ESCRT, autophagy, and frontotemporal dementia.

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Public Summary:
Many age-dependent neurodegenerative diseases are associated with the accumulation of abnormally folded proteins within neurons. One of the major proteolytic pathways in the cell is the autophagy pathway, which targets cytoplasmic contents and organelles to the lysosomes for bulk degradation under various physiological and stressful conditions. Although the importance of autophagy in cellular physiology is well appreciated, its precise roles in neurodegeneration remain largely unclear. Recent studies indicate that components of the endosomal sorting complex required for transport (ESCRT) are important in the autophagy pathway. Reduced activity of some ESCRT subunits leads to the accumulation of autophagosomes and failure to clear intracellular protein aggregates. Interestingly, rare mutations in CHMP2B, an ESCRT-III subunit, are associated with frontotemporal dementia linked to chromosome 3 (FTD3). Mutant CHMP2B proteins seem to disrupt the fusion of autophagosomes and lysosomes in cell culture models. These findings suggest a potential mechanism for the pathogenesis of FTD3 and possibly other neurodegenerative diseases as well.

Scientific Abstract:
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