

5th INTERNATIONAL MEETING STEROIDS AND NERVOUS SYSTEM TORINO, Italy, Villa Gualino, February 13 - 18, 2009

VITAMIN D, NERVOUS SYSTEM AND AGING

Tuohimaa P.1,2, Kalueff A.3, Keisala T.1 and Minasyan A.1

1Medical School, 33014 University of Tampere and 2Department of Clinical Chemistry, Tampere University Hospital, Finland and 3 Laboratory of Clinical Science, National Institute of Mental Health, NIMH/NIH, Bethesda, MD 20892, USA

Vitamin D3 endocrine system consist of 3 active hormones: the main circulating hormone, calcidiol (25 OH D3), calcitriol (1,25 (OH)₂ D3) and 24-calcidiol (24,25 (OH)₂). Serum calcidiol reflects best the biological action of the hormonal forms of vitamin D3. Therefore, low serum calcidiol is associated with an increased risk of several chronic diseases including osteoporosis, cancer, diabetes, autoimmune diseases, hypertension, atherosclerosis and muscle weakness, which are aging related diseases. Both high and low vitamin D actions seem to cause premature aging. Recent animal and human studies suggest that vitamin D insufficiency is associated with an abnormal development and function of the central nervous system (CNS). In epidemiological studies, vitamin D3 insufficiency seems to be associated with an increased risk of several diseases of CNS such as multiple sclerosis, Alzheimer's and Parkinson's disease as well as schizophrenia. We have used two strains (129S1 and NMRI) of vitamin D receptor knockout mice (VDRKO) and 1 α -hydroxylase KO mice for behavioural, biochemical and morphological studies. VDR-KOs were more anxious than the WT littermates, they also showed an abnormal grooming behaviour. An ectopic calcification of the thalamic area was found in VDR-KOs. Because VDR-KOs showed a vertical swimming pattern suggesting a balance deficit, we performed several balance tests. Both rotarod and tilting platform tests suggested a balance deficit in VDR-KOs. Auditory brain stem response (ABR) suggested a premature hearing loss in VDR-KOs. 1 α -hydroxylase KOs were similar to the control mice suggesting that calcitriol might be substituted with calcidiol and 24-calcidiol in hearing and balance functions. A premature aging is linked with an abnormal expression of p53, NF- κ B and IGF signalling system. We found that the expression of p53, NF- κ B and IGF-1 receptor were significantly lower in VDR-KOs than in the control mice. In conclusion, hormonal forms of vitamin D3 appear to be neuroactive and their imbalance causes functional disturbances in CNS and possibly a premature aging of the CNS.