# Effects of Transcranial Direct Current Stimulation (tDCS) on Cognition in Patients Treated for Normal Pressure Hydrocephalus

## Efeitos da Estimulação Transcraniana por Corrente Contínua (ETCC) na Cognição de Pacientes Tratados por Hidrocefalia de Pressão Normal

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## ABSTRACT

This study investigated the effects of transcranial direct current stimulation (tDCS) on the cognition of patients with normal pressure hydrocephalus (NPH) who underwent cerebrospinal fluid shunt surgery. Five participants, aged between 60 and 80 years, were assessed using neuropsychological instruments at three time points: before, three days after, and thirty days after the tDCS intervention. The results demonstrated significant cognitive improvements in the Mini-Mental State Examination (MMSE) and the Addenbrooke's Cognitive Examination (ACE), both of which assess global cognitive functions. In contrast, instruments targeting specific neuropsychological domains, such as the Stroop Test and the Rey Auditory Verbal Learning Test (RAVLT), did not show statistically significant differences. The discrepancy in the results highlights the sensitivity of broad cognitive assessments in detecting generalized cognitive changes promoted by the intervention. These findings suggest that tDCS is a promising approach for cognitive rehabilitation in patients with NPH, while emphasizing the need for future studies with larger sample sizes.

**Keywords:** Transcranial direct current stimulation; Normal pressure hydrocephalus; Cognition; Cognitive rehabilitation.

## RESUMO

Este estudo investigou os efeitos da estimulação transcraniana por corrente contínua (ETCC) na cognição de pacientes com hidrocefalia de pressão normal (HPN) que realizaram cirurgia de derivação liquórica. Cinco participantes, com idades entre 60 e 80 anos, foram avaliados por meio de instrumentos neuropsicológicos em três momentos: antes, três dias após e trinta dias após a intervenção com ETCC. Os resultados demonstraram melhorias cognitivas significativas nos testes Mini-Mental State Examination (MMSE) e Addenbrooke's Cognitive Examination (ACE), que avaliam funções cognitivas globais, enquanto os instrumentos com foco em domínios neuropsicológicos específicos, como o Stroop e o RAVLT, não apresentaram diferenças estatisticamente significativas. A discrepância nos resultados destaca a sensibilidade de avaliações amplas em identificar mudanças cognitivas generalizadas promovidas pelas intervenções. Os achados sugerem que a ETCC é uma abordagem promissora para reabilitação cognitiva em caso de pacientes com HPN, mas enfatizam a necessidade de estudos futuros com amostras maiores.

**Palavras-chave:** Estimulação transcraniana por corrente contínua; Hidrocefalia de pressão normal; Cognição; Reabilitação cognitiva.

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## INTRODUCTION

Population aging is a global phenomenon with substantial implications for healthcare systems and public policies. It is estimated that by 2050, the worldwide population aged 60 years and older will reach two billion people, with significant impacts on the prevalence of chronic and degenerative neurological conditions[1]. Normal pressure hydrocephalus (NPH) fits into this context as a syndrome that predominantly affects older adults, characterized by the classic triad of gait disturbances, urinary incontinence, and cognitive decline[2,3].

Although cerebrospinal fluid shunting is considered the gold-standard treatment for NPH, with recognized efficacy in improving motor and functional symptoms[4], cognitive deficits may persist in many patients even after the surgical procedure[5]. These deficits include impairments in memory, attention, processing speed, and executive functions, associated with dysfunction in fronto-subcortical circuits and compromised integrity of the periventricular white matter[6,7]. Such limitations significantly impact patients' functionality and quality of life, highlighting the need for complementary therapeutic strategies.

In this scenario, cognitive rehabilitation has gained prominence as an additional therapeutic alternative. It consists of a set of systematic interventions aimed at improving or compensating for impaired cognitive functions, with the goal of promoting greater functional autonomy and social participation[8]. In populations with chronic neurological disorders, cognitive rehabilitation-based interventions have shown efficacy in recovering higher cognitive functions, especially when combined with brain neuromodulation techniques[9].

Among these techniques, transcranial direct current stimulation (tDCS) stands out as a non-invasive, low-cost tool with a favorable safety profile. tDCS uses low-intensity electrical current to modulate cortical excitability and promote synaptic plasticity and has been increasingly applied in the rehabilitation of cognitive disorders associated with conditions such as stroke, Alzheimer's disease, schizophrenia, and Parkinson's disease[10-13]. The beneficial effects of tDCS on cognitive performance have been observed in domains such as working memory, verbal fluency, sustained attention, and inhibitory control[14-16].

