Is iron a hidden culprit in Alzheimer's disease?

PhD Sowmya Sunkara[1], Dr Marlene Leoni[2], Dr Johannes Haybäck[2,3], **Assoc. Prof. Dr Gerd Leitinger**[1]
[1]Division of Cell Biology, Histology and Embryology, Gottfried Schatz Research Center, Medical University of Graz, Graz, Austria, [2]Diagnostics & Research Institute for Pathology, Medical University of Graz, Graz, Austria, [3]Tyrolpath Obrist Brunhuber GmbH, Zams, Austria

Background incl. aims
Up to 80% of dementia cases globally are down to Alzheimer's disease (AD), a major neurodegenerative disorder[1]. The disease was discovered in 1906 by Alois Alzheimer[2], and in spite of great research efforts, therapeutic progress has been slow. This is probably because AD is characterized by several factors, namely amyloid beta (Aβ) deposits, neurofibrillary tangles (NFTs), and neuronal inflammation, with an unclear connection between these factors. It has been shown previously that iron is dysregulated in AD pathology [3]. Here we used an organotypic tissue culture model for studying the contribution of iron overload to the disease.

Methods
We established an organotypic tissue culture model of AD, for which we cultivate either human or porcine brain tissue and inject Aβ monomers into the tissue, which triggers aggregation of Aβ and the deposition of the aggregates in the tissue. In order to study the contribution of excess iron in this model we injected ferric citrate into the tissue.

Results
A careful analysis of the shape of the deposits in vitro showed that iron changes the shape of the deposits. Furthermore, we reveal that combined iron overload and Aβ injection exacerbated neuronal loss, enhancing the toxicity of Aβ on its own.

Conclusion
The advantage of our organotypic brain tissue culture model is that the natural organization of the cells within the tissue is preserved. This technique will eventually also open the possibility of reducing animal experiments. This integrated approach will elucidate the complex mechanisms underlying neuronal degeneration in AD, paving the way for targeted therapeutic interventions.
Grant sponsors : Austrian Science Fund FWF, grants P29370, P32058; MEFO Graz.

Keywords:

Azheimer's disease, Amyloid beta, iron

Reference:

[1] Alzheimers & Dementia in Austria. https://www.worldlifeexpectancy.com/austria-alzheimers-dementia.
[2] Stelzmann, R. A., Norman Schnitzlein, H. & Reed Murtagh, F. An english translation of alzheimer's 1907 paper, "über eine eigenartige erkankung der hirnrinde". Clinical Anatomy 8, 429–431 (1995).
[3] Peng, Y., Chang, X. & Lang, M. Iron Homeostasis Disorder and Alzheimer's Disease. International Journal of Molecular Sciences 2021, Vol. 22, Page 12442 22, 12442 (2021).

© The Authors, published by EDP Sciences. This is an open access article distributed under the terms of the Creative Commons Attribution License 4.0 (https://creativecommons.org/licenses/by/4.0/).