SURVIVAL ROLE OF EMBRYONAL PROTEINS IN ALZHEIMER'S DISEASE LINKED DEMENTIA VIA REGULATION OF OXIDATIVE STRESS AND LEVEL OF CATECHOLAMINES

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Purpose of the study

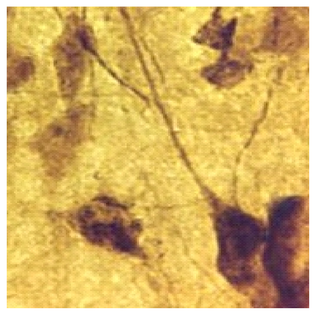
Main event in the pathogenesis of such a neurodegenerative disorder as Alzheimer's disease (AD) is generation and deposition of amyloid beta (Ab). Oxidative stress and generation of free radical species have implications in the formation of Ab and its subsequent neurotoxicity. Degeneration of aminergic brainstem nuclei such as the locus coeruleus which is very vulnerable to the free radicals and the selective exhaustion of catecholamines near the locus coeruleus of brainstem can appear as a potential pathogenesis of AD. That's why our study was focused to find some parallels between oxidative stress and changes in catecholamines concentration experimental model of AD, and find new biological agent which will be able to regulate them. As a bioregulator we choose the complex of proteoglycans of embryonal genesis (PEG). PEG contains the pool of proteoglycans of embryonal genesis which are associated with alpha-fetoprotein, chorionic gonadotrophin, beta1-glycoprotein, carcinoembryonic antigen, and carbohydrate antigens: Ca-19-9, Ca-125.

Methods used

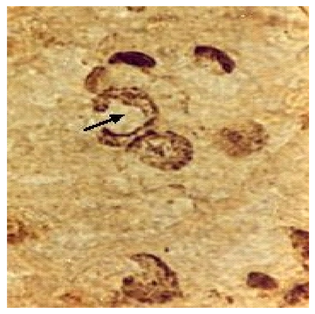
The experimental model of AD was made in rats by intracerebroventricular injection of aggregated Ab (fragment 25-35).The animals were divided into five groups: the control group consisted of vehicle-treated animals; the 1st experimental group (PEG-control) was subcutaneously injected with PEG (0.5 mg/100 g) only; the 2nd experimental group was i.c.v. injected with aggregated Ab; the 3rd experimental group was subcutaneously injected with PEG (0.5 mg/100 g) 7 days before Ab injection (group PEG-1); the 4th experimental group was subcutaneously administered PEG (0.5 mg/100 g) 7 days before Ab injection and on the 31st day after it (group PEG-2). Oxidative stress and antioxidant capacity were measured by use of chemo-luminescence method (spontaneous, induced by UV and Fe^{2+} ions) in cerebral cortex, hippocampus and brainstem. Adrenergic structures of brainstem were studied by glyoxylic acid condensation using luminescence microscope and accompanied by the HPLC study of norepinephrine (NE), adrenalin and metabolites of adrenergics.

Summary of results and conclusion

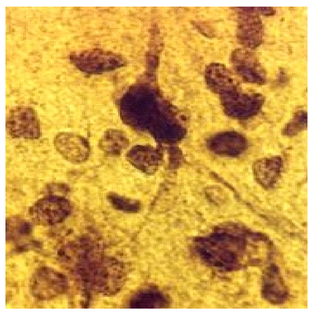
After injection of Ab received data testify the increase in the level of chemoluminescence (both spontaneous and inducible) in the cerebral cortex, hippocampus and brainstem. On the other hand the increase in intensity of luminescence of catecholamine granules near the locus coeruleus was also detected. At the same time HPLC results show high elevation in concentration of NE in the brainstem. In PEG treated animals all types of chemoluminescence in mentioned brain structures decreased and the antioxidant capacity increased without any significant difference between PEG-1 and PEG-2 groups. Almost no changes of adrenergic structures were shown compared with the control rats in all PEG treated groups. At the same time in PEG-1 group concentration of NE was less than in control, whereas in PEG-2 group it was about control level. It should be certainly pointed that the results of biochemical determination of NE and metabolites of adrenergics in brainstem were in unison with the luminescent study. Summarizing, it seems, that regulation of oxidative stress and disturbance in adrenergic structures can be of importance for neuronal rescue in Alzheimer's pathology and regulation of these both processes can lead to neuroprotection, which is also confirmedby morphological study of brain stem and cortical neurons.



