Multiple mechanisms of dimethyl fumarate in amyloid β-induced neurotoxicity in human neuronal cells

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Alzheimer disease (AD) is characterized by a complex heterogeneity of pathological changes and any therapeutic approach categorically requires a multi-targeted way. It has been demonstrated that together with the hallmarks of the disease such as neurofibrillary tangles and senile plaques, oxidative and inflammatory stress covered an important role. Dimethyl fumarate (DMF) is an orally bioavailable methyl ester of fumaric acid and activator of Nrf2 with potential neuroprotective and immunomodulating activities. Therefore, the aim of the present work was to evaluate the potential beneficial effects of DMF in an in vitro Alzheimer's model by using SH-SY5Y human neuroblastoma cell lines stimulated with amyloid-beta (Aβ). DMF pretreatment (30 μM) preserved cellular viability from Aβ 1μM stimulation, reducing tau hyper-phosphorylation. Moreover, DMF was able to induce an activation of manganese superoxide dismutase (Mn-SOD) and heme-oxygenase-1 (HO-1), decreasing the severity of oxidative stress. Our results showed important multi-protective effects of DMF pretreatment from Aβ stimulation in SH-SY5Y cells, highlighting a Nrf2/ NF-κB dependent mechanism, that could provide a valuable support to the therapies for neurodegenerative diseases today.