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Editorial

Diet, Drug and Inhibitor Therapy Prevent Toxic Protein Aggregation in Various Species

Ian James Martins[1,2,3]*

[1]*Centre of Excellence in Alzheimer's Disease Research and Care, Sarich Neuroscience Research Institute, Edith Cowan University, Australia*

[2]*School of Psychiatry and Clinical Neurosciences, The University of Western Australia, Australia*

[3]*McCusker Alzheimer's Research Foundation, Hollywood Medical Centre, Australia*

***Corresponding Author:** Ian James Martins, School of Medical and Health Sciences, Edith Cowan University, Western Australia, Australia.

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Protein aggregation has become of major concern to diabetes and neurodegenerative diseases [1]. The reversal of various diseases such as obesity, diabetes and neurodegenerative diseases is connected to accelerated protein aggregation that can lead to endoplasmic reticulum (ER) stress and mitochondrial apoptosis [2,3]. Diet, drug and inhibitor therapy have become of importance to prevent protein aggregation and important to the cellular quality-control system to prevent protein aggregation and ER stress related cell death. Polyunsaturated fatty acids such as docosahexaenoic acid (DHA) and various inhibitors [4-8] may reduce protein aggregation and prevent programmed cell death.

The generation of toxic amyloid beta has been connected to hypercholesterolemia with various cholesterol lowering drugs such as statins [9] important to the treatment of toxic amyloid beta in man and various species. Caffeine has been shown to lower amyloid beta levels and its excessive use is critical for species survival [10]. Indian spices such as curcumin are important to the prevention of toxic amyloid beta aggregation but in the current non-alcoholic fatty liver disease (NAFLD) epidemic curcumin doses should be carefully controlled with relevance to neuron toxicity [11]. The aggregation of amyloid beta indicates central importance to toxic protein aggregation in various species with specific doses of zinc and magnesium consumption essential to prevent toxic amyloid beta aggregation [12-17]. Other components such as 4-phenylbutyric acid has been used to prevent protein aggregation and ER stress [18] but excessive butyric acid consumption may lead to cell apoptosis [19].

In recent years the heat shock proteins (HSP) have become critical to amyloid beta aggregation and tau clearance [20] with HSP now critical to various diets, drug and inhibitor therapy with relevance to protein aggregation and mitochondrial apoptosis. HSP in various species is now critical for survival with heat shock genes [21,22] and (Figure 1) their regulation by diet and core body temperature is essential for adaptation to various environments. The heat shock gene Sirtuin 1 (Sirt 1) is now critical for survival with various Sirt 1 dietary activators [22] also relevant to prevent amyloid beta protein aggregation.

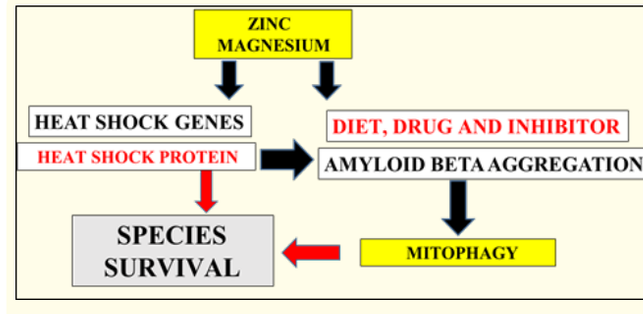

Figure 1: Zinc consumption determines heat shock gene activation and HSP-amyloid beta aggregation with relevance to mitophagy. Excessive zinc consumption may promote protein aggregation and inactivate beneficial effects of dietary magnesium, fatty acids, drug and inhibitor effects on prevention of protein aggregation.

Zinc levels with relevance to Sirt 1 expression and HSP metabolism is essential in various species [22,23] but excessive zinc levels may induce toxic immunogenic HSP-amyloid beta aggregation and mitochondrial apoptosis [12,22]. In the developing world elevated xenobiotic levels may override zinc/magnesium effects and lead to Sirt 1 inactivation with accelerated protein aggregation [13-17]. Inactivation of Sirt 1 leads to defective hepatic drug xenobiotic metabolism (statin) with delayed statin cytotoxicity associated with defective hepatic caffeine and curcumin metabolism and accelerated protein aggregation in various species [9-11].

Conclusion

Survival of the species and regulation of HSP levels are critical to prevent toxic protein aggregation and mitophagy. Dietary activators, drugs and inhibitors may reverse protein aggregation, but excessive caffeine and curcumin levels may inactivate and promote toxic amyloid beta aggregation. In various species zinc levels and core body temperature are critical to survival with HSP and amyloid regulation important to toxic protein aggregation with relevance to programmed cell death.

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