




# CLINICAL AND NEUROPHYSIOLOGICAL EFFECTS OF ANODAL TRANSCRANIAL DIRECT CURRENT STIMULATION IN PATIENTS WITH REFRACTORY CHRONIC CLUSTER HEADACHE

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**Background.** Chronic cluster headache (CCH) is a disabling disorder that remains refractory to available preventive therapies in a substantial proportion of patients. Growing evidence suggests that dysfunctional pain-processing networks and abnormal cortical excitability contribute to its pathophysiology (1). Anodal transcranial direct current stimulation (tDCS) may modulate these dysfunctional networks through changes in cortical excitability and neuroplasticity (2). We investigated the clinical and neurophysiological effects of anodal tDCS using high-density electroencephalography (HD-EEG).

**Methods.** Fifteen patients with ICHD-3 refractory chronic cluster headache underwent ten sessions of anodal tDCS (2 mA, 20 min, five sessions/week for two weeks), with the anode positioned over C3 (targeting the left dorsolateral prefrontal cortex) and the cathode over FP2. Clinical outcomes and resting-state HD-EEG were assessed at baseline (T0), immediately after treatment (T1), and one month later (T2). Functional connectivity (FC) was analysed using Network-Based Statistics, as previously described (3).

**Results.** Significant clinical improvement was observed after treatment. MIDAS scores decreased from 31.8 ± 18.4 to 23.2 ± 7.1 (p=0.01), and HIT-6 scores from 66.7 ± 0.7 to 60.2 ± 7.8 (p=0.01). Significant improvements were also observed in CHIQ (p=0.03), BDI (p=0.02), ESS (p=0.04), and PSQI (p=0.04). Clinical benefits persisted at one-month follow-up, with further improvement in MIDAS (p=0.04 vs T1; p=0.006 vs T0) and sustained reductions in HIT-6 (p=0.009), CHIQ (p=0.04), and BDI (p=0.02) compared with baseline. HD-EEG revealed frequency-specific FC modulation, with reduced theta connectivity across occipital, parietal, and limbic regions, increased alpha connectivity within temporal, prefrontal, and insular networks persisting at follow-up, and enhanced low-gamma connectivity immediately after treatment with partial persistence at one month.

**Conclusions.** Anodal tDCS over the left dorsolateral prefrontal cortex was associated with sustained clinical improvement and reorganization of cortical functional connectivity in patients with refractory CCH. The observed increase in alpha and low-gamma connectivity together with reduced theta synchronization suggests adaptive neuroplastic changes within pain-processing networks. These preliminary findings suggest that tDCS may represent a promising adjunctive treatment for refractory CCH and warrant confirmation in larger randomized sham-controlled trials.