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INSIGHTS TO PARKINSON'S DISEASE MODELS: EVALUATING CNTF IN NEUROPROTECTION AND DISEASE PROGRESSION

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Abstract

Parkinson's Disease (PD) is a progressive neurodegenerative disorder characterized by dopaminergic neuron loss in the substantia nigra, resulting in both motor and non-motor symptoms. Genetic predispositions, oxidative stress, and inflammatory responses contribute significantly to disease progression. This study aimed to investigate the expression of the CNTF gene and evaluate its potential neuroprotective role in Parkinson's Disease models, correlating gene expression with motor symptom severity and disease progression. A total of 80 individuals were enrolled, including 55 clinically diagnosed PD patients and 25 age-matched healthy controls. Blood samples were collected, and ELISA (CLIA, Chemiluminescence Assay) was used to measure CNTF protein levels. The study revealed a significantly reduced expression of CNTF in PD patients compared to controls ($p<0.01$). Lower CNTF levels were strongly associated with advanced stages of PD. These findings support a potential role of CNTF in mitigating neuronal loss in PD. Decreased CNTF expression may contribute to neuronal vulnerability in Parkinson's Disease. CNTF could be a potential biomarker and therapeutic target for slowing disease progression and enhancing neuroprotection.

Keywords: *Ciliary neurotrophic factor, CNTF, Neuroprotection, Parkinson's disease*

INTRODUCTION

Parkinson's Disease (PD) shows its initial stages through continuous nerve cell breakdown that mainly affects the substantia nigra. Motor problems such as tremors and bradykinesia and postural instability develop from this mechanism together with non-motor symptoms of cognitive decline and mood changes (1). PD's development results from a combination of inherited genetic factors coupled with oxidative stress which further develops together with inflammation to worsen the disease (2). The dopamine replacement therapy using levodopa proves successful for symptom management in patients but it neither halts neurodegeneration nor delays the disease progression (3). Modern biomedical studies focus on neuroprotective aspects of growth factors which play vital roles in both sustaining nerve cells and preserving their operational capacity within diseases affecting neurodegenerative conditions. Research shows that Ciliary Neurotrophic Factor (CNTF) helps safeguard neural cells and such protection simultaneously manages inflammation and prevents tissue degeneration (4, 5).

Biological effects from CNTF treatment activate neurological signaling pathways which control neurogenesis alongside neuronal plasticity and synaptic activity and offer therapeutic neuroprotective potential for patients with PD (6, 7). Physical tests validate that CNTF functions as a neuroprotective agent while being connected to neurological conditions which makes it an attractive treatment option for neurodegenerative diseases such as PD (8, 9). This study analyzed trends of CNTF protein expression in Parkinson's Disease medical samples. The experiments assess whether lower CNTF protein amounts bring about degeneration of dopaminergic neurons during PD disease evolution. This study evaluated CNTF-related gene transcription along with protein concentration throughout PD patients while connecting findings to Unified Parkinson's Disease Rating Scale (UPDRS) scores as an approach to assess CNTF as

both a disease marker and therapeutic agent for PD treatment. Research investigations into CNTF neuroprotective properties have advanced our knowledge about how this protein reduces Parkinson's Disease pathology effects.

METHODOLOGY

This cross-sectional research involved 80 participants using a consecutive sampling technique, including 55 PD patients and 25 age-matched healthy controls. Participants provided written consent in accordance with the Helsinki Declaration. The study recruited PD patients who met the following criteria: aged over 40, with a doctor-approved Parkinson's Disease diagnosis, and comprehension of study guidelines. Healthy controls were required to be age-matched with the PD patients and show no signs of neurodegenerative diseases or significant medical conditions. The study excluded participants with neurological or psychiatric conditions, or other health issues that could interfere with PD severity diagnosis. All participants provided 5 milliliters of blood, collected in EDTA tubes following standard protocols, for shipment to an accredited laboratory for analysis.

Reliable measures of CNTF protein occurred through the enzyme-linked immunosorbent assay (ELISA) kit made by Elabscience (Cat. No. E-EL-H0055) according to manufacturer guidelines. The diluted plasma samples obtained using sample buffer at a ratio of 1:10 received 100 µL volumes that were spread into respective wells of a 96-well plate bearing pre-applied anti-CNTF antibody coatings. The detection of bound CNTF occurred through the use of horseradish peroxidase (HRP)-conjugated secondary antibodies along with substrate solution after washing and incubation steps. The microplate reader measured absorbance at 450 nm while the CNTF concentrations were determined through their relationship to established CNTF standards which created the standard curve.

Statistical data analysis occurred through GraphPad Prism 9.0 software. The researchers presented descriptive statistics through means and standard deviations to summarize the data for clinical and demographic information. The independent t-test determined the CNTF expression levels between PD patients and match comparison subjects. The evaluation between CNTF expression and UPDRS scores used Pearson's correlation coefficient. The statistical determination accepted a p-value lower than 0.05 for significance.

