Abstract View

HIGH-RESOLUTION LARGE-SCALE -D MAPPING STUDIES OF ALPHA-SYNUCLEIN IMMUNOREACTIVITY IN TRANSGENIC MICE OVEREXPRESSING HUMAN ALPHA-SYNUCLEIN.

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Lewy body formations, a hallmark feature of Parkinson's disease pathology, are protein aggregates comprised largely of alpha-synuclein (α-SYN). Mutation of the α-SYN gene is associated with familial forms of Parkinson's disease. Transgenic mice overexpressing human α-SYN exhibit motor deficits in Rotorod studies, and have α-SYN inclusions in neuronal cell bodies, neurites and glial cells. We have extended these earlier observations using 2-photon microscopy to acquire high-resolution large-scale 3-D maps of α-SYN immunoreactivity in whole brain slices from wildtype and α-SYN overexpressing transgenic mice. Using a 2-photon microscope equipped with a high precision montaging stage we mapped α-SYN immunoreactivity in coronal brain slices at the levels of anterior striatum, hippocampus and cerebellum. Examination of these high-resolution datasets from transgenic animals revealed widespread neuritic α-SYN aggregates as well as nuclear inclusions in subsets of neurons throughout many neural regions. In the cortex and striatum, a subset of neurons with the characteristics of interneurons were intensely labeled. Aggregates were not observed in wildtype animals. Immunolabeling studies are underway to identify the heavily labeled neurons, as well as ultrastructural examination of protein aggregates in transgenic mice using electron tomography. These findings extend the observations of α-SYN protein aggregation to additional neural regions in transgenic mice overexpressing α-SYN. A discussion of the utility of the large scale mapping technique in characterizing neuropathology in mouse models of human disease will also be presented.
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