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Cotinine, a tobacco-derived compound as a new drug to improve memory and reduce plaques in Alzheimer's disease

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Alzheimer's disease (AD) is the main cause of dementia in the elderly and is characterized by memory loss and presence of amyloid plaques formed by aggregated β–amyloid (Aβ) peptide. Epidemiological studies have shown a negative correlation between tobacco consumption and the development of AD. The beneficial effects of tobacco have been attributed to nicotine; nonetheless, due to its toxicity, nicotine is not considered an adequate therapeutic agent. Notably, more than 80% of nicotine is metabolized into cotinine, a metabolite with a longer half-life (2-3 h *vs.* 19-24 h for nicotine and cotinine, respectively) that has a good safety profile in humans. We studied the effect of cotinine on cognitive performance, Aβ levels, and plaque deposition in a mouse model of Aβ neuropathology, the transgenic (Tg)6799 mice. We performed memory testing using the radial arm water maze, circular platform, and interference tasks. Additionally, we examined the effects of cotinine on Aβ levels and aggregation using Western blot, dot-blot immunoassays, atomic force microscopy, ELISA, and immunohistochemical techniques. We also modeled the $Aβ_{1-42}$/cotinine interaction using molecular modeling. Our results show that cotinine decreased plaque deposition and improved working and reference memories as well as reduced oligomeric Aβ levels in the brains of Tg6799 mice. Cotinine also stimulated the Akt/glycogen synthase kinase 3β pathway downstream of the α7nAChRs, a cascade involved in memory, neuronal survival, and tau phosphorylation in the brains of mice. Molecular dynamics simulation of the Aβ/cotinine interaction showed that cotinine can interact with key histidine residues that may affect its aggregation.

Biography

I am a female scientist obtained my Biochemist degree, M.S., and Ph.D. from the University of Concepción in Chile. After, I pursued postdoctoral studies at the National Center of Biotechnology in Spain, McGill University in Canada, and the Johns Hopkins University in the USA. I spent a year as a scientist at the Columbia University in New York City before moving to Florida where I am a scientist at the Bay Pines VA Healthcare System and an assistant professor at the University of South Florida. I authored more than 21 papers in scientific journals and three book chapters. I filed four patents applications and serve as editorial board member of several scientific journals. My laboratory work in the search of new drugs to assess the memory impairment and/or loss associated with dementia and other mental health disorders such as Posttraumatic stress disorders. We have found two drugs that prevented (cotinine) and reverted (Sorafenib) memory impairment in AD. The effect of these drugs on Alzheimer's disease need to be further characterized but I have not funding from NIH and still I am not eligible for applying for Veterans Affairs funding.