Galantamine inhibits aggregation of α-synuclein in human neuroblastoma SH-SY5Y cells

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Synucleinopathies such as Parkinson's disease (PD) and dementia with Lewy bodies (DLB) are neurodegenerative disorders featured by the abnormal accumulation of α-synuclein protein (α-syn). Recent studies showed exogenous pre-formed fibrils (PFFs) of recombinant α-syn induced endogenous α-syn aggregates in human SH-SY5Y cells. In this study, we focused on nicotinic acetylcholine receptor (nAChR) as the therapeutic targets for synucleinopathies through α-syn clearance. PFFs were generated from α-syn by agitation followed by sonication. SH-SY5Y cells overexpressing α-syn gene were treated with PFFs for 24 h. After the incubation for 48 h, immunocytochemical analysis revealed the localization of α-syn. PFFs induced the aggregation of α-syn, which were detected with anti-phosphorylated-α-syn antibody and thioflavin-T. These data indicated that intracellular aggregation of α-syn were Lewy body-like aggregates. In addition, we examined galantamine effect, because some reports showed nAChR signaling increased autophagic activity. Galantamine were treated for 48 h after preincubation with PFFs, and then α-syn aggregation was decreased. These observations suggest that nAChR may be a novel target for synucleinopathies through α-syn clearance by autophagic activation.