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Can mental stress cause Parkinson's disease ?

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Abstract :

Parkinson's disease (PD) is a neurodegenerative disease characterized by the loss of dopaminergic (DA) neurons in the substantia nigra pars compacta (SNpc) and, to a lesser extent, in the noradrenergic neurons of the locus coeruleus (LC). Most cases of PD are idiopathic and sporadic and are believed to be the result of both environmental and genetic factors. At this report two articles were chosen to discuss the possible relationship between chronic resistant stress and Parkinson's disease . The first one is a case report about patient who had traumatic stress . The second is a case study was made on rats by exposing them to severe and prolonged stress . Both articles indicated that the ongoing exposure to stress causes neurodegeneration, specifically causes neural damage in SN and LC . Which is the hole mark for Parkison's disease .

Introduction

There has been no constant definition of stress , whereas people have different ideas with respect to the definition of stress , it is known as physical , mental , emotional factor that causes bodily or mental tension .

There are different types of stress , such as physical stress which refers to physical activities and events that wreak havoc on the human body, emotional and traumatic stress which are the most common .

Stress may be acute or chronic, according to the American Psychological Association , chronic stress refers to an extended stress that may last for years and even decades .

Mental (Chronic) stress occurs when the individual is exposed to ongoing stressors without relief, which leads to the activation of complex neurologic and endocrinologic reactions that stimulate the secretion of specific hormones.

The constant release of stress hormones causes changes in brain and body chemistry and function . These hormones are typically involved in the flight or fight reaction. When an individual is exposed to high levels of stress on an ongoing basis, the constant production of stress hormones causes them to build up in the body, the glands that produce them become fatigued, and mental and physical illness and disease can set in.¹

An example of such diseases are neurodegenerative diseases which leads to neuron death , with the most common being Parkinson's disease .

which is a neurodegenerative disease characterized by the loss of dopaminergic (DA) neurons in the nigrostriatal and mesolimbic pathways including ventral tegmental area (VTA) .¹

Causes of PD include viral infection, head trauma, herbicides, pesticides, heavy metal exposure, and genetic mutations . Genetic PD is estimated to account for approximately 5% of the PD cases, and at least 90% of the PD cases are sporadic and have unknown etiology.

Recent studies found that the exposure to chronic stress may simultaneously induce multiple neuronal loss of dopaminergic DA systems, which then leads to Parkinson's disease .¹

This report will discuss the possibility of chronic stress to cause Parkinson's disease .

Materials and Methods

An experiment was made by searching in google scholar using key-words like (Mental stress , Chronic stress , Parkinson's disease) .

The results of the search revealed many articles , two of them were chosen to be discussed in this report .

The first one is a case study was made on rats . It was made by exposing them to chronic stress . It was done by housing the animals in a room maintained at 20–22°C with a 12-h light/12-h dark cycle and food and water were provided .

The procedure was repeated in a schedule of 1 day in 2 , 4 , 8 , 16 weeks of chronic resistant stress .

Tissues were collected after the latest session to be examined .¹

The second one is a case report was published on July/ 7th/ 2019 , revealed that a 38 year-woman experienced an emotional trauma after learning that her beloved husband was cheating on her .

Certain testes and investigations were made after her going through repeated cycles of insomnia , anxiety and anorexia .

One week later , she had sudden onset of rest tremor in her left arm .²

Results

In the first article , tests were made and they gave the following results :

1- Tyrosine hydroxylase neuron loss in the substantia nigra .

2- Tyrosine hydroxylase neural loss in in the locus coeruleus .

3- Fluoro-jade-B immunoreactive cells were detected as markers of degeneration in the SN and LC .¹

In the second article , tests were made to the patient and revealed as following ;

After going through traumatic stress ; the patient suffered from insomnia and anorexia .

One week after, she experienced sudden onset of rest tremors in her left arm .

