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Sex hormones, Alzheimer's disease and mitochondria

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Metabolic impairments are common hallmarks of Alzheimer's disease (AD), and amyloid- β (A β) peptide and hyperphosphorylated tau protein – the two foremost histopathological signs of AD - have been implicated in mitochondrial dysfunction. Epidemiological studies showed that women represent two thirds of AD patients and exhibit a greater vulnerability to the disease compared to men but little is known about the influence of sex steroid hormones on AD-related mitochondrial dysfunction. Thus, we aimed to investigate whether sex hormones could attenuate the toxic effects of A β and abnormal tau on bioenergetic parameters, such as ATP production, mitochondrial membrane potential (MMP), mitochondrial respiration and glycolysis, in cellular models of AD (SH-SY5Y neuroblastoma cells overexpressing either the human amyloid precursor protein (APP) or mutant tau (P301L)). After a treatment of 24 h, the majority of these steroids were effective in enhancing bioenergetic outcomes in cells overexpressing APP and mutant tau, attenuating the mitochondrial dysfunction that is present in these cell lines when compared to the respective control cells. Interestingly, testosterone (the main male sex hormone) was more efficient in alleviating A β -induced mitochondrial deficits, while progesterone and estrogen (the female sex hormones) were the most effective steroids in our model of AD-related tauopathy. Thus, our results provide new insights in re-defining the biological model of how steroids control neuronal and bioenergetic functions, and may open new avenues for the development of gender-based therapeutic approaches in AD.

Biography

Amandine Grimm has performed a joint PhD between the University of Strasbourg, France, specialty Neuroscience, and the University of Basel, Switzerland, specialty Pharmaceutical Sciences. She has obtained her PhD degree in January 2015, and is currently a Postdoctoral fellow in the Neurobiology Lab for Brain Aging and Mental Health (Psychiatric University Clinic of Basel (Switzerland)). In the course of her Joint-PhD and Postdoctoral researches, she has published 9 papers, including 6 original articles, reviews and book chapters signed as first author.

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