

Ruggero G Fariello (BioNeuroFar, Switzerland)

α -Synuclein (α -syn) and its aggregation tendency plays a pivotal role in the pathogenesis of LBD, PD and MSA. Less clear is the pathogenic role of α -syn in Hallervorden Spatz Disease. Particularly in LBD there is general agreement that dissolving α -syn aggregates would take care of the most important pathogenic process leading to dementia. True, in AD all the attempt to obtain symptomatic benefits by dissolving β -amyloid (amy) aggregates have miserably failed. However, β -amy aggregation is only one pathogenic factor in AD. Thus, clearance of β -amyloid from brains cannot be expected to have the same beneficial results of clearing α -syn in the synucleopathies. Said this, the very high risk of successfully translating benefits obtained in animal models of neurodegenerative diseases to the clinical setting still remains. At present no molecule in development impedes both the antifibrillogenic and the anti-oligomerization of the protein which may key to the pathogenic process. Several compounds, are in various phase of development, at least two are mab and claim "vaccination" potential. The certainty that encephalitic processes will result from prolonged treatment has not been reached yet. Also the consequences of blocking α -syn throughout the brain (and in other parts of the bodies) have not been fully explored. The field of a disease modifying treatment addressing α -syn aggregation in PD may move forward more expeditely using small molecules or peptides.