Although scarce, studies with NPH patients suggest that the combination of tDCS with clinical or surgical treatment may enhance neurocognitive recovery, amplifying therapeutic effects in the medium term[17]. Considering the progressive and multifactorial nature of cognitive impairments in NPH, the introduction of neuromodulation methods into therapeutic plans represents a promising intervention pathway. Furthermore, tDCS has been recognized as a viable rehabilitation strategy in outpatient settings, especially among older adults with multiple comorbidities[18]. Given the therapeutic potential of tDCS, it becomes essential to accurately assess its effects on cognition, particularly in conditions such as NPH.

To adequately measure the cognitive effects of the proposed interventions, it is crucial to adopt standardized, sensitive, and validated psychometric instruments, especially given the clinical and neuropsychological complexity characteristic of NPH.

In this regard, clinical decision-making requires distinguishing between neuropsychological screening instruments and formal neuropsychological assessments. Screening tools, such as the Mini-Mental State Examination (MMSE) and the Addenbrooke's Cognitive Examination (ACE), are widely used for the initial detection of global cognitive changes in exploratory contexts. On the other hand, formal neuropsychological assessments require more extensive batteries, composed of standardized tests with robust evidence of validity and reliability, capable of accurately discriminating the affected cognitive domains. The rigorous use of these tools is essential to ensure the reliability of clinical inferences and the scientific replicability of findings.

In the present study, instruments from both categories—screening and neuropsychological assessment—were used. The MMSE and ACE were employed for global screening. For the evaluation of specific cognitive domains, the RAVLT, the Stroop Test, the Trail Making Test-A (TRAIL-A), and the Digit Span subtests (Forward and Backward) from the WAIS-III were used to assess episodic memory, inhibitory control, sustained attention, and working memory. For phonemic verbal fluency, the FAS test, often used in screening contexts, was applied, and as a control for emotional variables, the Geriatric Depression Scale (GDS) was administered.

These instruments were selected based on their adaptation and validation for the Brazilian population, presenting robust psychometric properties, as evidenced by recent studies[19-25].

Given this background, the present study aims to evaluate the effects of transcranial direct current stimulation (tDCS), in combination with cerebrospinal fluid shunting, on the cognition of patients diagnosed with normal pressure hydrocephalus. Specifically, it aims to determine whether the observed cognitive changes are generalized or specific to certain domains, contributing to the consolidation of evidence-based strategies for neuropsychological rehabilitation in NPH patients.

## METHOD

This study adopted a quasi-experimental design with repeated measures to investigate the effects of transcranial direct current stimulation (tDCS) on cognition in patients diagnosed with normal pressure hydrocephalus (NPH) who had previously undergone cerebrospinal fluid shunt surgery.

Five individuals with NPH participated in the study in 2019, including three women and two men, aged between 63 and 83 years (M = 72.6; SD = 7.3), all residing in the state of São Paulo, Brazil. Educational levels ranged from 8 to 21 years of schooling (M = 15.8; SD = 5.1). Inclusion criteria were: having undergone cerebrospinal fluid shunting at least 12 months prior, being clinically stable, presenting persistent cognitive complaints, and having availability to participate in the stimulation sessions. Sociodemographic and clinical data were collected through participant interviews and review of medical records.

Neuropsychological assessment and screening instruments were used to evaluate cognitive performance at three time points: before the tDCS intervention (pre), three days after the end of the sessions (P3), and thirty days after (P30). The instruments applied in this study were: Mini-Mental State Examination (MMSE), Addenbrooke's Cognitive Examination (ACE), Rey Auditory Verbal Learning Test (RAVLT), Stroop Color and Word Test, Digit Span (Forward and Backward, WAIS-III), Trail Making Test A (TRAIL-A), Geriatric Depression Scale (GDS), and the Controlled Oral Word Association Test (FAS). The MMSE and ACE are global cognitive screening tools, composed of direct and objective response items, widely used in clinical practice for the initial detection of cognitive changes, especially in elderly populations. Both are adapted and validated for the Brazilian population.

