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Application of non-invasive brain stimulation with the use of repetitive transcranial magnetic stimulation or transcranial direct current stimulation in the treatment of dysphagia following an ischemic stroke

Zastosowanie nieinwazyjnej stymulacji mózgu z wykorzystaniem przezczaszkowej stymulacji magnetycznej lub przezczaszkowej stymulacji prądem stałym w terapii dysfagii w następstwie udaru niedokrwiennego mózgu

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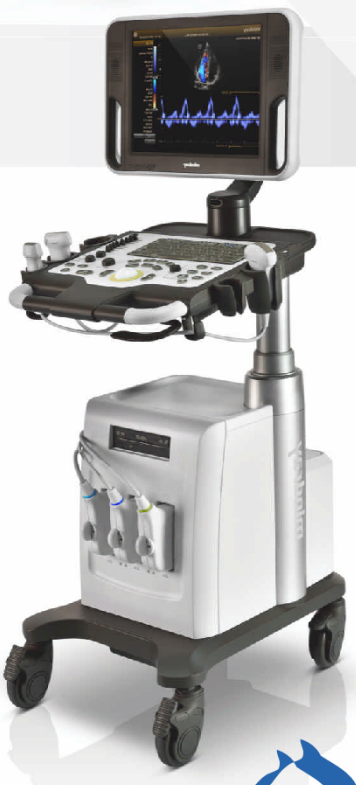

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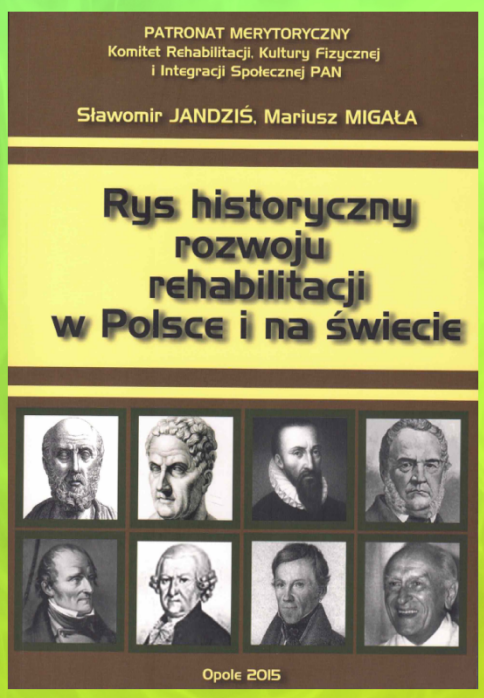

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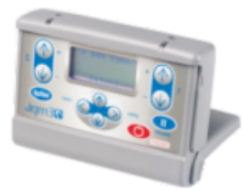

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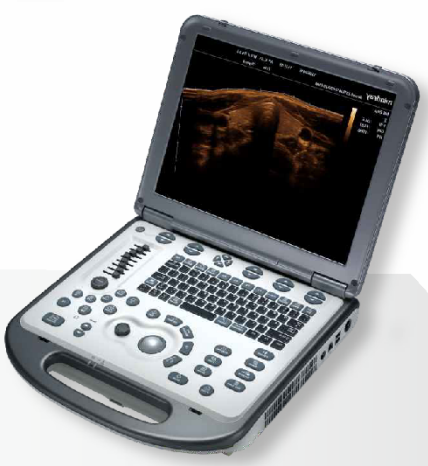

