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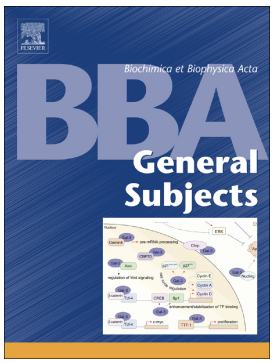

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In vitro Neurotoxicity of Salsolinol is Attenuated by the Presynaptic Protein α-Synuclein

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ABSTRACT

Background: Salsolinol (SALSO), a product from the reaction of dopamine (DA) with acetaldehyde, is found increased in dopaminergic neurons of Parkinson's disease (PD) patients. The administration of SALSO in rats causes myenteric neurodegeneration followed by the formation of deposits of the protein α-synuclein (aS), whose aggregation is intimately associated to PD.

Methods: NMR, isothermal titration calorimetry and MS were used to evaluate the interaction of SALSO with aS. The toxicity of SALSO and *in vitro*-produced aS-SALSO species was evaluated on mesencephalic primary neurons from mice.

Results: SALSO, under oxidative conditions, stabilizes the monomeric state besides a minor population of oligomers of aS, resulting in a strong inhibition of the fibrillation process. SALSO does not promote any chemical modification of the protein. Instead, the interaction of SALSO with aS seems to occur via hydrophobic effect, likely mediated by the NAC (non-amyloid component) domain of the protein. aS-SALSO species were found to be innocuous on primary neurons, while SALSO alone induces apoptosis via caspase-3 activation. Importantly, exogenous aS monomer was