Abstract:

Clearance of cellular debris is a critical feature of the developing nervous system, as evidenced by the severe neurological consequences of lysosomal storage diseases in children. An important developmental process, which generates considerable cellular debris, is synapse elimination, in which many axonal branches are pruned. The fate of these pruned branches is not known. Here, we investigate the role of lysosomal activity in neurons and glia in the removal of axon branches during early postnatal life. Using a probe for lysosomal activity, we observed robust staining associated with retreating motor axons. Lysosomal function was involved in axon removal because retreating axons were cleared more slowly in a mouse model of a lysosomal storage disease. In addition, we found lysosomal activity in the cerebellum at the time of, and at sites where, climbing fibers are eliminated. We propose that lysosomal activity is a central feature of synapse elimination. Moreover, staining for lysosomal activity may serve as a marker for regions of the developing nervous system undergoing axon pruning.