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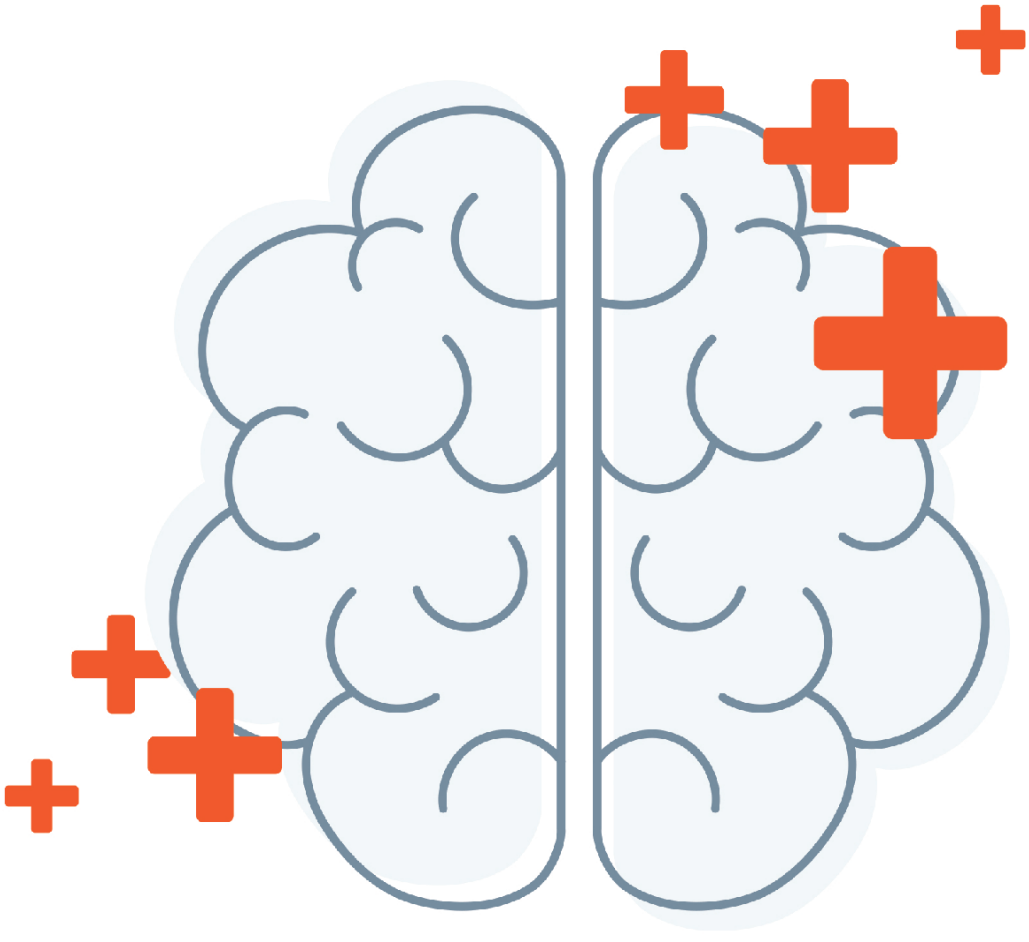

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Application of non-invasive brain stimulation with the use of repetitive transcranial magnetic stimulation (rTMS) or transcranial direct current stimulation (tDCS) in the treatment of dysphagia following an ischemic stroke – analysis of research reports

Zastosowanie nieinwazyjnej stymulacji mózgu z wykorzystaniem przezczaszkowej stymulacji magnetycznej (rTMS) lub przezczaszkowej stymulacji prądem stałym (tDCS) w terapii dysfagii w następstwie udaru niedokrwiennego mózgu – analiza doniesień z badań

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Abstract

Stroke is one of the significant problems and causes of death, in particular in highly developed countries. It is also the most common cause of dysphagia. This study is devoted to the analysis of publications from the last decade concerning research on the use of non-invasive brain stimulation (TMS, tDCS) in the treatment of dysphagia following an ischemic stroke. The following databases were searched for publications: PUBMED, Polish Scientific Journals Database, EBSCO, ScienceDirect. Out of 358 articles found, only two met all the inclusion conditions.

The studies discussed in this article included patients who had their first unilateral ischemic stroke, followed by dysphagia.

Findings from pilot studies on the effectiveness of the use of tDCS in the treatment of dysphagia following an ischemic stroke were analysed. Fourteen patients aged 50-92 were randomly assigned to two groups. The study group was treated with anodic stimulation, and the control group with sham brain stimulation. The results showed that patients in the study group obtained a statistically significant result, indicating an improvement in the swallowing function as measured by the Dysphagia Score and Severity Scale. The above data may indicate the effectiveness of the use of tDCS in the treatment of dysphagia.