Cortical neurons in norma
Mag x1000

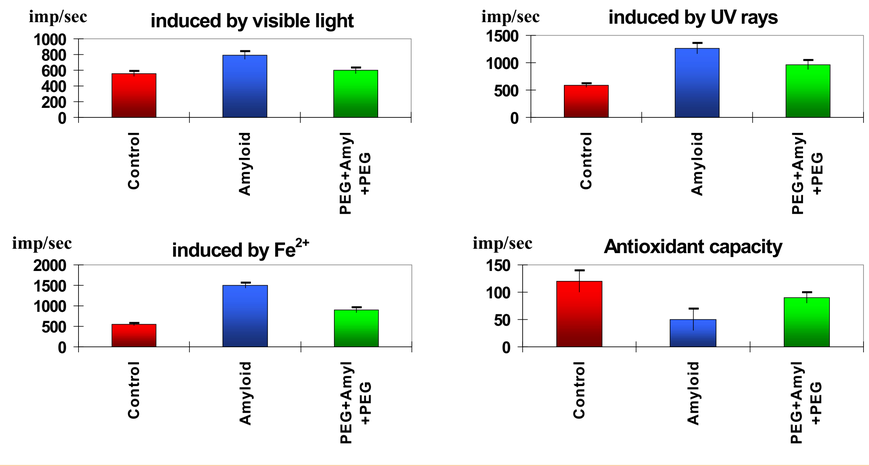


Cortical neurons after Abetta
Mag x1000

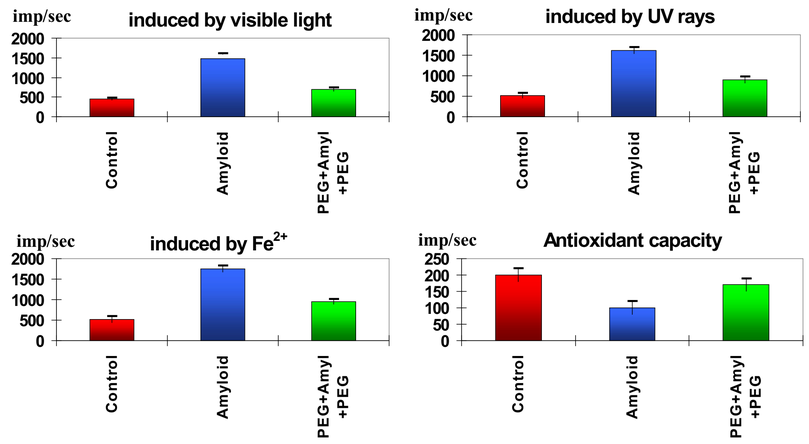


Cortical neurons treated with PEG
Mag x1000

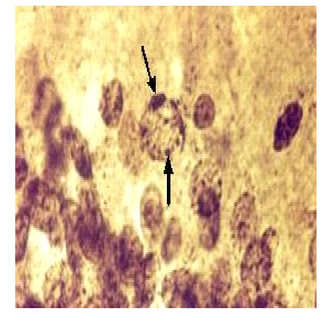
Chemoluminescence and antioxidant capacity in cortical neurons



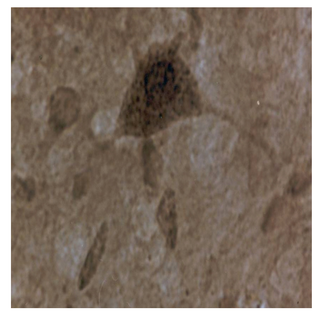
Chemoluminescence and antioxidant capacity in hippocampal neurons



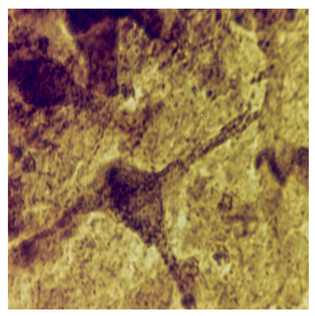
Hippocampal neurons in norma
Mag x1000



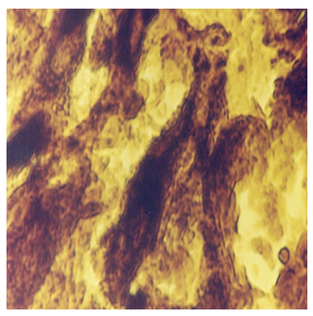
Hippocampal neurons after Abetta
Mag x1000



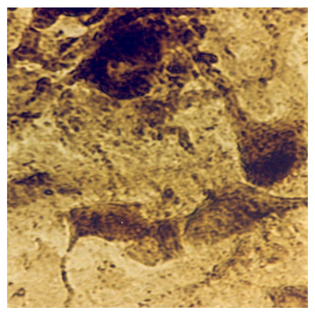
Hippocampal neurons treated with PEG
Mag x1000



