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A31
EFFECTS OF EXPERIMENTAL INTRACEREBRO-VENTRICULAR INJECTION OF AMYLOID BETA PEPTIDE (1-42) ON THE DAILY BAX AND BCL-2 EXPRESSION IN THE RAT HIPPOCAMPUS

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Alzheimer's disease (AD) is a neurodegenerative disorder marked by cognitive and behavioral impairment. The accumulations of amyloid-β (Aβ) peptides in the brain are believed to be associated with perturbations of synaptic function leading to cognitive deficits. The proto-oncogene Bax (Bcl-2-associated X protein) and related protein Bcl-2 (B-cell chronic lymphocytic leukemia/lymphoma-2) genes are triggers of apoptosis in Alzheimer's disease (AD). Besides the cognitive deficit, AD patients also show alterations in their circadian rhythms. The objective of this study was to investigate the effects of an intracerebroventricular (i.c.v.) injection of amyloid beta peptide (1-42) on daily patterns of Bax and Bcl-2 expression, as well as of clock proteins in the hippocampus and on temporal profiles of cognitive performance of four-month-old males Holtzman rats. Groups were defined as: control (CO) and Aβ-injected (Aβ). Rats were maintained under 12 h-light:12 h-dark conditions and received food and water *ad libitum* throughout the entire experimental. Daily rhythms of Bax and Bcl-2 expression were analyzed by RT-PCR and protein levels by Western blots, in hippocampus samples isolated every 4 h during a 24 h period. Regulatory regions of Bax and Bcl-2 were scanned for E-box sites. The Novel Object Recognition (NOR) test was used to evaluate cognition, particularly recognition memory. We found E-box sites on regulatory regions of Bax and Bcl-2 genes, which display a daily oscillation of expression in the rat hippocampus. The i.c.v. injection of Aβ (1-42) modified daily variation of Bax and Bcl-2, and clock proteins. It was observed that the group injected with Aβ explored the novel object for less time compared to the control group, during the day and night periods. Thus, elevated Aβ peptide levels might affect the temporal patterns of cognitive function and apoptotic genes, probably by altering daily rhythms of clock proteins.

A32
EFFECTS OF PIOGLITAZONE-VALPROIC ACID ON DAILY RHYTHMS OF NEP EXPRESSION IN AN EXPERIMENTAL MODEL OF ALZHEIMER DISEASE

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Alzheimer's disease (AD) is a primary cause of dementia in the elderly. AD late onset, which constitutes 90% of cases, could be mainly attributable to deficiencies in the clearance of the Aβ peptide. Direct degradation of Aβ by endopeptidases has emerged as one important pathway for clearance. Neprilysin (Nep) is one of the most important Aβ-degrading enzymes. Neurogranin (Rc3) and neuromodulin (Gap-43) play an important role in learning and memory. Recently, PPAR-γ agonists (Pioglitazone) have shown neuroprotective effects in neurodegenerative disorders. Numerous studies have shown that the intraperitoneal administration of valproic acid (VA), an inhibitor of histone deacetylases, caused an increase in NEP activity in different areas of the brain, including the hippocampus, in an experimental model of AD. AD patients also show alterations in their circadian rhythms. Taking into account these observations, the objective of this study was to evaluate the effect of Pio/VA on the 24 h rhythms of Aβ; Nep, Rc3, and Gap-43 expression in the hippocampus of Aβ-injected rats. Four-month-old males Holtzman rats were divided into three groups defined as: (1) control, (2) Aβ-injected, (3) Aβ-injected treated with Pio-VA. Rats were maintained under 12 h-light: 12 h-dark conditions. Tissues samples were isolated every 6 h during a 24 h period. Nep, Rc3, and Gap-43 mRNA levels were determined by RT-PCR. Aβ protein levels were analyzed by immunoblotting. We found that the treatment of Pio-VA reestablished rhythmicity of those temporal patterns. These findings might constitute, at least in part, molecular and biochemical basis of restoration of circadian rhythmicity by the administration of Pio-VA in neurodegenerative disorders.

A33
CYTOKERATIN 5 EXPRESSION IN SERTOLI CELLS OF HGSNAT KNOCKOUT MICE

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The somatic Sertoli cells of the testis are involved in secretion and endocytosis of proteins, phagocytosis of residual bodies, and in the formation of the blood-testis barrier. Sertoli cells rest on a well characterized and elaborate basement membrane (BM) benefitting cell growth, differentiation, and sperm development. The BM is a thin extracellular layer composed of glycoproteins, type IV collagen, and the proteoglycan heparan sulphate (HS). Degradation of HS occurs in the lysosome in a stepwise manner, involving heparin α-glucosaminide N-acetyltransferase (HGSNAT) enzyme. A