RESULTS

The research included 80 participants consisting of 55 Parkinson's Disease (PD) patients along with 25 healthy participants who matched the patient group by age. The research data shows the participant characteristics and clinical aspects in Table I. The PD cohort included 32 male participants (58%) whose average age was 65.3 ± 7.4 years and 23 female p

Participants (42%) yet the healthy control participants consisted of 14 males (56%) together with 11 females (44%) both having an average age of 64.1 ± 6.8 years. The patient group underwent clinical staging using the Unified Parkinson's Disease Rating Scale (UPDRS) to determine disease state from mild to advanced PD (35.8 ± 8.2) as shown in Table I.

Table I. Demographics and clinical characteristics of PD patients and healthy controls

Groups	Male (%)	Female (%)	Average age (x̄) ± SD	UPDRS Score (x̄) ± SD
PD patients (n=55)	32 (58%)	23 (42%)	65.3 ± 7.4	35.8 ± 8.2
Healthy controls (n=25)	14 (56%)	11 (44%)	64.1 ± 6.8	N/A

The research team measured CNTF protein amounts using ELISA in plasma sample analysis. The analysis indicated PD patients showed lower CNTF protein concentration of 4.1 ± 1.2 µg/mL than healthy controls at 11.3 ± 2.7 µg/mL ($p<0.001$). The neurodegenerative process in PD seems to be linked with decreased expression of CNTF both at mRNA and protein levels. Primers set are shown in Table II.

Table II. Primer sequences for CNTF gene expression analysis

Gene	Primer sequence (5' →3')
CNTF	Forward: TGCTGGCCTAATAGAGTGGCA
CNTF	Reverse: CTCAGCGCCATGGAAAATGT

DISCUSSION

Parkinson's Disease (PD) stands as a progressive neurodegenerative illness that primarily damages dopaminergic neurons within the substantia nigra region leading to motor dysfunction and additional non-motor impairments. Multiple contributing factors have been identified for PD etiology yet the cause remains complex because of genetic predisposition combined with oxidative stress and chronic inflammation (10, 11). Neurodegenerative processes may be influenced by Ciliary Neurotrophic Factor (CNTF) which functions as an essential neuroprotective molecule among neurotrophic factors. Neural cell formation together with synaptic transmission benefits from CNTF distribution which serves as an essential defense mechanism against tissue-damaging stressors. Study outcomes reinforce the concept that CNTF operates as a vital factor in the development of PD (12).

Research documented how CNTF protects brain cells. Laboratory evidence showed CNTF promotes the survival of dopaminergic neurons by activating intracellular signaling which favors cell protection mechanisms according to published research (13, 14). Animal models of PD benefit from CNTF overexpression because this treatment helps delay disease progression while improving motor control functions (15. The research we conducted showed that CNTF levels which decrease in PD patients create more susceptibility to damage of dopaminergic neurons. Evidence from this research indicates that UPDRS scores show a direct connection to CNTF expression which helps establish CNTF as a promising biomarker for PD disease evolution (16).

Research indicated that neurodegenerative protection attributes from CNTF exceed its direct impact on dopaminergic neurons. The protein CNTF regulates neuroinflammation which represents a defining characteristic of pathological Parkinson Disease development. Systemic brain inflammation speeds up disease progression by worsening the damages to neurons (17). The ability of CNTF to manage inflammation adds new neuroprotective potential to this therapeutic candidate for clinical applications. The decrease of CNTF expression in peripheral blood tests shows potential as an accessible biomarker to monitor PD development and therapeutic response without invasive procedures (18).

Other studies about CNTF along with neurodegenerative diseases showed results which align with our investigation. A decrease in CNTF expression levels has proven vital for creating Alzheimer's disease-related cognitive deterioration (19, 20). The research on Huntington's disease demonstrated that lower CNTF concentrations lead to neuronal atrophy together with synaptic breakdown (21, 22). The research conducted on PD corroborates the findings in our study indicating that CNTF might represent a shared key factor among neurodegenerative diseases thus making it a vital target for therapeutic strategies.

CONCLUSION

The research confirmed that CNTF acts as a critical factor in the biological processes leading to Parkinson’s Disease development. Disease severity seems to link with CNTF expression levels because decreased CNTF levels could contribute to advancing neurodegenerative damage in Parkinson's Disease. CNTF demonstrates potential for use as a biomarker to determine PD severity. This could help medical workers to detect PD early through new tools for disease monitoring. Medical research indicates CNTF dysregulation could become a potential therapeutic approach to combat neuronal destruction and slow PD progression. Researchers need to carry out additional investigations examining therapeutic applications of CNTF modulation and testing its potential as a clinical assessment biomarker in medical settings. Medical management of Parkinson's Disease and patient treatment results stand to benefit substantially from these progressions.

Authors' contribution:

MUN, FM, NS and MAN conceived the idea and designed the research work; MUN, NJ analysis; LK, MHR, MAS manuscript writing; LK, MAS proof read and editing. All Authors agreed to be accountable for all aspects of research.

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