Contribution of non-invasive brain stimulation to the evaluation and treatment of dysphagia

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Non-Invasive Brain Stimulation (NIBS): main techniques

- Transcranial magnetic stimulation (TMS)
- Transcranial electrical stimulation (TES)
Transcranial magnetic stimulation (TMS)

TMS is based on the principle of electromagnetic induction
Transcranial magnetic stimulation (TMS)

Barker, 1984
Transcranial magnetic stimulation (TMS)

Effects of coil geometry on the stimulated cortical surface
Transcranial magnetic stimulation (TMS)

Paradigms of TMS

- Single-pulse TMS (spTMS)
- Paired-pulse TMS (ppTMS)
- Repetitive TMS (rTMS)
  - Theta burst stimulation (TBS)
  - Paired associative stimulation (PAS)
Transcranial direct current stimulation (tDCS)
tDCS: Mechanism of action
It modulates the basal activity (spontaneous neuronal firing) of the stimulated cortical area, increasing it (anode currents) or reducing it (cathode currents)
Characterizing the application of transcranial direct current stimulation in human pharyngeal motor cortex

Samantha Jefferson, Satish Mistry, Salil Singh, John Rothwell, and Shaheen Hamdy

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Fig. 3. Overlaid traces of pharyngeal MEPs from the stimulated hemisphere of 1 subject, showing typical responses to 3 different tDCS paradigms [sham (C), anodal (A), and cathodal (B)]. Note the changes in amplitude following anodal and cathodal stimulation, which are not seen with sham stimulation alone.

tDCS applied to the motor cortex of the pharynx (right hemisphere)
Cortical control of swallowing: Cooperation between homologous cortical areas
Task-concurrent anodal tDCS modulates bilateral plasticity in the human suprahyoid motor cortex

Shaofeng Zhao, Zulin Dou*, Xiaomei Wei, Jin Li, Meng Dai, Yujue Wang, Qingfu Yang and Hual He

**FIGURE 1** | Flow diagram of experiment protocols showing the time points for measurements and interventions. tDCS, transcranial direct current stimulation.
FIGURE 2 | tDCS over the stronger hemisphere concurrent with the swallowing task. (A) a-tDCS increased suprathyroid cortical excitability in the stronger hemisphere. (B) a-tDCS had no effects on the weaker hemisphere (*p < 0.05; **p < 0.001, compared with sham, respectively).

Zhao et al., 2015
Unbalanced hemispheric cooperation between homologous cortical areas involved in the control of swallowing
Magnetoencephalographic evidence for the modulation of cortical swallowing processing by transcranial direct current stimulation

Sonja Suntrup, Inga Teismann, Andreas Wollbrink, Martin Winkels, Tobias Warnecke, Agnes Höfl, Christo Pantev, Rainer Dziewas

- **Left hemisphere**: main role in controlling the oral phase
- **Right hemisphere**: greater role in the control of the pharyngeal phase

**a.** ↑ ERD related to *rapid swallowing task* after anodal tDCS of the **left hemisphere**

**b.** ↑ ERD related to *challenged swallowing task* post-anodal tDCS of the **right hemisphere**

- **Bilateral activation**
- **Unilateral (right)**
rTMS: rationale for therapeutic approaches

<table>
<thead>
<tr>
<th>Inhibitory Stimulation over the contra-lesioned (healthy) M1.</th>
<th>Decrease in the transcallosal inhibition to the affected hemisphere and an increase in the excitability of healthy hemisphere.</th>
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<tbody>
<tr>
<td><img src="image1.png" alt="Brain Image" /></td>
<td><img src="image2.png" alt="Brain Image" /></td>
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<tr>
<th>Excitatory Stimulation over the lesioned M1</th>
<th>Increase in cortical excitability of the lesioned hemisphere</th>
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<td><img src="image3.png" alt="Brain Image" /></td>
<td><img src="image4.png" alt="Brain Image" /></td>
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<tr>
<th>Excitatory Stimulation over the contra-lesioned M1</th>
<th>Undamaged hemisphere will promote recovery.</th>
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<td><img src="image5.png" alt="Brain Image" /></td>
<td><img src="image6.png" alt="Brain Image" /></td>
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<th>Bilateral excitatory stimulation</th>
<th>Clinical identification of the dominant hemisphere is frequently difficult. Bilateral stimulation method may generalize the effects.</th>
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<td><img src="image7.png" alt="Brain Image" /></td>
<td><img src="image8.png" alt="Brain Image" /></td>
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Therapeutic approaches using tDCS in post-stroke dysphagia

- Ipsilesional anodal and contralesional cathodal stimulation
- Contralesional anodal stimulation
- Ipsilesional anodal stimulation
- Bilateral anodal stimulation
Suntrup-Krueger et al., 2018
Ann Neurol. 2018