Fifty patients were qualified for the research on the effectiveness of rTMS in the treatment of dysphagia. Three groups were created: the first group treated with high frequency rTMS, where patients received rTMS stimulation – 3Hz; the second group with low frequency rTMS – 1Hz; and the control group. The effectiveness of the therapy used was assessed on the fifth day and after 1, 2 and 3 months. After 5 days the groups where active rTMS stimulation was used showed greater improvement in the swallowing function compared to the sham stimulation group. Improved results in the Standardized Swallowing Assessment were also recorded after 3 months in the 1Hz and 3Hz groups, but this did not apply to the control group. In three groups, the results of the water swallow test and the degree of dysphagia improved after 3 months.

This analysis shows that non-invasive brain stimulation using tDCS and rTMS in the treatment of dysphagia is associated with improved swallowing function. However, the small number of studies conducted in this area does not allow for extrapolation of their results.

Key words:

dysphagia, transcranial magnetic stimulation (TMS), transcranial direct current stimulation (tDCS)

Streszczenie

Udar mózgu jest jednym z istotnych problemów i powodów śmiertelności szczególnie krajów wysoko rozwiniętych. Stanowi on również najczęstszą przyczynę dysfagii.

Niniejsza praca poświęcona została analizie publikacji z ostatniej dekady, dotyczących badań nad wykorzystaniem nieinwazyjnej stymulacji mózgu (TMS, tDCS) w terapii dysfagii w następstwie udaru niedokrwiennego mózgu. W celu odnalezienia publikacji przeszukane zostały bazy danych: PubMed, Polish Scientific Journals Datebase, EBSCO, ScienceDirect. Wśród 358 odnalezionych artykułów jedynie 2 spełniły wszystkie warunki włączenia.

Omawiane w niniejszym artykule badania obejmowały pacjentów, którzy przebyli pierwszy w życiu udar jednostronny niedokrwienny, w następstwie którego wystąpiła dysfagia.

Analizie poddane zostały doniesienia z badań pilotażowych skuteczności zastosowania tDCS w terapii zaburzeń połykania w następstwie udaru niedokrwiennego mózgu. 14 pacjentów w wieku od 50 do 92 lat w sposób losowy przydzielono do dwóch grup. Grupie badanej stosowano stymulację anodową, a w grupie kontrolnej pozorowaną stymulację mózgu. Wyniki wykazały, iż pacjenci w grupie badanej uzyskali wynik istotny statystycznie, wskazujący na poprawę funkcji połykania mierzonych na podstawie Skali Wyników i Nasilenia Dysfagii. Powyższe dane mogą wskazywać na skuteczność wykorzystania metody tDCS w terapii dysfagii.

Do badań na skutecznością rTMS w terapii dysfagii zakwalifikowano 50 pacjentów. Utworzono trzy grupy: pierwszą – wysokiej częstotliwości rTMS, gdzie pacjenci otrzymywali stymulację rTMS – 3 Hz; niskiej częstotliwości rTMS – 1 Hz oraz kontrolną. Oceniano skuteczność zastosowanej terapii w piątym dniu oraz po 1, 2 i 3 miesiącach. Grupy objęte aktywną stymulacją rTMS po 5 dniach prezentowały większą poprawę funkcji połykania w stosunku do grupy pozorowanej stymulacji. Lepsze wyniki w Standaryzowanej Ocenie Połykania odnotowano także po 3 miesiącach w grupach 1 Hz i 3 Hz, nie dotyczyło to natomiast grupy kontrolnej. W trzech grupach po 3 miesiącach poprawiły się wyniki testu połykania wody oraz stopnia dysfagii.

Niniejsza analiza badań wskazuje, że nieinwazyjna stymulacja mózgu z wykorzystaniem metod tDCS i rTMS w procesie terapii dysfagii powiązana jest z poprawą funkcji połykania. Jednak niewielka ilość przeprowadzonych badań w tym zakresie nie pozwala na ekstrapolowanie ich wyników.

Słowa kluczowe:

dysfagia, przezczaszkowa stymulacja magnetyczna (TMS), przezczaszkowa stymulacja prądem stałym (tDCS)

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Introduction

Every year in Poland there are 70,000 strokes, 80% of which are ischemic strokes [1]. Other sources state that ischemic strokes may constitute up to 85%. According to the guidelines of the World Health Organization, a stroke is a sudden global or focal disturbance of brain function following abnormalities in cerebral blood flow, lasting not less than 24 hours [2].