The RAVLT assesses episodic verbal memory through learning and recall of word lists, with acquisition, interference, and delayed recall measures. The Stroop Test measures inhibitory control and selective attention using conflicting visual stimuli that require executive processing. The Digit Span subtests (Forward and Backward) assess working memory, respectively immediate auditory memory and information manipulation capacity. The TRAIL-A evaluates sustained attention, processing speed, and visual scanning, being sensitive to fronto-subcortical alterations.

The FAS (Controlled Oral Word Association Test) is a measure of phonemic verbal fluency, often used as an indirect indicator of executive functions, and the Geriatric Depression Scale (GDS) was included to control for possible emotional interference on cognitive performance. All instruments mentioned were administered in their Brazilian-adapted and validated versions, following the standards of the Federal Council of Psychology.

It is important to note that although some of these tests are individually used as markers of specific domain performance, the battery used in this study has a predominantly screening character and does not constitute, in its current scope, a comprehensive neuropsychological assessment. Thus, the results obtained should be interpreted as preliminary indicators of cognitive change and not as sufficient data for differential diagnosis or individualized therapeutic planning.

Stimulation was performed using the DC-Stimulator Mobile device (NeuroConn), provided on loan by the company Proibras. The protocol consisted of applying 2 mA for forty minutes per session, over three consecutive weeks (five sessions per week, totaling fifteen sessions). The anode was initially positioned over the right dorsolateral prefrontal cortex and then over the left hemisphere, with the cathode fixed on the contralateral deltoid muscle in both phases.

For statistical analysis, non-parametric repeated measures tests (Friedman) were applied due to the small sample size. Post hoc analyses were conducted using the paired Wilcoxon test, with a significance level of $\alpha < 0.05$. Effect size was also calculated using Kendall's W for complementary interpretation of the findings.

This study was approved by the Research Ethics Committee of the Hospital das Clínicas, Faculty of Medicine, University of São Paulo (CAAE: 00259818.0.0000.0068; approval number: 3.011.572). All participants signed the Informed Consent Form.

## RESULTS

**Table 01 –** Results of the neuropsychological assessments conducted

| Test | Descriptive | Pre | P3 | P30 | Friedman Test | Multiple 2x2 Comparisons (Wilcoxon Test) | Results |
|---|---|---|---|---|---|---|---|
| MME | Mean | 26,2 | 26,6 | 27,4 | X2=8,375 (2); p=0,015 W=0,83 (Large effect) | Pre x P3 (Z = -1,414; p=0,157) | Pre = 3 |
| | Median | 26 | 27 | 27 | | Pre x P30 (Z= -2,121; p=0,034) | |
| | SD | 1,6 | 1,3 | 1,3 | | | Pre < 30 |
| | N | 5 | 5 | 5 | | P3 x P30 (Z= -2,000; p=0,046) | P3 < P30 |
| ACE | Mean | 82,6 | 85 | 56,8 | X2=6,400 (2); p=0,041 W=0,64 (Moderate effect) | Pre x P3 (Z= -1,625; p=0,104) | Pre = 3 |
| | Median | 86 | 88 | 92 | | Pre x P30 (Z= -2,060; p=0,039) | |
| | SD | 6,8 | 4,6 | 7,1 | | | Pre< 30 |
| | N | 5 | 5 | 5 | | P3 x P30 (Z=-1,214; p=0,225) | P3 = P30 |
| RAVLT | Mean | 31,2 | 30 | 33,8 | X2=2,000 (2); p=0,368 | | There were no significant differences |
| | Median | 31 | 28 | 33 | | | |
| | SD | 2,4 | 6,4 | 6,9 | | | |
| | N | 5 | 5 | 5 | | | |
| STROOP | Mean | 18,6 | 17,8 | 18,6 | X2=2,333 (2); p=0,311 | | There were no significant differences |
| | Median | 18 | 17 | 18 | | | |
| | SD | 2,5 | 4,7 | 5,1 | | | |
| | N | 5 | 5 | 5 | | | |
| Digit Span Forward | Mean | 7 | 8,4 | 7,4 | X2=2,333 (2); p=0,311 | | There were no significant differences |
| | Median | 6 | 8 | 7 | | | |
| | SD | 1,7 | 1,9 | 1,4 | | | |
| | N | 5 | 5 | 5 | | | |
| Digit Span Backward | Mean | 5,4 | 5,4 | 5,2 | X2=0,824 (2); p=0,662 | | There were no significant differences |
| | Median | 5 | 5 | 4 | | | |
| | SD | 1,4 | 2,4 | 2,4 | | | |
| | N | 5 | 5 | 5 | | | |
| TRAIL A | Mean | 52,2 | 58 | 55 | X2=1,200 (2); p=0,549 | | There were no significant differences |
| | Median | 60 | 64 | 40 | | | |
| | SD | 22 | 19,5 | 23,4 | | | |
| | N | 5 | 5 | 5 | | | |
| FAS | Mean | 34,2 | 29,4 | 33,4 | X2=1,600 (2); p=0,449 | | There were no significant differences |
| | Median | 36 | 31 | 35 | | | |
| | SD | 4,7 | 6 | 3,3 | | | |
| | N | 5 | 5 | 5 | | | |
| GDS | Mean | 4,2 | 3 | 2,6 | X2=0,353 (2); p=0,838 | | There were no significant differences |
| | Median | 3 | 3 | 3 | | | |
| | SD | 3,2 | 2 | 1,4 | | | |
| | N | 5 | 5 | 5 | | | |

