BMC Neuroscience

Poster presentation

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Transient overexpression of alpha-Synuclein in OLN-93 oligodendroglial cells is not cytotoxic and not affected by HSP70

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from Annual Meeting of the Study Group Neurochemistry. International Conference of the Gesellschaft für Biochemie und Molekularbiologie 2006 (GBM 2006): Molecular pathways in health and disease of the nervous system
Witten, Germany. 28–30 September 2006

Published: 23 March 2007

BMC Neuroscience 2007, **8**(Suppl 1):P11 doi:10.1186/1471-2202-8-S1-P11

Alpha-Synuclein (alpha-syn) accumulates in neurons and glia in a number of neurodegenerative disorders. The cytotoxicity and solubility of alpha-syn can be modified by the molecular chaperone HSP70. In multiple system atrophy (MSA), alpha-syn-positive glial cytoplasmic inclusions (GCIs) originating in oligodendrocytes are specifically prominent. Alpha-Synuclein is not detectable in mature oligodendrocytes in the normal brain, but we have shown previously that it is present in cultured rat brain oligodendrocytes [1] and down-regulated as the cultures mature. Hence, GCI formation might be causally related to a specific upregulation of the protein during pathological situations.

To test if alpha-syn at a high level is cytotoxic to oligodendroglial cells and that HSP70 modifies its properties, we have transiently transfected OLN-93 cells, a cell line with oligodendroglia characteristics, and also OLN-93 cells permanently expressing HSP70 (OLN-HSP70), with plasmids encoding alpha-syn. The data show that alpha-syn does not cause cell death, but leads to a disorganisation of the microtubule network to a similar extent in both cell lines. Furthermore, HSP70 did not improve the solubility of alpha-syn, as investigated by determining the amount of alpha-syn in the detergent insoluble fraction. When cells were treated with oxidative stress, exerted by hydrogen peroxide, alpha-syn overexpressing cells did not reveal an altered or enhanced sensitivity to the stress situation as compared to control OLN-93 cells. Also, alpha-syn did not protect cells from oxidative stress, which has been suggested before, since it shares similarities with small heat shock proteins. However, OLN-HSP70 cells showed a higher resistance to oxidative stress, both in the presence and absence of alpha-syn. After treatment with hydrogen peroxide thioflavine S-positive staining, indicating fibrillary protein deposits, was not observable. Thioflavine S staining was only detectable, when cells were treated with hydrogen peroxide first and then with the proteasomal inhibitor MG-132. This was seen independently of the presence of HSP70. Thus, in the present cell system, alpha-syn overexpression is not cytotoxic, and HSP70 is not the major player in altering the properties of alpha-syn.

References

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