Research and Reviews: The Neurosurgery Journal

Extended Abstract
Vol. 2, Iss. 2
2019

Euro Dementia 2019: RTP801 is a critical factor in the neurodegeneration process of A53T α-synuclein in a mouse model of Parkinson's disease under chronic restraint stress

Naihong Chen
Chinese Academy of Medical Sciences and Peking Union Medical College, China

Background and Purpose: Recently, the incidence of Parkinson's disease has shown a tendency to move to a younger population, linked to the constantly increasing stressors of modern society. However, this relationship remains obscure. Here, we have investigated the contribution of stress and the mechanisms underlying this change.

Experimental Approach: Ten-month-old α-synuclein A53T mice, a model of Parkinson's disease (PD), were treated with chronic restraint stress (CRS) to simulate a PD-sensitive person with constant stress stimulation. PD-like behavioural tests and pathological changes were evaluated. Differentiated PC12-A53T cells were treated with corticosterone in vitro. We used Western blot, microRNA expression analysis, immunofluorescence staining, dual luciferase reporter assay and HPLC electrochemical detection to assess cellular and molecular networks after stress treatment. In vivo, stereotaxic injection of shRNA lentivirus was used to confirm our in vitro results.

Parkinson's disease (PD) is characterised by a loss of dopaminergic neurons within the nucleus niger (SN) and also the formation of Lewy bodies with aggregation of α-synuclein (αSyn). metal has emerged because the second most typical neurodegenerative disorder. There are not any medicine obtainable to delay or forestall the progression of metal , however studies have known some factors contributory to deterioration during this condition, as well as ageing, trauma, and stress. Elucidation of their mechanisms could offer novel clues for this issues in developing medicine for the treatment of metal.

The increasing stress in trendy society means the general public area unit subjected to long-term anxiety and major affective disorder. we've got targeted on the contribution of this increasing stress to the sooner age of onset of metal and to the sweetening of metal morbidity. Mounting proof indicates that stress enhances the progression of metal. In rodents, stress, like tail pinch, redoubled striatal Dopastat unleash and turnover and excitation of striatal dopaminergic nerve terminals, that resulted in necrobiosis. Sequent studies incontestable that stress caused by a unilateral 6-hydroxydopamine lesion within the nigrostriatal bundle accelerated neural degeneration, that exaggerated motor symptoms in rats (Smith et al., 2008). Chronic stress results in reduced dopaminergic activity among the ventral tegmental space in rodents and caused redoubled corticoid levels in metal patients.

One case rumored that a 38-year-old girl suddenly old associate degree early onset of metal symptoms one week when learning grievous news, that more aroused attention to the results of stress on systema nervosum. there have been some indications of correlations between stress and metal, like the contribution of reduced T-lymphocytes to dopaminergic cell loss, activation of the HPA axis by unhealthy cytokines and chemokines, and a shift of catecholamines into the cytoplasm to become toxic via toxic. However, there's no robust proof of the incidence and deterioration of metal induced by stress.

This work is partly presented at on 15th International Conference and Exhibition on Alzheimer Disease, Dementia & Ageing on April 22-23, 2019 held at Rome, Italy.

The macromolecule RTP801 is additionally called Dig2 or REDD1, and is encoded by the stress-responsive cistron cistron transcript four (DDIT4). RTP801 may be a GR target cistron, one in all the genes activated by glucocorticoids and by stress, like drive, DNA damage, and nutrient or energy deprivation. Mice lacking RTP801 (RTP801 KO) area unit proof against proof against pathological conditions and should suppress the adverse effects of glucocorticoids. Abnormalities in RTP801 signaling might also disturb energy physiological condition. A comparison of RTP801 expression in post-mortem brains from metal and management patients found that RTP801 was extremely elevated among neuromelanin-containing neurons of the tin, however not in neural structure neurons. Therefore, RTP801 was outlined as a stress-coping regulator however conjointly as a pro-apoptotic agent in neurodegenerative disorders. the current study used 10-month-old A53T mutant human αSyn transgenic mice as a PD-sensitive model. In these mice, we have a tendency to known RTP801 because the reactive think about think about. These results support the chance of targeting RTP801, as a method of preventing the tendency to earlier onset of metal which can result from constant social stress.

Key results: The protein RTP801 is encoded by DNA-damage-inducible transcript 4, and it was specifically increased in dopaminergic neurons of the substantia nigra after CRS treatment. RTP801 was post-transcriptionally inhibited by the down-regulation of miR-7. Delayed turnover of RTP801, through the inhibition of proteasome degradation also contributed to its high content. Elevated RTP801 blocked autophagy, thus increasing accumulation of oligomeric α-synuclein and aggravating endoplasmic reticulum stress. RTP801 inhibition alleviated the symptoms of neurodegeneration during this process.

Conclusions and implications: RTP801 is a promising target for the treatment of PD, especially for PD-sensitive patients who live under increased social pressure. Down-regulation of RTP801 could inhibit the current tendency to an earlier onset of PD.

This work is partly presented at on 15th International Conference and Exhibition on Alzheimer Disease, Dementia & Ageing on April 22-23, 2019 held at Rome, Italy.