**Legend:** Mini-Mental State Examination (MMSE), Addenbrooke's Cognitive Examination (ACE), RAVLT (Rey Auditory Verbal Learning Test), and Stroop Color and Word Test (Stroop), Controlled Oral Word Association Test (FAS), Geriatric Depression Scale (GDS).

The study results were initially analyzed using the Friedman test, employed to compare repeated measures in related samples, considering the data structure. The Mini-

Mental State Examination (MMSE) revealed statistically significant differences among the analyzed conditions ($\chi^2$ = 8.375, df = 2, p = 0.015), with a large effect size (W = 0.83), according to Kendall's interpretation criteria. Given the significant result, post hoc analyses were conducted using the paired Wilcoxon test to identify which condition pairs showed statistically significant differences.

Multiple comparisons between conditions showed no significant difference between the Pre and P3 time points (Z = -1.414, p = 0.157). However, significant differences were identified between Pre and P30 (Z = -2.121, p = 0.034) and between P3 and P30 (Z = -2.000, p = 0.046).

Nevertheless, no formal corrections for multiple comparisons, such as the Bonferroni correction, were applied. This decision was based on the small sample size (N = 5), which already represents an important limitation to the statistical power of the analyses. Conservative corrections like Bonferroni, although effective in mitigating Type I errors, substantially increase the risk of Type II errors, i.e., the failure to detect real differences between conditions. Therefore, maintaining unadjusted p-values was deemed more appropriate to preserve statistical power and allow the identification of consistent patterns in the data. Despite this, the results were interpreted with caution, considering the methodological limitations and the exploratory nature of the research.

Another instrument analyzed in the study was the ACE, whose performance also revealed significant correlations between the evaluated time points ($\chi^2$ = 6.400, df = 2, p = 0.041, W = 0.64, moderate effect). The test, widely recognized for its sensitivity in assessing global cognitive abilities, showed associations reflecting changes over the course of the applied interventions: Pre vs. P3 (Z = -1.625; p = 0.104), Pre vs. P30 (Z = -2.060; p = 0.039, with Pre < P30), and P3 vs. P30 (Z = -1.214; p = 0.225). These correlations indicate a positive impact of the implemented strategies, reinforcing the hypothesis that targeted interventions can promote measurable progress, even in a small sample like that of this study. The detailed analysis revealed a pattern of continuous improvement across conditions, corroborating the efficacy of the adopted procedures.

However, the other instruments used, which specifically focus on assessing isolated neuropsychological functions, did not present statistically significant results in the conducted analyses. This discrepancy may be related to the fact that the instruments showing significant changes assess cognitive functioning in a broader and more integrated manner, whereas domain-specific tests, by focusing on restricted areas, may require more pronounced changes to capture statistically significant differences. This result highlights the greater sensitivity of generalized assessments in detecting the effects of interventions in contexts with small samples or more subtle changes.

## DISCUSSION

The findings of this study suggest that transcranial direct current stimulation (tDCS) may positively contribute to the cognitive performance of patients with normal pressure hydrocephalus (NPH). Statistically significant differences were observed in the Mini-Mental State Examination (MMSE) and the Addenbrooke's Cognitive Examination (ACE) scores, both commonly used instruments for broadly screening cognitive dysfunction. In contrast, the other applied tests, which are more specific and focused on isolated domains (such as the Stroop, RAVLT, Digit Span, and FAS), did not show significant changes across the three assessment phases.

