Glucocorticoid excess enhances 5-HT-ir fibre degeneration in aged rats

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Published in:
Journal of Neurochemistry

Publication date:
2001

Reference
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P01-30

Increased clusterin in brain tissue but not in CSF in Alzheimer's disease

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Clusterin is suggested to be involved in the pathogenesis of Alzheimer's disease (AD). We quantified clusterin in AD-brain tissue using immunoblotting, showing significantly increased levels in frontal cortex (150% of controls) and hippocampus (179%), but not in cerebellum (104%). As cerebrospinal fluid (CSF) is continuous with the extracellular space in the brain biochemical brain processes can be reflected by CSF analysis. For analysis of a possible concomitant increase in AD-CSF, clusterin was quantified by ELISA. However, no change in CSF-clusterin was found in any diagnostic group (AD, vascular dementia, Parkinson's disease), as compared to controls. In longitudinal samples from stroke patients no change in CSF-clusterin was found in contrast to increased GFAP in the early, acute phase, probably indicating an astrocytosis. Brain clusterin is synthesised by astrocytes. Thus, despite the indication of reactive astrocytes no elevation of the CSF-clusterin level was detected. We show that the increased levels of clusterin in AD-brain tissue are not followed by any increase in the CSF. Thus, CSF-clusterin cannot be used as an indicator or a diagnostic marker for neurodegeneration. The reason for the lack of change in CSF-clusterin is unclear. **Explanations may include:** (a) up- and down regulations in different brain regions (b) affected leakage of proteins from brain into CSF, or (c) an increased uptake of clusterin by neurons, all with a net effect in CSF zero. Also, CSF-samples are collected at earlier stages of the disease than post-mortem brain tissue samples, which are from terminal AD patients. This may partly explain discrepancies between the two types of studies, but has to be further examined.

P01-31

Functional gene networks in neurodegenerative diseases

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Kelman presents the SPRAB (Specific Protein Recognition and Binding) technology for *in silico* protein–protein interaction mapping. We are able to construct a GeneNetwork, which provides an in-depth understanding of gene interplay, involving gene products in all their molecular versions. Visualization of data as well as navigation within this network of physical protein–protein interactions is possible with the tool GeneViator™. It enables scientists to extract knowledge according to certain filter criteria. The application of Kelman's tools is exemplified here by means of a case study. Object of our *in silico* investigations are the genes for several proteins, which are known to play a multi-facetted but poorly understood role in the pathogenesis of neurodegenerative diseases: amyloid precursor protein (APP), presenilin 1 (PSEN1), microtubule-associated protein tau (MAPT) and Apolipoprotein-E4 (APOE4). The genes selected were analysed in all of their molecular versions known (allelic variants, splice forms, mutations). The computational analyses were aimed to reveal interrelations between these genes as well as interrelations between them and other interacting partners, completely unknown until now. We mainly focussed on events connected with the processing of PSEN1 and APP. They are considered to be very important for the understanding of neurodegenerative processes but the results of experimental approaches were not satisfying so far. The gene network Kelman constructed for the described inquiry uncovered molecular connections and interaction partners, which otherwise wouldn't have attracted attention. The protein–protein interaction network provides us with information necessary for valuable functional annotations and with promising hypotheses formulated for the search for target candidates in drug discovery.

P01-32

Abstract withdrawn

P01-33

Glucocorticoid excess enhances 5-HT-ir fibre degeneration in aged rats

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The excess of corticosterone (CORT) in aged rats is considered as a risk factor for neuronal survival. Among the different neurotransmitter systems serotonergic (5-HT) neurones are vulnerable to ageing and their axons spontaneously degenerate in a number of brain areas of ageing rats. We investigated the effect of sc. implantation of CORT pellets at the age of 24 months on 5-HT and cholinergic fibre degenerations in several brain areas including the hippocampus and anteroventral thalamus (AVT). Immunocytochemical stainings for 5-HT and choline acetyltransferase (ChAT) were used and the degree of fibre degeneration and the amount of fibre aberrations were quantified with the Quantimet 600 program. Learning and spontaneous behaviours as well as the function of pituitary-adrenocortical axis (plasma ACTH and CORT) were also measured under baseline and stress conditions. By the age of 26 months CORT increased 5-HT fibre degeneration in the hippocampus and AVT. ChAT-ir fibre degeneration in the AVT was not influenced by CORT. CORT-implanted rats displayed higher plasma CORT levels up to 6 weeks after implantation. Passive avoidance learning was inhibited by the steroid implant. In conclusion, excess amount of CORT selectively enhances 5-HT axon degeneration as compared to cholinergic fibre degeneration during ageing in rats.

P01-34

Ageing and oxidative stress

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Because of their low functional status and high incidence of chronic disease, most elderly experience the syndrome of physical frailty. Exercise can be the only way to treat the losses of functional capacity. Senescence associated loss of functional capacity could be due to the accumulation of molecular oxidative damage: oxygen use although necessary for survival, may be hazardous to long-term existence. Today is well accepted the concept that cells are chronically under oxidative stress and that ageing