Routine examinations were normal, and there were no abnormalities in ceruloplasmin level or thyroid hormone tests.²

Discussion

The previous results of the study (In the first article) indicates that the exposure to chronic RS markedly reduced the number of DA neurons in the SNpc and that of noradrenergic neurons in the LC. In addition, neuronal loss was accompanied by excessive microglial activation; the oxidative stress marker NT was markedly increased in the SN and LC. These observations indicates significant DA neuron loss in rat SN after only 2 weeks of RS and further intensification following continuous exposure to chronic stress for up to 16 weeks. Chronic stress also reduced the levels of TH mRNA and protein as well as the levels of DA neurotransmitter measured using in situ hybridization, Western blot analysis, and HPLC assays, respectively. To ensure that the observed loss of TH immunoreactivity reflected neuronal loss rather than altered TH expression, cell numbers were evaluated using cresyl violet staining of Nissl bodies and by FJB immunofluorescence labeling of degenerating cells, regardless of whether they were apoptotic or necrotic. Therefore, the number of Nissl-stained cells was similar to that of TH-ir cells. Importantly, FJB-positive cells initially appeared in the SN after only 2 weeks of chronic RS, indicating early degeneration with TH-ir loss.

Furthermore, FJB-staining was specific for cells that showed shrinking morphology, indicating that the induction of DA neurodegeneration was caused by chronic stress in the SN.

Noradrenergic neurodegeneration reportedly occurs in conjunction with DA neuron loss in PD. Accordingly, the present data show neurodegenerative changes in the LC after only 8 weeks of RS, suggesting that chronic stress alone induces both DA and noradrenergic neurodegeneration.

Previous studies have shown that acute stress increased excessive microglial activation in the brain, microglial changes after chronic stress was investigated in the previous study and it revealed continuous and gradual microglial activation in the whole brain and the SN and LC.

Importantly, in the previous study it highlighted that the style and amount of stress that the rats expressed was severe and prolonged, and it was made intentionally to indicate the relationship between the chronic stress and neurodegeneration, but it is not yet confirmed to what extent it can be compared to human.¹

As for the second article, the case was diagnosed with PD. The evidence as reported in the case were at first, it was verified that she had no severe or acute medical conditions. Second, the EMG results were consistent with features of the typical resting tremor. Third, at the early stage of PD, D2 receptors in the striatum were upregulated,^{3,4} and D2-receptor binding in both the caudate nucleus and putamen had a positive correlation with the metabolic rate for glucose in early PD. Eidelberg et al suggested that in early stages of PD, increased glucose metabolism in the putamen was related to the complex feedback mechanism induced by striatal dopamine dysfunction. Thus, the increased glucose metabolism in the putamen, seen on PET scan, is consistent with the early stages of the disease. Lastly, antiparkinsonian medications were effective.

It is important to know that such disease (Parkinson's) is rarely seen before 40's .

But for this patient, stress was an important role in her symptoms, and was proposed that stress increased motor symptoms .

It was also suggested that appearance of the clinical PD symptoms during a stressful period may reflect damage to the nigrostriatal system that had been masked during the preclinical stage.²

Other studies supported the previous results . As for in some studies ex-prisoners of war had a significantly higher incidence of developing PD several decades after their release.³

Conclusion

Both studies show that stress triggers DA and noradrenergic neurodegeneration, potentially contributing to the etiology of PD . These observations indicate that severe and prolonged stress may trigger dopaminergic cell loss in susceptible individuals and propose that functional somatic syndromes are commonly seen in patients with PD. the onset of sporadic PD, thereby contributing to its progression , depending on the type of stress .

References

1. Sugama, S., Sekiyama, K., Kodama, T., Takamatsu, Y., Takenouchi, T., Hashimoto, M., Bruno, C., & Kakinuma, Y. (2016). Chronic restraint stress triggers dopaminergic and noradrenergic neurodegeneration: Possible role of chronic stress in the onset of Parkinson's disease. *Brain, behavior, and immunity*, 51, 39–46. <https://doi.org/10.1016/j.bbi.2015.08.015> .
2. Zou, K., Guo, W., Tang, G., Zheng, B., & Zheng, Z. (2013). A Case of early onset Parkinson's disease after major stress. *Neuropsychiatric disease and treatment*, 9, 1067–1069. <https://doi.org/10.2147/NDT.S48455> .
3. Djamshidian A, Lees AJ. Can stress trigger Parkinson's disease? *Journal of Neurology, Neurosurgery & Psychiatry* 2014;85:878-881.