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Alzheimer Theories: Tau Pathologies Induced by Brain Protein Nanoparticles Agglomeration

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Abstract

Tubulin binding protein (Tau) represents the subunit protein of one of the major hallmarks of Alzheimer disease (AD) and could be used as an indicator of disease mechanisms. Tau pathologies could be explained by unfolded protein and can be considered by nanoscience as non-linked nanoparticles (NPs). Interestingly, non-linked NPs have large number of conformations. Pathological aggregation of Tau protein is limited to non-linked NPs giving motifs forming β structures. The aggregation of Tau is toxic in cell and animal models. Alzheimer theory point to a mechanism of toxicity related to structural conformations of coated NPs to non-linked NPs under natural or artificial electromagnetic field. However, research-using nanosciences associated to electromagnetic field in neurodegenerative disease, as Tau pathology, were poorly understood. Brain protein considered as Nps could agglomerate and enhance protein 3D conversion; leading to Tau pathologies as neurodegenerative disease (Alzheimer diseases, Parkinson diseases…).

Keywords:* *Tau pathology; Alzheimer; Nanoparticle; Folding; Unfolding; Brain

1. Introduction

For cell biologists and neuroscientist, Tubulin binding protein (Tau) was one of the first microtubule-associated proteins (MAPs) to be characterized. Tau research aim to identify the components of the abnormal protein in the brain of Alzheimer patients. One of them, Aβ, was considered as extracellular amyloid plaques. The highly acidic carboxy-terminal ~30 residues of tubulin are important for tight binding [1], but they are also natively unfolded and Tau projection domain is about ~18 nm in length [2] with a radius of gyration in solution of ~6.5 nm.

The major interest in Tau stems from its aggregation in AD and other tauopathies could be an excellent of area of research in nanobiology. There has been a debate on whether Tau is causal to the disease or just a byproduct of some disease process. For the case of AD the case is still open, and changes in Tau are mostly viewed as a consequence of Aβ pathology. However,

the discovery of mutations in the Tau gene causing frontotemporal dementias has confirmed a causative role of Tau in neurodegeneration. For Tau aggregation the consequences of phosphorylation are even less clear. The fact that Tau phosphorylation precedes aggregation in AD has led to the assumption that phosphorylation drives Tau into aggregation, and certain highly phosphorylated states of Tau may be prone to aggregation [3]. In our view, it is therefore questionable whether strategies to reduce phosphorylation (e.g., kinase inhibitors) will be effective in preventing Tau aggregation (even though they may be beneficial for other reasons).

One hypothesis is that affected neurons release pathological Tau, which is taken up by neighboring cells and thus spreads the pathology in a prion-like fashion [4]. Several mechanisms can be envisaged for this release and re-. Alternatively, affected neurons could release factors (e.g., cytokines) that then challenge other neurons, either directly or via intermediate cells; an example is the cytosolic accumulation of Tau in neurons encountering activated microglia or exposed to tumor necrosis factor α [5].

Researchers believe that at the heart of Tau Pathologies is the conversion of a particular protein from a normal (Tau protein) to an abnormal, "Tau protein", shape. Both forms of the protein consist of the same building blocks but different final products – just like the Transformers toys that could assume two shapes, one benign and the other aggressive. In the Alzheimer theory of disease, normal (Tau protein) recruits and re-shapes abnormal, "Tau protein" to match its own form. Alzheimer diseases by a simple conversion from linked-nanoparticles (linked-Tau) which are a normal form of protein to an abnormal form, which is the non-linked nanoparticles (non-linked-Tau). It is important to mention that the linked-Tau or (non-linked-Tau) sizes can be considered as nanoparticles in reference to nanosciences definitions. In nanosciences the non-linked nanoparticles agglomerate with chemical and physical laws as show previously in different studies [6,7,4]. Moreover, toxic effects of non-linked-Tau nanoparticles in different nervous system animal species were poorly discussed by different researchers related to the increase of relativities of the nanoparticles with different compounds of the nervous system.

Human and animal brains were exposed to different concentrations of non-linked-Tau protein nanoparticles and contain naturally in its structure linked-Tau protein nanoparticles probably inducing and inversion of Tau protein ratio = Non-linked-Tau protein/linked-Tau protein. In physiological environment, the Tau ratio is equal to zero. Following the generation of the non-linked NPs the ratio increase and reach high values. In exposures to linked-NPs, particles induced lower cytotoxicity than non-linked particles. Analysis showed that non-linked NPs were more cytotoxic to the nervous system. Changes in sub-cellular architecture were observed with non-linked-Tau protein.