Brainstem neurons in norma
Mag x1000

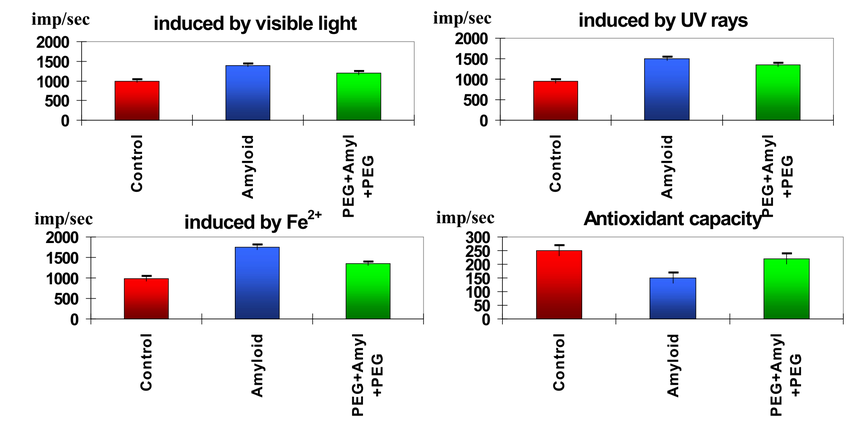


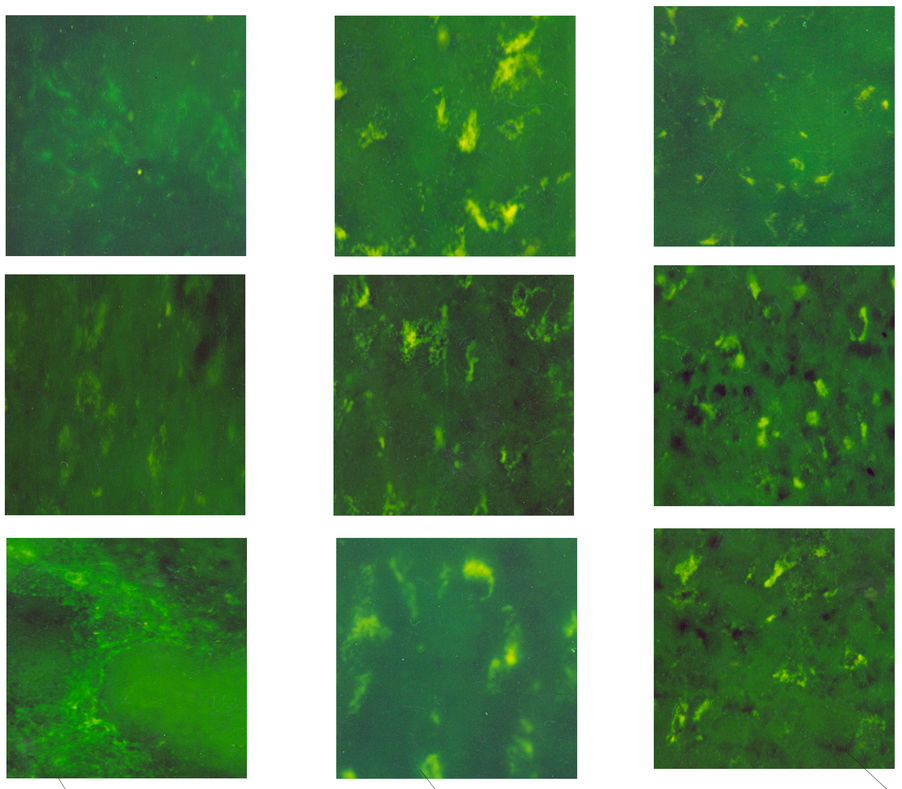
Brainstem neurons after Abetta
Mag x1000



Brainstem neurons treated with PEG
Mag x1000

Chemoluminescence and antioxidant capacity in brainstem neurons





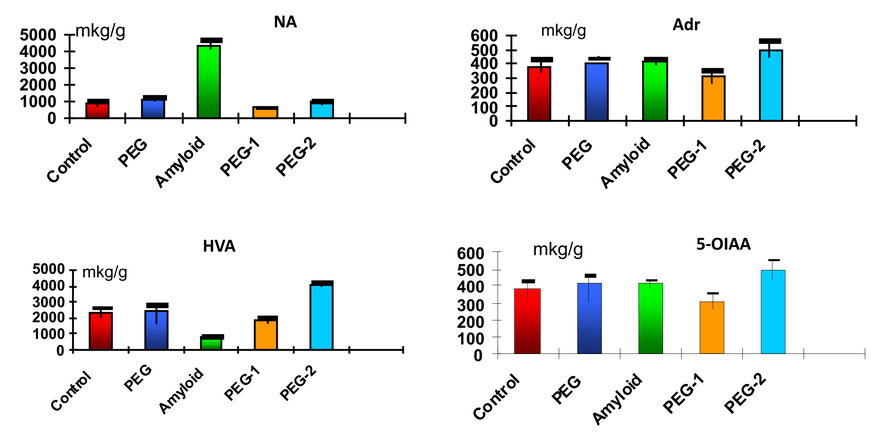
Mag x1000

Luminescence of catecholamine granules near locus cereleus in norma

Luminescence of catecholamine granules near locus cereleus after Abetta

Luminescence of catecholamine granules near locus cereleus treated with PEG

HPLC study of norepinephrine (NE), adrenalin and metabolites of adrenergics - 5-oxyindole acetic acid (5-OIAA) and homovanillic acid (HVA)



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