

**P015** Effect of disease-associated mutants of the endosomal sorting protein CHMP2B on post-synaptic glutamate receptors and spines of hippocampal neurons

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Mutations of the ESCRT-III subunit CHMP2B have been reported to be linked with cases of fronto-temporal dementia (FTD), which is the second most common cause of presenile dementia, characterised by a severe cortical atrophy and with non SOD1-ALS, associated with degeneration of motor neurons. One mutation in intron 5 results in expression of proteins with truncated (CHMP2B<sup>intron5</sup>) or abnormal C-terminal part (CHMP2B<sup>Δ10</sup>). According to results of several laboratories, deletion of the C-terminal part of CHMP2B could lead to a constitutive activation of the protein and thereby formation of aberrant endosomes. The cellular mechanisms by which these mutants induce neurodegeneration may be intimately connected to the control of cell death through autophagy, but also to that of synaptic plasticity. We present evidence that in hippocampal neurons, expression of mutant CHMP2B at low doses perturbs the traffic of neuronal AMPA receptors and the maintenance of dendritic spines, while leaving dendritic shafts intact.