REEP and reticulon mutant phenotypes in *Drosophila*

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Several causative genes for hereditary spastic paraplegia encode proteins with intramembrane hairpin loops that contribute to curvature of the endoplasmic reticulum (ER), but the relevance of this function to axonal degeneration is not understood. These genes include *reticulon2* and *REEP1*. In contrast to mammals, *Drosophila* has only one widely expressed reticulon ortholog, *Rtnl1*, and two REEP othologs, ReepA and ReepB. We therefore used *Drosophila* to test the importance of these proteins in ER organization and axonal function. Rtnl1 and ReepB distribution overlapped with that of ER, but in contrast to rough ER, was enriched in axons. Loss of Rtnl1 or ReepA,ReepB double mutants led to expansion of sheet ER in larval epidermis. Loss of Rtnl1 also caused abnormalities specifically in the distal portions of longer motor neuron axons and terminals, including in smooth ER, the microtubule cytoskeleton, and mitochondria. In contrast proximal axon portions and shorter axons appeared unaffected. Our results show a preferential requirement for reticulon function in distal longer axons, and support a model in which spastic paraplegia is caused by impairment of axonal smooth ER.