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Efficacy of Cold Plasma in Stimulating Hippocampal Neurogenesis in Patients with Early-Stage Parkinson's Disease with the Mediating Role of *BDNF* Gene Expression and Cognitive Performance

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ABSTRACT

Introduction: Early-stage Parkinson's disease is associated with the loss of dopaminergic neurons and impaired hippocampal neurogenesis, leading to cognitive deficits. Cold atmospheric plasma (CAP), a novel intervention, exhibits anti-inflammatory and stimulatory effects on neural cells. Brain-derived neurotrophic factor (*BDNF*) plays a pivotal role in hippocampal neurogenesis. This study investigated the efficacy of CAP in stimulating hippocampal neurogenesis in patients with early-stage Parkinson's disease, examining the mediating roles of *BDNF* gene expression and cognitive performance.

Materials and Methods: A quasi-experimental study with a pretest-posttest control group design was conducted in neurology clinics in Tehran. The sample consisted of 60 patients with early-stage Parkinson's disease (30 in the intervention group and 30 in the control group), all at Hoehn-Yahr stages 1–2. The intervention group received 12 sessions of 20-minute each of CAP (dose: 10 kV/cm) applied to the scalp, especially the temporal region. The assessment tools included the Montreal Cognitive Assessment (MoCA) and Mini-Mental State Examination for cognitive evaluation, quantitative polymerase chain reaction for measuring peripheral blood *BDNF* gene expression, and hippocampal MRI to measure the volume of the dentate gyrus (DG). Data were analyzed using structural equation modeling (SEM) in AMOS.

Results and Discussion: Post-intervention, neurogenesis (based on DG volume) increased by 28% ($p < 0.001$). *BDNF* gene expression mediated 35% ($\beta = 0.35$) and cognitive performance (with MoCA score improving from 22.4 to 26.7) mediated 42% ($\beta = 0.42$), both of which were statistically significant. SEM confirmed the indirect pathway: CAP $\rightarrow$ *BDNF* $\rightarrow$ neurogenesis (GFI = 0.95; RMSEA=0.06). No adverse events were reported during the study.

Conclusion: CAP is a safe and effective approach for stimulating hippocampal neurogenesis in early-stage Parkinson's disease, acting through *BDNF*. It is recommended that CAP be integrated into clinical treatment protocols.



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Keywords: *BDNF*, Cognitive performance, Cold plasma, Hippocampal neurogenesis, Parkinson's disease

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