The above data indicates the scale of the problem. Strokes remain one of the most important causes of death. This is especially true in the case of highly developed countries [1]. Concerning the aetiology of dysphagia, brain dysfunctions resulting from abnormalities in blood flow constitute the most common cause of strokes. In the acute phase of a stroke, dysphagia may occur in more than 50% up to 80% of cases. Complications as a result of chyme aspiration may occur in 30% of patients. About 90% of symptoms usually disappear within two weeks. In 8% of cases, dysphagia is observed for six months [3].

Dysphagia is a difficulty in the process of food intake and its passage from the oral cavity to the throat, oesophagus and stomach [4]. Dysphagia in the course of a stroke occurs suddenly, preventing the patient from adapting to the situation. As a consequence, aspiration pneumonia and malnutrition may occur. It is important to recognize it as early as possible and counteract its negative consequences [5].

Post-stroke rehabilitation is a process that requires multi-profile patient rehabilitation. One of the methods used in the rehabilitation process is transcranial magnetic stimulation (TMS). This method uses electromagnetic induction. By generating an electromagnetic pulse, it is supposed to induce electrical activity in specific areas of the cerebral cortex. There are two ways of stimulation using this method: giving a single impulse and several impulses at short intervals (rTMS - repetitive transcranial magnetic stimulation) [6].

Another method of neuromodulation used in the process of post-stroke rehabilitation is tDCS. The method of transcranial direct current stimulation (tDCS) is based on the administration of a weak current through electrodes placed on the scalp. The brain may be stimulated in two ways, namely using single-hemispheric stimulation and dual-hemispheric stimulation. In the first way, one target electrode and a second reference electrode are normally placed on the scalp. In the second case, the electrodes are attached bihemispherically to stimulate the cortical areas of both hemispheres of the brain [7].

Objective

The objective of this study is to analyse the current state of research on the use of non-invasive brain stimulation (TMS, tDCS) in the treatment of dysphagia following an ischemic stroke. The analysis of the collected materials is to enable the understanding of the effectiveness of using TMS and tDCS in the treatment of dysphagia following an ischemic stroke and indicate the directions of the process of improving the swallowing function.

doi.org/10.56984/8ZG20ANp0

Material and methods

For the purposes of this analysis, the following databases were reviewed: PUBMED, Polish Scientific Journals Database, EBSCO, ScienceDirect. The words dysphagia, ischemic stroke, and swallowing therapy were used for precise search results. 794 publications were found. By narrowing the search field in ScienceDirect to scientific and review articles, the number of publications found in this database was limited to 280. Then, 371 articles were qualified for the next stage of work, 13 of which were duplicates. The next step was to read the titles and abstracts of 358 publications and qualify or exclude them for the purposes of this study. The following inclusion criteria were used in the analysis:

- The study group consisted of people diagnosed with dysphagia following an ischemic stroke. Age, gender and ethnic origin did not constitute limitations;
- The research concerned the use of tDCS or TMS in the treatment of dysphagia following an ischemic stroke. Comprehensive interactions, i.e. tDCS or TMS, used in combination with other methods in the treatment of dysphagia were allowed;
- These were randomized controlled trials, controlled clinical trials and pilot trials;
- Research results published in the last decade.

The following exclusion criteria were used in the analysis:

- The research was based on a case study;
- The research concerned dysphagia as a result of a haemorrhagic stroke;
- The group of patients diagnosed with dysphagia included both ischemic and haemorrhagic stroke patients, without indicating two separate groups of respondents, taking into account the mechanism of a stroke.

Based on the analysis of titles and abstracts, four articles were qualified for further analysis. After reading their content, two were excluded due to the failure to meet the inclusion criteria (Fig. 1).

Fifty-four patients participated in the study. The patients experienced their first unilateral ischemic stroke, as a result of which they developed dysphagia.

The group of pilot studies on the effectiveness of tDCS included 14 patients aged 50 to 92. The patients qualified for the study were 24-168 hours after the onset of a stroke [9]. In the case of the second study, where the effectiveness of rTMS was assessed, the upper time limit for entering the study was 2 months after a neurological ischemic event [10]. Patients with cognitive impairments, contraindications to the use of the therapy specified in the study design (tDCS, rTMS) were not included in the qualification. In the study conducted by Ju D., Yang F., Liu L. et al. the exclusion criterion also took into account the burden of coexistence with other neurological diseases, infections, fever, profound disorders of linguistic communication in the form of aphasia, prior administration of a sedative or inability to participate in the follow-up [10]. The second study took into account difficulties in following orders due to dementia [9].

