# XBP-1 deficiency in the nervous system reveals a homeostatic switch to activate autophagy

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Endoplasmic reticulum (ER) stress has been extensively described in many protein misfolding disorders including amyotrophic lateral sclerosis (ALS). Adaptation to ER stress is mediated by the activation of an integrated signal transduction pathway known as the unfolded protein response (UPR). We have recently defined the contribution of X-Box binding protein-1 (XBP-1) to ALS, a key UPR transcription factor that regulates genes involved in protein folding and quality control. Despite expectations that XBP-1 deficiency would enhance the severity of experimental ALS, these mice were instead markedly more resistant to developing the disease. This phenotype was associated with enhanced clearance of abnormal protein aggregates by macroautophagy, a cellular pathway involved in lysosome-mediated protein degradation. Our results reveal a critical crosstalk between these two stress pathways that can provide protection against neurodegeneration. Here, we discuss possible signaling pathways that m