- RCT on 60 patients with acute post-stroke dysphagia
- Parameters: 1 mA x 20 min, 4 consecutive days
- Concomitant swallowing maneuvers

Score changes at FEDSS:

- 1,3 real group
- 0,4 sham group

P<0.0005

- The benefit is greater the earlier the treatment is started
- Less improvement in patients with right ischemic operculo-insular lesions
Anodal bihemispheric stimulation

- Unilateral ischemic stroke, chronic dysphagia > 6 months
- Parameters: 1 mA x 20 min, 2 weeks
- Concomitant intensive dysphagia therapy

**ORIGINAL REPORT**

*EFFECT OF BIHEMISPHERIC ANODAL TRANSCRANIAL DIRECT CURRENT STIMULATION FOR DYSPHAGIA IN CHRONIC STROKE PATIENTS: A RANDOMIZED CLINICAL TRIAL*

Young Hyun AHN, MD1, Hyun-Joo SOHN, MD, PhD1, Jin-Sung PARK1, Tae Gyu AHN2, Yong Beom SHIN, MD1, Minsu PARK1, Sung-Hwa KO, MD1, and Yong-II SHIN, MD, PhD1, 4

From the 1Department of Rehabilitation Medicine, Mekwiil Hospital, Busan, 2Department of Rehabilitation Medicine, Pusan National University School of Medicine, Yangsan, 3Biomedical Research Institute, Pusan National University Hospital, Busan, and 4Research Institute for Convergence of Biomedical Science and Technology, Pusan National University Yangsan Hospital, Yangsan, Korea

*J Rehabil Med 2017; 49: 30–35*
Anodal bihemispheric stimulation

- Unilateral ischemic injury, stabilized > 6 months (26 patients, sham vs real stim.)
- Parameters: 1 mA x 20 min, 2 weeks
- Concomitant intensive dysphagia therapy

Therapeutic approaches using tDCS in post-stroke dysphagia
Therapeutic approaches using tDCS in other forms of neurogenic dysphagia

Anodal tDCS pharyngeal motor cortex (dominant hemisphere for swallowing)

Anodal tDCS swallowing motor cortex (right hemisphere)

Restivo et al., 2019
Effects of anodal tDCS (1.5 mA x 20 min, 5 days) vs intermittent TBS (right hemisphere) in patients with primary and secondary presbydysphagia

The improvement in the DOSS score correlates with an increase in the reproducibility of the swallowing act