This discrepancy between screening instruments and more targeted assessments may indicate that the effects of tDCS, in this clinical context, promote generalized but subtle improvements in global cognition, without substantially impacting specific cognitive functions. Previous studies have pointed out that the MMSE and ACE are more sensitive to broad changes in cognitive functioning, which may explain the detection of differences in these scales in small and exploratory samples[14,15]. However, it is essential to emphasize that such instruments do not constitute, by themselves, a formal neuropsychological assessment and should not be used in isolation to support clinical decisions in cognitive rehabilitation[8,9].

The present investigation predominantly used neuropsychological screening measures, limiting inferences about the impact of tDCS on specific cognitive functions. Additionally, the small sample size and absence of a control group compromise the statistical power and generalizability of the findings. These limitations are recognized in the literature on neurological interventions in elderly populations with comorbidities, where logistical and ethical obstacles often hinder more robust research designs[17,18].

Literature has demonstrated that tDCS promotes neuromodulatory effects through the induction of long-term potentiation (LTP), a mechanism associated with synaptic plasticity and the consolidation of cognitive functions such as learning and memory[10,11]. When applied over the dorsolateral prefrontal cortex—a region involved in executive control, working memory, and sustained attention—tDCS can facilitate the functional reorganization of impaired neural networks, as observed in patients with fronto-subcortical dysfunctions typical of normal pressure hydrocephalus.

In tDCS application, the anodal (positive) electrode increases cortical excitability in the underlying brain region, while the cathodal (negative) electrode tends to reduce excitability, inhibiting local neural activity[12,13]. The protocol adopted in this study, which alternated anodal stimulation between the right and left hemispheres with the cathode

fixed on the contralateral deltoid muscle, was based on evidence suggesting that bilateral and repeated stimulation may amplify the cognitive effects of the intervention[14–16]. This strategy aims to synergistically target different functional networks of the prefrontal cortex, respecting the lateralization of functions such as verbal fluency (left hemisphere) and sustained attention (right hemisphere), thus reinforcing the theoretical foundation of the model employed.

Finally, it is important to highlight that cognitive rehabilitation in patients with NPH represents a relevant clinical challenge, especially given the persistence of deficits even after cerebrospinal fluid shunting. The combination of neuromodulation techniques, such as tDCS, with structured rehabilitation programs may represent a viable and innovative alternative for this group, considering their predominantly subcortical dysfunction profile and the risk of progression to dementia syndromes[5,6,17].

Nevertheless, it is reinforced that clinical decisions aimed at rehabilitation should rely on formal neuropsychological assessments, using standardized, sensitive, and validated instruments capable of accurately discriminating the affected cognitive domains and their severity[8,9]. The use of screening scales, although useful in exploratory contexts or when resources are limited, does not replace this process and, therefore, should not serve as the sole basis for therapeutic effect inferences.

In this regard, the findings of this study should be understood as preliminary but relevant, indicating the feasibility and safety of tDCS application in patients with NPH. Future studies should investigate, with greater methodological control, the efficacy of the technique in combination with multidisciplinary rehabilitation programs, including longitudinal analyses, control groups, and more comprehensive neuropsychological batteries. Additionally, it would be desirable to investigate the specific modulation of domains such as episodic memory, verbal fluency, and executive functions, aiming to identify subgroups of patients more responsive to the intervention and expand the clinical applicability of the findings.

## CONCLUSION

The results of this study indicate that transcranial direct current stimulation (tDCS) presents potential as a complementary strategy in the cognitive rehabilitation of patients with normal pressure hydrocephalus (NPH), especially in improving general aspects of cognition, as evidenced by widely used screening instruments in clinical practice. The intervention proved to be feasible and safe, although its effects were primarily observed in global cognitive performance measures.

However, methodological limitations—such as the small sample size, absence of a control group, and predominant use of screening instruments—impose constraints on the generalization of the findings and their direct application in clinical practice. Thus, the data presented here should be understood as preliminary, serving as a foundation for more robust future investigations.

It is recommended that subsequent studies employ controlled designs, larger samples, and formal neuropsychological assessments capable of more precisely discriminating the effects of tDCS on specific cognitive domains. The combination of tDCS with structured multidisciplinary rehabilitation programs may enhance its applicability and efficacy, contributing significantly to improving the functionality and quality of life of individuals with NPH.

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