because **PEMF** has proven long ago delaying cellular senescence [23]. Moreover, it can affect the redox status within cells, thus evoking a general stress response. Accordingly, in an AD mice model, high-frequency **PEMF** treatment induced an improvement of cognitive functions - probably by an enhanced clearance of the amyloid plaques, increased neuronal activity, and increased cerebral blood flow [24]. This is all the more remarkable since - despite numerous studies - there is no real evidence that high-frequency electromagnetic field (**EMF**) exposure is a risk to human health. To the contrary, this presents the first evidence that long-term EMF exposure directly associated with cell phone use (918 MHz) provides cognitive benefits. Naturally with the restriction that caution should be taken in extrapolating these mouse studies to humans.

On the other hand, it has been demonstrated, that - in vitro - low-frequency **EMFs** can modulate gene expression, that allows a rapid adaptation of protein levels to changing environmental conditions and as to how a somatic cell behaves [25]. Obviously so-called miRNAs are responsible, since they are predicted to regulate up to 90 % of human genes [26]. So, a recent study demonstrated the ability of a low-frequency **PEMF** to modulate gene expression in cell functions that are dysregulated in AD [27]. And in a current study of 2021, repeated **PEMF** exposure lowers a beta-amyloid level in primary human mixed brain tissue cultures [28]

According to a recent study, rats that got an artificial created AD, showed that the mean escape latency * was reduced by 66 % under the exposure of **PEMF**. Furthermore, the IGF-2 gene expression significantly increased compared to the control group [29]. This indicates that **PEMF** exposure can improve the ability of learning and memory in dementia rats and this effect may be related to the process of IGF signal transduction.

Escape latency time:
For experiments with rats typical maze dimensions are a tank with a diameter of 1 to 2 meters, in which a 10–15 cm platform is placed. One of the most commonly used performance measures is the escape latency, defined as the time for the animal to find the platform and escape the maze. It says a lot about hippocampal-dependent learning, including acquisition of spatial memory and long-term spatial memory

In further studies an application of ELF-PEMF not only has improving effect on different cognitive disorder signs of AD animals, but also disrupts the processes of AD rat model formation [30] and reduced the number of Aβ plaques in the cortex and hippocampus of mice [31]. So **PEMF** could be used at least at early stage of neural degeneration in case of AD and other diseases with amyloid protein deposition in other tissues.

Constraints

Despite the reported positive effect of **PEMF** on dementia rats, some studies reported controversial findings. For example: No effects on learning and memory abilities in rats [32]. Or other results indicated that magnetic field can damage the cognition function in rats [33],[34]. But these inconsistencies may be attributed to the differences of **PEMF** parameters such as intensity and duration of the applied **PEMF**.

Conclusion

Although the **PEMF** has therapeutic potential for dementia, the associated neurobiological mechanisms are yet unclear. Nevertheless we can conclude that **EMF** exposure may represent a non-invasive, non-pharmacologic therapeutic against Alzheimer's disease and an effective memory-enhancing approach in general.

PEMF in vascular dementia

Admittedly, studies mentioned all relate to AD. Therefore question arises whether there are publications in the field of vascular dementia and **PEMF** too.

Applied **ELF-MF** has possible neuroprotective function in the hippocampus, as the most sensitive brain structure in the model of global cerebral ischemia, through reduction of neuronal death and activation of astrocytes and microglial cells [35]. And it is well known that PEMF effects are mediated by increased nitric oxide (NO), which is a vasodilator, creating a sharp increase in microvascular perfusion, for example in rat brain [36] or an increase in capillary permeability by a significant increase capillary vasodilation [37] An initial study showed, that 30 minutes of **PEMF** treatment induced cerebral dilation leading to an increase in microvascular blood flow and tissue oxygenation that persisted for at least 3 hours. This results suggest that **PEMF** may be an effective treatment for at least patients after traumatic or ischemic brain injury [38]. And for instance: with **QRS-treatment** that happens after 3 minutes But that is not a proof for a vascular dementia.

There is only a study form the 1990's where **PEMF** in picoTesla range resulted in a dramatic improvement in visual memory and enhancement of visuoconstructive performance which was associated clinically with improvement in other cognitive functions such as short term memory, calculations, spatial orientation, judgement and reasoning as well as level of energy, social interactions, and mood [39] 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., neuritic plaques) disruption of neuronal communication in the central nervous system.

But possibly, we should consider a vascular dementia from another point of view. Because many studies have shown that hypertension increases the risk of cognitive disorders, Alzheimer's dementia, and vascular dementia [40]. A hypertension-induced damage can also include changes to cerebrovascular structural and function, which

in turn can cause the neuropathological abnormalities responsible for cognitive deficits, such as micro-infarcts, microbleeds, silent brain infarcts, and brain atrophy [41],[42]. Other structural damages to the brain caused by arterial hypertension include remodeling of the cerebral artery and endothelial dysfunction, which cause altered cerebral blood flow (CBF) autoregulation, blood-brain barrier disruption, and cerebrovascular regulatory mechanism impairment. Therefore managing and controlling hypertension and blood pressure variability could preserve cognitive functions. And the detection of hypertension, and the reduction and control of blood pressure are protective measures against later-life cognitive decline [43]. And **PEMF** treatment offers reductions in systolic and pulse blood pressure and suggests that this might be linked to improvements in peripheral resistance or circulation [44].

Setting recommendations:

Proram:	Basic or Relax
Intensity:	Evidence for pT, µT and mT
Duration:	a. AD: 24 - 60 minutes / 1 - 2 times a day
	b. Vascular dementia: 8 - 16 minutes / 1 - 2 times a day
Applicator:	Pillow

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