In both studies, neurological and speech therapy examinations were also used to assess the degree of dysphagia. A neurologist assessed dysphagia using: physical

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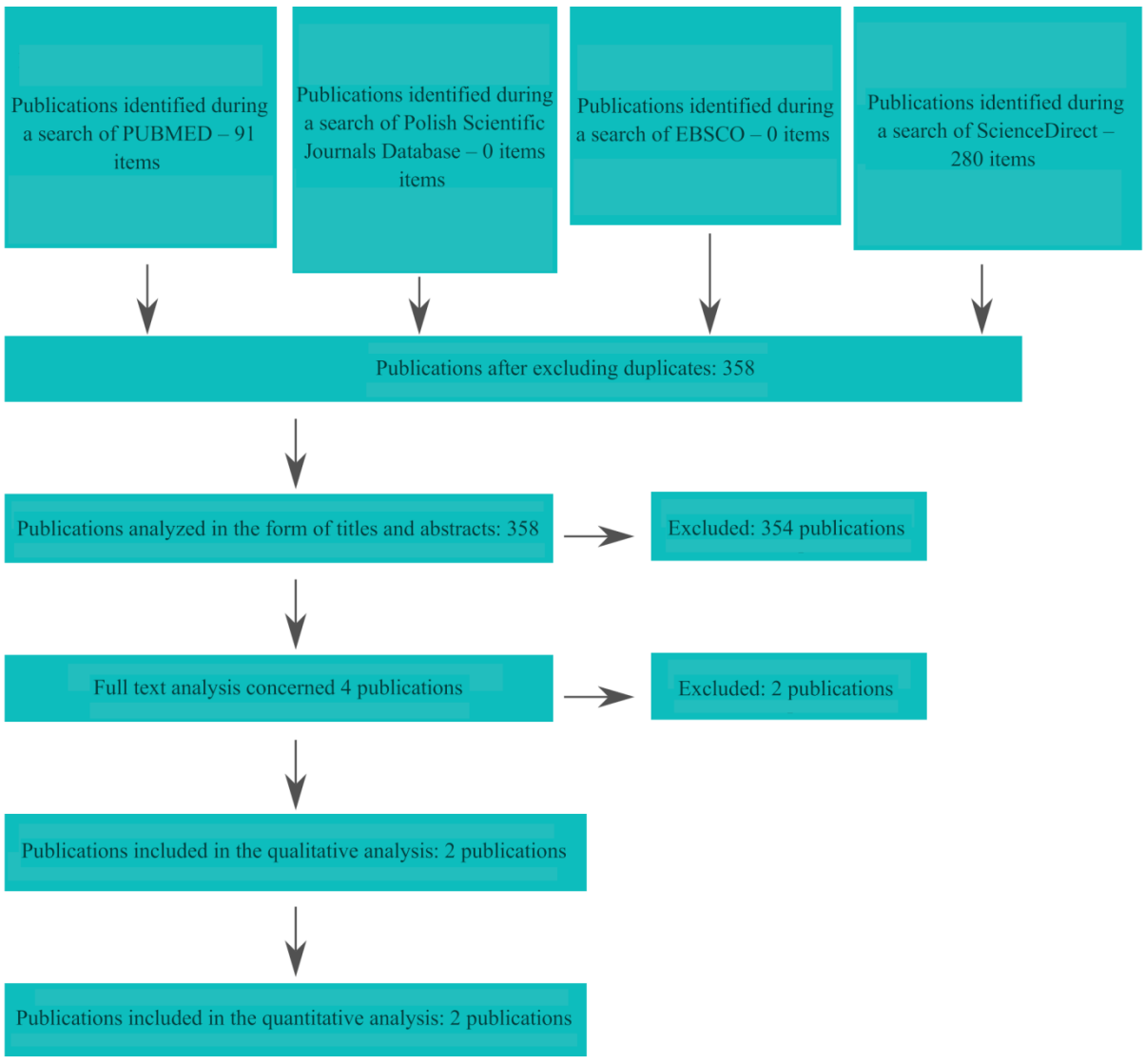