Moreover, while non-linked-NPs resulted in decreased quality and functionality of nervous system. In nowadays, the complete nature of the Alzheimer theory remains unknown as far as we know and some of the fundamental issues are unresolved. The real question is by any mechanism we have the conversion of linked-Tau protein to non-linked-Tau protein probably by different agents like electromagnetic field, pesticides, heavy metals, and other xenobiotics. Both forms of the protein-linked nanoparticles to non-linked nanoparticles consist of the same building blocks but different final products – just like the transformers toys that could assume two shapes, one benign and the other aggressive (FIG. 1).

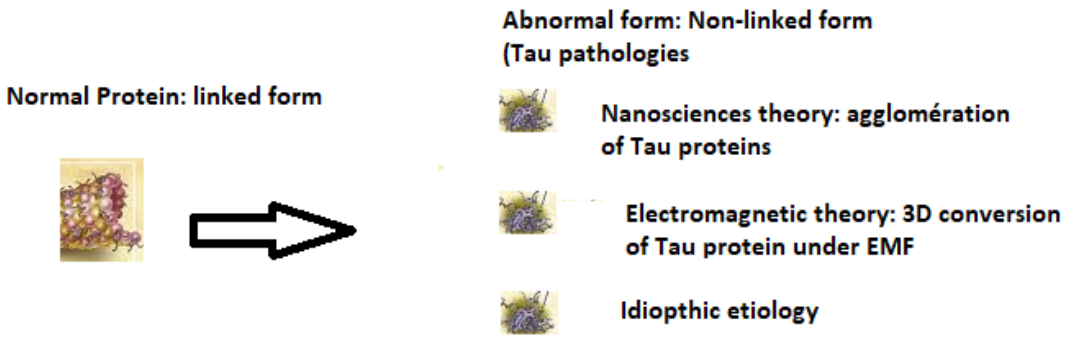

FIG. 1. **Alzheimer theories and Tau pathologies induced by brain protein nanoparticles agglomeration under electromagnetic field (EMF).**

2. Nanoparticle Theory of Tau Pathologies

Linked and non-linked nanoparticles, like other nano-sized particles, exhibit special properties relative to their bulk counterparts partly due to their very small size and greater surface area. Because of production of different types of NPs as a ratio=non-linked-Tau NPs/linked-tau NPs which the pathogen form can be considered as non-linked NPs. New applications under development, rigorous knowledge are needed about the potential impacts of this pathogen non-linked-Tau NPs on Human brain and/or animal brain. Over the past decade, research on neurobiological effects of various NP types' non-linked-Tau NPs & linked-Tau NPs has been performed on various cell lines, and animal models. In vitro toxicity studies have indicated effects of NP types (non-linked-Tau NPs) & NPs (linked-Tau NPs) on neuron cells. In vivo, exposures of NPs (non-linked-Tau NPs) have shown toxic effects in various mammalian models. Moreover, studies in rats and mice have demonstrated toxicity of NPs in a variety of target of the Human and animal brains. From these in vitro and in vivo studies, the proposed mechanisms of linked and non-linked NPs-induced toxicity are the increase of reactivity of the non-linked NPs with the nervous system related to their high specific surface. Even though, there is growing evidence that non-linked NPs are toxic in various test models, the exact mechanisms of non-linked NPs toxicity remain unclear leading to neurodegenerative disease (Alzheimer, Parkinson diseases…). Toxicological studies of non-linked-Tau NPs have demonstrated that physicochemical properties of NPs including size, shape, surface coating, surface charge, solubility, and chemical composition could dramatically affect NPs behaviour in biological systems and thus influence the toxicity of NPs in the nervous system of different animal models. A number of studies reported that non-linked NPs toxicity was dependent on their size and surface. Similarly to other NPs, the size of non-linked NPs probably is linked to cellular uptake processes in the brain. The surface has been shown to affect the affinity of NPs for the neuron cell surface and the dissolution or the release of compounds from non-linked NPs, which could explain the toxicity mechanism of non-linked NPs compared to link NPs. The investigation of the physicochemical characteristics and their impact on the biological effects of non-linked NPs is important for the better understanding of neurotoxic mechanism. The study provides scientific insight relating physical/chemical characteristics of non-linked NPs to cell damage and possible toxicity mechanisms of these NPs in the central nervous system [6,7,8]; explaining in part the etio-pathogeny of neurodegenerative diseases especially Tau pathologies (FIG. 1).

