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EFFICACY AND SAFETY OF TRANSCRANIAL PULSE STIMULATION (TPS) IN OLDER ADULTS WITH MILD NEUROCOGNITIVE DISORDER e AN OPEN-LABEL TRIAL

Pak Wing Calvin Cheng, Kwan Hin Tommy Fong. University of Hong Kong, Hong Kong, Hong Kong

Abstract

Background: Neurocognitive disorder (NCD) is becoming a worldwide health burden. Non-invasive brain stimulation (NIBS) is increasingly recognized as a potential alternative than pharmacological approach in tackling this problem. Transcranial Pulse Stimulation (TPS) is a kind of NIBS that uses repetitive single ultrashort pulses in the ultrasound frequency range to stimulate the brain, and it can provide better spatial precision and reach deeper brain regions comparing to transcranial direct current stimulation (tDCS) and transcranial magnetic stimulation (TMS). Despite evidence showing significant improvement in using TPS in treating AD, there has been no study investigating the effect of TPS on older adults with mild NCD.

Objectives: This study is an open-label study to assess the effectiveness and tolerability of TPS on cognition in older adults with mild NCD. We hypothesized that a 2-week TPS intervention could significantly improve patient's global cognition.

Methods: All participants receive a six-session TPS intervention for 2 weeks with three sessions per week. Their cognitive status will be assessed immediately before and after the intervention.

Current Findings: 10 participants with mild NCD were recruited. Paired sample t-tests showed there was a significant improvement in the executive function measured by the Stroop interference scores, t (9) = -2.27, p < .05, indicating that participants use less time in completing the Stroop test after the intervention (M = 13.14, SD = 11.87) than before (M = 25.16, SD = 18.65). Trends of cognitive improvement have also been found in global and other cognitive domains despite not statistically significant, which is probably due to small sample size. All participants finished six-session and reported no severe side effects.

Practice Implications: The results of current study could provide empirical support on the effectiveness and tolerability of TPS as a new treatment in patients with mild NCD.

Keywords: Neurocognitive disorder (NCD), Non-invasive brain stimulation (NIBS), Transcranial Pulse Stimulation (TPS)
Introduction

- Neurocognitive disorder (NCD) is becoming a worldwide health burden. Non-invasive brain stimulation (NIBS) is increasingly recognized as a potential alternative than pharmacological approach in tackling this problem.
- Transcranial Pulse Stimulation (TPS) is a kind of NIBS that uses repetitive single ultrashort pulses in the ultrasound frequency range to stimulate the brain, and it can provide better spatial precision and reach deeper brain regions comparing to transcranial direct current stimulation (tDCS) and transcranial magnetic stimulation (TMS).
- Despite evidence showing significant improvement in using TPS in treating Alzheimer’s disease, there has been no study investigating the effect of TPS on older adults with mild NCD.

Objectives

This study is an open-label study to assess the effectiveness and tolerability of TPS on cognition in older adults with mild NCD. We hypothesized that a 2-week TPS intervention could significantly improve patient’s global cognition.

Methods

- Subjects identified by case medical officers and screened for eligibility from local public psychiatric outpatient clinic.
- Cantonese speaking elderly who aged ≥ 60 years old, diagnosed with mild neurocognitive disorder (NCD; DSM-V) were included.
- Major NCD / dementia subjects were excluded from study.
- All participants received three 30-minute TPS sessions every other day per week for 2 weeks.

Transcranial Pulse Stimulation

- A global brain stimulation approach, which homogenously distributes the total energy of 6000 TPS pulses per session over all accessible brain areas.
- Prefrontal, Temporal and Occipital brain areas were stimulated by ultrashort (3 μs) ultrasound pulses with typical energy levels of 0.2-0.25 μl/m2 and pulse frequencies of 4-5 Hz (pulses per second).

Results

Table 1. Repeated Measures ANOVA – Overall Time Effects due to TPS.

<table>
<thead>
<tr>
<th>Domains</th>
<th>Measures</th>
<th>Baseline (t0 (N=11))</th>
<th>12-Week TAU (t1 (N=11))</th>
<th>2-Week TPS (t2 (N=11))</th>
<th>12-Week Follow-up (t3 (N=11))</th>
<th>One-way Repeated ANOVA Effect of Time</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Mean (SD)</td>
<td>Mean (SD)</td>
<td>Mean (SD)</td>
<td>Mean (SD)</td>
<td></td>
</tr>
<tr>
<td>Global Cognition</td>
<td>HK-MoCA Total</td>
<td>19.36 (2.84)</td>
<td>19.45 (2.30)</td>
<td>21.45 (2.50)</td>
<td>21.45 (2.30)</td>
<td>F (3,30) = 4.107, p = 0.015*</td>
</tr>
<tr>
<td></td>
<td>Stroop Interference</td>
<td>22.28 (16.18)</td>
<td>23.35 (18.69)</td>
<td>13.02 (12.17)</td>
<td>18.09 (15.06)</td>
<td>F (3,30) = 1.863, p = 0.157</td>
</tr>
<tr>
<td></td>
<td>TMT Interference</td>
<td>119.48 (111.64)</td>
<td>89.14 (99.94)</td>
<td>92.64 (66.13)</td>
<td>70.41 (47.58)</td>
<td>F (3,30) = 2.222, p = 0.108</td>
</tr>
<tr>
<td>Cognitive Functioning</td>
<td>Forward DS Total</td>
<td>8.88 (2.00)</td>
<td>10.00 (2.58)</td>
<td>9.75 (2.72)</td>
<td>9.64 (2.91)</td>
<td>F (3,30) = 3.606, p = 0.025*</td>
</tr>
<tr>
<td></td>
<td>Backward DS Total</td>
<td>4.19 (1.91)</td>
<td>4.13 (1.63)</td>
<td>4.38 (2.00)</td>
<td>4.91 (1.76)</td>
<td>F (3,30) = 1.878, p = 0.201</td>
</tr>
<tr>
<td></td>
<td>Verbal Fluency Test</td>
<td>30-second Interval</td>
<td>24.06 (3.82)</td>
<td>26.25 (5.31)</td>
<td>20.98 (5.50)</td>
<td>F (3,30) = 3.755, p = 0.021*</td>
</tr>
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<td></td>
<td></td>
<td>60-second Interval</td>
<td>32.69 (4.29)</td>
<td>34.38 (7.74)</td>
<td>33.75 (8.35)</td>
<td>F (3,30) = 2.960, p = 0.116</td>
</tr>
<tr>
<td>Depressive Symptoms</td>
<td>HAMD-D Total</td>
<td>7.25 (4.68)</td>
<td>6.69 (4.30)</td>
<td>5.63 (4.69)</td>
<td>6.45 (3.96)</td>
<td>F (3,30) = 2.069, p = 0.181</td>
</tr>
<tr>
<td>Daily Functioning</td>
<td>Chinese IADL Total</td>
<td>23.31 (3.46)</td>
<td>22.31 (4.09)</td>
<td>22.94 (3.26)</td>
<td>23.27 (2.97)</td>
<td>F (3,30) = 1.066, p = 0.378</td>
</tr>
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</table>

* p < 0.05. TAU = Treatment-as-usual; DS = Digit Span.

Discussion

- TPS is likely to have an immediate effect on global cognition and executive functioning of older adults with mild NCD, and the improvements seemed to be sustainable.
- Despite statistical insignificance, trends of improvement were observed in depressive symptoms after receiving TPS.
- There might be a placebo effect by queueing TPS treatment, as reflected by the slight improvements shown between baseline and after 12-week treatment-as-usual period.

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References