Cosentino et al., 2020
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<tr>
<th>NIBS Technique</th>
<th>Number of RCTs Included (Total Number of Patients Involved, When Reported)</th>
<th>Time Period</th>
<th>Disease</th>
<th>Main Conclusions</th>
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<tr>
<td>Bakr et al., 2022</td>
<td>rTMS, tDCS 6 studies on rTMS; 4 studies on DCS</td>
<td>From inception to August 2021</td>
<td>Post-stroke dysphagia</td>
<td>All rTMS studies and 3 of the 4 DCS studies show enhanced recovery of dysphagia. Bilateral rTMS stimulation and combined treatment with rTMS and DBS have a more pronounced therapeutic impact.</td>
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<td>He et al., 2022</td>
<td>tDCS 15 studies (787 patients)</td>
<td>From inception to December 31, 2021</td>
<td>Post-stroke dysphagia</td>
<td>tDCS has a positive effect on post-stroke dysphagia. Bilateral stimulation and high-intensity stimulation (1.6–2 mA) may have better effects.</td>
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<td>Li et al., 2022</td>
<td>rTMS 9 studies (393 patients)</td>
<td>From inception to September 31, 2021</td>
<td>Post-stroke dysphagia</td>
<td>rTMS can improve dysphagia of post-stroke patients, especially in the presence of unilateral hemispheric stroke lesions. No significant difference was observed among the different stimulation sites subgroups.</td>
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<td>Lin et al., 2022</td>
<td>tDCS 10 studies (343 patients)</td>
<td>From inception to January 15, 2021</td>
<td>Post-stroke dysphagia</td>
<td>Compared to sham tDCS, anodal tDCS applied both unilaterally (to the affected or unaffected hemisphere) or bilaterally can foster recovery of the swallowing function. A larger effect size is observed for acute compared to chronic stroke. The therapeutic effect is greater when the unaffected hemisphere is targeted.</td>
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<td>Qiao et al., 2022</td>
<td>rTMS 12 studies (433 patients)</td>
<td>From inception to June 2021</td>
<td>Post-stroke dysphagia</td>
<td>rTMS has positive therapeutic effect when applied for &gt;30 days and in the subacute phase after stroke. No significant therapeutic effect were observed when stimulation duration was &lt;3 days. Patients recover better when treated in the subacute rather than the chronic phase. Both low-frequency rTMS applied to the unaffected hemisphere and high-frequency rTMS applied to the affected hemisphere could achieve a therapeutic effect.</td>
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<td>Speyer et al., 2022 (part II)</td>
<td>rTMS, tDCS 15 studies on rTMS; 9 studies on tDCS (728 patients)</td>
<td>From inception to March 6, 2021</td>
<td>Oropharyngeal dysphagia due to stroke (21 studies), PD (1 study), brain injury (1 study), dysphagia (1 study)</td>
<td>Large pre-post intervention effect sizes were observed for both types of brain neurostimulation. Significant small and moderate post-intervention between-group effects in favour of rTMS and tDCS were shown respectively.</td>
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<td>Tan et al., 2022</td>
<td>rTMS, tDCS 9 studies on rTMS and 9 studies on tDCS (453 patients)</td>
<td>From inception to January 5, 2021</td>
<td>Post-stroke dysphagia</td>
<td>Transcranial stimulation is effective in improving the swallowing function even at 1 and 3 months after the intervention. No difference in efficacy between rTMS and tDCS in terms of the reduction of dysphagia scale scores were observed. Higher effects on the improvement of the swallowing function are seen in middle-aged rather than older adults.</td>
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<td>Wen et al., 2022</td>
<td>rTMS 11 studies (463 patients)</td>
<td>Not specified</td>
<td>Post-stroke dysphagia</td>
<td>rTMS demonstrated a great beneficial effect for post-stroke dysphagia when combined with traditional swallowing exercises. A better efficacy was noted for high frequency vs. low frequency stimulation. No significant difference was observed based on stimulation site (affected vs. unaffected hemisphere).</td>
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<tr>
<td>Xie et al., 2022</td>
<td>rTMS 10 studies (246 patients)</td>
<td>From inception to December 20, 2021</td>
<td>Post-stroke dysphagia</td>
<td>rTMS of the bilateral hemisphere and the contralateral hemisphere significantly improves swallowing function after stroke. Low-frequency rTMS is more effective than high-frequency rTMS.</td>
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<tr>
<td>Zhao et al., 2022</td>
<td>tDCS 16 studies</td>
<td>From inception to June 2021</td>
<td>Post-stroke dysphagia</td>
<td>Anodal tDCS on both the ipsilesional and contralateral hemisphere is statistically significant in the improvement of post-stroke dysphagia. Stimulation of the affected hemisphere has a larger effect size than stimulation of the unaffected one. Significant therapeutic effect was observed only for patients in the chronic phase but not in the acute phase (0–14 days).</td>
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<tr>
<td>Zhu et al., 2022</td>
<td>rTMS, tDCS 7 studies on rTMS and 7 studies on tDCS</td>
<td>From inception to March 2021</td>
<td>Post-stroke dysphagia</td>
<td>Both high-frequency rTMS and tDCS applied over the pharyngeal motor cortex may improve the swallowing function in patients with poststroke dysphagia. No sufficient numbers of studies to investigate the effect of low-frequency rTMS on poststroke dysphagia.</td>
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Cosentino et al., in press
Systematic reviews with metanalyses on NIBS for treatment of neurogenic dysphagia published in 2022

• Almost all metanalyses focused exclusively on post-stroke dysphagia
• Both rTMS and tDCS can improve the outcome of patients with post-stroke dysphagia, especially when applied in combination with traditional DT
• Methodological heterogeneity among studies and limitations:
  ▪ Variability in the definition of the stimulated area
  ▪ Neuronavigation not used in most of the studies
  ▪ Broad areas of disagreement
TMS studies

• Both bilateral stimulation and unilateral stimulation of the contralesional hemisphere can induce improvement of dysphagia in patients with hemispheric stroke (Xie et al., 2022)

• A minimum number of 5 sessions is required for rTMS to obtain a significant clinical benefit on dysphagia (Qiao et al., 2022)

• High-frequency rTMS can improve dysphagia when applied to the ipsilesional hemisphere, low-frequency rTMS mainly acts when applied to the contralesional hemisphere in patients with hemispheric stroke (Qiao et al., 2022)
tDCS studies

• Greater accessibility to treatment and possibility of home therapy thanks to portable devices

• Most studies have demonstrated the efficacy of the anodal (facilitatory) current when applied both over the ipsilesional and contralesional hemisphere (Zhao et al., 2022)
TMS and tDCS studies

- Greater efficacy of NIBS in middle-aged rather than older adults (Tan et al., 2022)
- Greater efficacy of NIBS when performed in the acute and subacute phases of stroke (Lin et al., 2022; Qiao et al., 2022).
- Effects of rTMS seem to be greater than those of tDCS (Tan et al., 2022; Speyer et al., 2022)
- Both rTMS and tDCS are well-tolerated and no serious adverse effects have been reported
Combined peripheral (neuromuscular) and cortical stimulation treatment for post-stroke and PD dysphagia?

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- IRCCS Mondino Foundation (G. Cosentino)
- San Paolo Hospital (T. Bocci)
- Sacco Hospital (N. Pizzorni)

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Thanks