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Effect Of Bromelain On BDNF Level And Memory Loss After 6-OHDA Injection Into The Intra-Medial Forebrain Bundle In Rats With A Parkinson's Disease model.

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Abstract

Introduction:
A sophisticated cognitive process called episodic memory enables the recording, storage, and retrieval of particular events along with the context in which they occurred. However, the brain-derived neurotrophic factor (BDNF), which is extensively produced in the brain, is functionally lost in Parkinson's disease (PD), which affects memory function. Therefore, the purpose of this investigation was to determine whether or not pre/post bromelain treatment had an impact on BDNF level and memory function in 6-OHDA injected rat model of Parkinsonism.

Methods:
Neurotoxin 6-OHDA was stereotaxically administered into male Sprague-Dawley rats. A portion of the rats were given the anti-inflammatory drug bromelain (40 mg/kg i.p.) before to or 24 hours after the 6-OHDA lesion. The novel object recognition test was used to measure the rats that had received neurotoxic injections' discrimination index. Using an enzyme-linked immunosorbent test, the levels of BDNF in the plasma, PFC, and hippocampus were determined.

Results:
The treatment with bromelain before to the lesion prevented the significant drop in the discrimination index caused by 6-OHDA injection. The 6-OHDA injection and bromelain treatment raised the plasma level of BDNF, while the 6-OHDA injection pre- and post-injection lowered the plasma level of BDNF in the neurotoxin-injected rats. With post-injection bromelain therapy, a substantial rise in cortical BDNF was seen.

Conclusion

In the 6-OHDA rat model of PD, BDNF levels in plasma rose. Plasma BDNF levels may serve as a crucial early indicator of brain injury and memory loss. Treatment with bromelain corrected the neurotoxin-induced rise in plasma BDNF levels and memory deficit, indicating that bromelain may be helpful in preventing memory loss in people with Parkinson's disease (PD).

Keywords:
BDNF,6-OHDA,Hippocampus,Pre-frontal cortex,Bromelain

Introduction

Episodic memory is a sophisticated collection of cognitive processes in humans that enable the conscious recording, storage, and retrieval of singular events and the context in which they occurred [1]. Studies on neurological patients show that the prefrontal cortex (PFC) and, particularly, the hippocampus, are associated with learning and memory [2, 3]. Patients with neurodegenerative diseases frequently experience cognitive impairment, which can range in severity from moderate cognitive impairment to dementia [4] depending on how severe the neuroinflammation is.

Brain derived neurotrophic factor (BDNF), which is essential for learning and memory and is strongly expressed in the hippocampus [5], is a target for research on the cognitive deficiencies associated with neurodegenerative disorders like Parkinson's disease (PD). BDNF and other neurotrophin family members carry out critical tasks including neuron development, differentiation, and survival [6]. Some investigations have revealed substantial deterioration and atrophy of spatial memory together with hippocampus shrinkage.

of nerve cells in PD patients [7,8]. BDNF affects the survival and performance of certain groups of dopaminergic, serotonergic, and GABAergic neurons in the brain [9]. Additionally, nerve regeneration or BDNF-mediated inhibition of neuronal loss was reported to be a successful management strategy for PD [10].

BDNF is produced by peripheral blood mononuclear cells and vascular endothelial cells in the periphery, where it is present in the plasma and platelets [11, 12]. BDNF can traverse the blood-brain barrier [13] in both directions, from the brain to the periphery and from the periphery to the brain [14], despite the protein's size (27 kDa), thanks to a high capacity saturable transporter system. BDNF levels in the brain and serum have been shown to be positively correlated [15].

Human longitudinal studies have demonstrated that BDNF polymorphisms are related with neuroinflammation and hippocampus shrinkage, which is consistent with evidence from animal models [16,17]. The

expression of the neurotrophin family, which includes nerve growth factor and other neuropeptides that share structural similarities with it, such as BDNF, is upregulated in the hippocampus after neuroinflammation [18] and is linked to a higher risk of memory loss [19]. Additionally, when the symptoms are severely exaggerated, inflammatory responses have been linked to the advancement of numerous neurological illnesses, including PD. Additionally, this opens up the possibility of using anti-inflammatory drugs to treat these disorders [20]. In the current work, we sought to examine how memory loss in a 6-OHDA rat model of PD was affected by bromelain as an anti-inflammatory medication, as well as any potential effect on the plasma and specific brain regions' levels of BDNF.

Results

For the novel object recognition test, we examined the amount of time the rats in the four groups—NN, 6N, Br6, and 24Br—spent interacting with the novel object (n=10 per group). The effect of 6-OHDA was shown by two-way repeated measures ANOVA as substantially less time spent with the novel item (6N post vs. NN post, p 0.05); F(1, 36) = 33.86, p 0.001. Additionally, bromelain pre-treatment of 6-OHDA-injected rats (6N post vs. Br6 post) significantly enhanced the amount of time spent with the new object (6N post vs. Br6 post), p 0.05. Similar to this, presurgical bromelain treatment (6N vs. Br6) significantly reversed the reduction in the percentage discrimination index caused by 6-OHDA injection F(1, 36) = 7.72, p 0.001. The index of percentage discrimination was compared to a 6-OHDA injection after surgery, although the difference was not statistically significant.

The neurotoxic (6-OHDA) significantly raised the plasma level of BDNF in comparison to the control group (NN), F(3, 20) = 5.806, p = 0.0059, Figure 2A. Bromelain pretreatment significantly decreased systemic BDNF (6N vs. Br6), p 0.05. Additionally, bromelain post-surgery treatment significantly decreased plasma BDNF level (6N vs. Br6), p 0.05. The level of BDNF in the cortex was affected by treatment F(3, 20) = 3.914, p = 0.0259, Figure 2B. Although 6-OHDA injection had no effect on the cortical BDNF level, post-surgery bromelain treatment was shown to considerably raise it (6N vs. 24Br), p 0.05. Additionally, pretreatment with bromelain had no discernible impact on the amount of BDNF in the cortex. 6-OHDA injection led to an increase but not significantly, in the hypothalamic concentration of BDNF. Pretreatment with bromelain decreased the hypothalamus concentration of BDNF, however this effect was not statistically significant. In addition, when compared to 6-OHDA injection, the hippocampus level of BDNF was unaffected by the post-treatment with bromelain.

Conclusion

In conclusion, our research revealed that the 6-OHDA rat model of Parkinson's disease significantly increased the plasma level of BDNF. The increase in plasma BDNF levels was reversed by bromelain therapy. As a result, it is possible to speculate that bromelain, along with a significant reduction in BDNF level, may play a crucial role in the memory impairment during PD and serve as an important early marker of brain injury.

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