3. Electromagnetic Field Theory of Tau Pathologies

In our days all peoples were exposed to electromagnetic pollution; mobile phone; WIFI, etc. Ammari et al., [9] demonstrated that a long period of exposure to EMF induce gliosis and affect the working memory in the rats. Some studies signalized that the EMF increased the risk factors of Alzheimer diseases. A few studies concerning the long-term effects of EMF in the Alzheimer's mice; [10], In Alzheimer's disease mice, long-term EMF exposure reduced brain amyloid-β (Aβ) deposition through Aβ anti-aggregation actions and increased brain temperature during exposure periods. However, never study concerning the effects of WIFI in Alzheimer's mice.

In this new view, we will discuss the literature that has investigated the topic of magnetic field effects in proteins and the implication of the size/shape of the NPs on the pathogenicity of Tau diseases in the nervous system. The lack of complete mechanism related to Tau diseases encourages us to propose a new view and theory related to these exceptional diseases. Electromagnetic field and spin effects have proven to be useful mechanistic tools for radical mechanism and protein folding-misfolding model in neurobiology. Magnetic fields can influence the course of chemical reactions on linked NPs to transform them on non-linked NPs via different mechanism using nanosciences laws. The proposed research will investigate non-linked NPs reactions in neuron cells under the influence of magnetic fields with a particular focus on the effects of magnetic fields on the conversion from coated to non-linked NPs and the behaviour of non-linked NPs near neurons or glial cells [11]. Additionally, prompted by theoretical predictions, the protein folding-misfolding depend on magnetic field effects directly or indirectly via free radicals to generate Alzheimer diseases (FIG. 1).

4. Conclusion

The Alzheimer theory based on nanosciences and electromagnetic bioeffects on protein folding give the scientific community an innovative research approach that enhanced nano-protein to do a pathological folding or misfolding implicated in the generation of large numbers of non-linked protein leading to Alzheimer diseases.

REFERENCES

1. Littauer UZ, Giveon D, Thierauf M, et al. Common and distinct tubulin binding sites for microtubule-associated proteins. Proc Natl Acad Sci USA. 1986;83(19):7162-6.
2. Hirokawa N, Shiomura Y, Okabe S. Tau proteins: the molecular structure and mode of binding on microtubules. J Cell Biol. 1988;107(4):1449-59.
3. Khalid I, Liu F, Gong CX, et al. Tau in Alzheimer Disease and Related Tauopathies. Curr Alzheimer Res. 2010;7(8):656-64.
4. Amel H, Rjeb A, Abdelmelek H. Prion theory: Induction of Prion Diseases by Nanoparticles Conversion (Prpc To Prpsc) Related to Electromagnetic Field. Open Access J Neurol Neurosurg. 2017;6(1):555676.
5. Gorlovoy IP, Gallick GE, Gorlova OY, et al. GWAS meets microarray: are the results of genome-wide association studies and gene-expression profiling consistent? Prostate cancer as an example. PLoS One. 2009;4(8):e6511.
6. Hanini A, Schmitt A, Kacem K, et al. Evaluation of iron oxide nanoparticle biocompatibility. Int J Nanomedicine. 2011;6:787-94.

7. Ferchichi S, Trabelsi H, Azzouz I, et al. Evaluation of oxidative response and tissular damage in rat lungs exposed to silica-coated gold nanoparticles under static magnetic fields. Int J Nanomedicine. 2016;11:2711-9.
8. Baratli Y, Charles AL, Wolff V, et al. Impact of iron oxide nanoparticles on brain, heart, lung, liver and kidneys mitochondrial respiratory chain complexes activities and coupling. Toxicol In Vitro. 2013;27(8):2142-8.
9. Ammari M, Gamez C, Lecomte A, et al. GFAP expression in the rat brain following sub-chronic exposure to a 900 MHz electromagnetic field signal. Int J Radiat Biol. 2010 May;86(5):367-75.
10. Arendash GW, Sanchez-Ramos J, Mori T, et al. Electromagnetic field treatment protects against and reverses cognitive impairment in Alzheimer's disease mice. J Alzheimers Dis. 2010;19(1):191-210.
11. Banaceur S, Banasr S, Abdelmelek H, et al. Whole body exposure to 2.4 GHz WIFI signals: effects on cognitive impairment in adult triple transgenic mouse models of Alzheimer's disease (3xTg-AD). Behav Brain Res. 2013;240:197-201.