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The hypothalamus in alzheimer's disease

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Abbreviations: AD, Alzheimer's Disease; GA, Golgi Apparatus; ER, Endoplasmic Reticulum; SCN, Suprachiasmatic Nucleus; PVN, Paraventricular Nucleus; SST, somatostatin; CRs, Circadian Rhythms

Editorial

Alzheimer's disease (AD) is a progressive devastating neurodegenerative disease causing serious irreversible cognitive decline in presenile and senile age, having considerable social, legal, ethical[1] and economic impact.[2] The clinical phenomena of the disease include prominent memory and learning impairment, attention deficit, gradual deterioration of judgment,executive dysfunction,language disturbances, visuospatial disorientation, which sometimes is obvious even at the initial stages of the disease, behavioral and mood disturbances associated with personality alterations and progressively autonomic dysfunction, changes in the endocrine system and physical decline, which become particularly prominent as the disease advances.[3]

The neuropathological alterations include neurofibrillary tangles consisting of highly phosphorylated tau proteins, extracellular aggregates of Aβ peptide in the form of neuritic plaques, dendritic alterations, synaptic loss, selective neuronal loss[4] affecting mostly the limbic and neocortical areas and blood–brain barrier disruption and microvascular lesions, which contribute also in plotting the neuropathological profile of AD.[5]

Electron microscopy enlarges the horizons of morphological alterations in AD visualizing clearly the substantial synaptic loss in association with marked alterations of the organelle involving mostly mitochondria,[6] Golgi apparatus (GA),[7,8] and endoplasmic reticulum (ER)[9] clearly observed even in areas of the brain, where dendritic plaques and neurofibrillary tangles are infrequent.

Autonomic dysfunction has been frequently reported in ADeither as hyperactivity or as failure of the autonomic system.[10] The autonomic responses to emotional or cognitive stimuli may be impaired, even in the initial stages of AD. Hypothalamic nuclei may be implicated in AD,[11] although all of them are not involved simultaneously and in the same extend. Microinflammation of the hypothalamus on the other hand may occur in aging and age related diseases such as AD.[12] In the field of clinical investigation was noticed that substance P and hypocretin (orexin), which plays an important role in sleep-wake cycle and food intake, were elevated in the CSF in a substantial number of AD patients in comparison with normal controls.[13,14] Somatostatin (SST) is consistently reduced in the hypothalamus and neocortical areas in AD,[15,16] correlating with cognitive decline, although it is well documented that the SST system is also implicated in stress, anxiety and depression.[17]

Neuropathological studies based on silver impregnation techniques in association with the Golgi - Nissl method, revealed marked dendritic alterations. Loss of dendritic spines, abnormal spines, a considerable decrease in spine density, and substantial decrease in the neuronal population in the hypothalamic nuclei in AD, affecting primarily the suprachiasmatic nucleus (SCN). Electron microscopy revealed marked mitochondrial alterations in the soma and dendritic branches and fragmentation of Golgi apparatus in a substantial number of neurons of the SCN and PVNof the hypothalamus.[18]

Among the hypothalamic nuclei the SCN seems to be more seriously affected in aging[19] and in a dramatic way in AD,[18,20] a fact that might explain the phenomenon of desynchronization of circadian rhythms (CRs) in the majority of the patients who suffer from AD,[21] since SCN is of substantial importance for the generation and the synchronization of CRs in man.[22]

In addition the involvement of the hypothalamic nuclei in the course of AD may explain the sleep disturbances,[23] the changes of feeding behavior, energy homeostasis, and thermoregulation of the body, as well as the autonomic dysfunction, which are gradually manifested as the diseases advances and contribute in the tragic physical decline of the patients eventually.[24]

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None.

Conflicts of interest

None.

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