Fig. 1. A schematic summary of the results of individual stages of the search process and research selection in accordance with the PRISMA assumptions [8]

examination, swallowing questionnaire: Standardized Swallowing Assessment (SSA), water swallow test, degree of dysphagia (DD). The National Institutes of Health Stroke Scale (NIHSS), Barthel Index (BI), modified Rnakin Scale were used to assess the patient's functioning after a stroke and the severity of the vascular incident [10]. The volume of the ischemic area was not included here. Speech and language pathologists who specialize in dysphagia who were not informed about the allocation of patients to groups performed the swallowing tests. The study used the Dysphagia Outcome and Severity Scale (DOSS). Videofluoroscopy was required in 7 patients. Patients who obtained the DOSS result: $X \leq 5$ were qualified for tDCS therapy; where $X = 1$ – severe dysphagia, and $X = 7$ – normal result. In this case, the NIHSS was also used to assess the severity of the stroke. The volume of acute ischemic lesions was determined on the basis of MRI in the DWI sequence.

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In the case of two patients in whom MRI could not be performed, the volume of the ischemic structure was calculated on the basis of a CT [9].
In both cases, the selection of patients into groups was randomized. Each of the studies, in addition to traditional methods of rebuilding the swallowing function, used non-invasive brain stimulation. However, two different methods, tools and mechanisms of action were used for this. In the study conducted by Ju D., Yang F., Liu L. et al. fifty-seven patients were recruited, of which 17 were not qualified for the study due to the failure to meet the inclusion criteria (11 people) and refusal to participate in the study (6 people). Three groups were created: the first group in the case of which high-frequency rTMS (3 Hz) was used consisted of 15 people aged 58.2 ± 2.78 – 13 men and 2 women. In the second, low-frequency rTMS (1 Hz) was used; there were 13 patients aged 57.92 ± 2.47 – 7 men and 6 women. The third control group consisted of 12 people aged 58.83 ± 3.35 – 6 women and 6 men. Based on the assessment of the motor potential evoked by the mylohyoid muscles, the point of stimulation, i.e. the cortical area of the representation of the mylohyoid muscles, was established. Therapy lasted 5 consecutive days. Patients from the high-frequency group received rTMS stimulation of the hemisphere affected by the stroke: 3Hz for 10 seconds with a pause of 10 seconds between trains, a total of 40 trains, which gives 1,200 pulses at 90% rMT. The low-frequency group received stimulation of the hemisphere not affected by the stroke: 1 Hz for 30 seconds with a two-second pause between trains, a total of 40 trains and 1,200 pulses at 100% rTM. The control group received sham stimulation. The effectiveness of the applied therapy was assessed on the fifth day and after 1, 2 and 3 months. [10].

Results and discussion

In the study conducted by Kumar S., Wagner C.W., Frayne C., et al. two groups were formed. A group of 7 included 3 men and 4 women subjected to tDCS and a control group consisting of 4 men and 3 women. The location of the anode electrodes was planned in advance. The electrodes were placed on the scalp of the undamaged hemisphere halfway between points C_3 and T_3 (left) or C_4 and T_4 (right). The reference electrode was positioned over the supraorbital region of the opposite hemisphere. During 5 consecutive days, when they were performing traditional swallowing exercises, the patients were given 2 mA stimulation for 30 minutes in the study group or sham stimulation in the control group [9].
No adverse events were reported in patients undergoing tDCS stimulation. In the case of rTMS, 3 people (one with sham stimulation) reported transient headaches, and one person in the group undergoing stimulation reported tingling in the head after the first session.
After 5 days the groups undergoing active rTMS stimulation showed greater improvement in the swallowing function as compared to the sham stimulation group. Better results in the Standardized Swallowing Assessment were maintained after 3 months in the 1 Hz and 3 Hz groups, and not in the control group. In three groups, after 3 months, the results of the water swallow test and the degree of dysphagia improved in relation to the starting value. In

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9 patients (3 persons from the 1 Hz group; 4 persons from the 3 Hz group and 2 persons from the sham group) there was no evoked response, therefore they were not subjected to neurophysiological assessment. The results of low-frequency rTMS stimulation showed a weakening of the excitability of the cortex of the hemisphere not affected by the ischemic lesion and a contralateral increase in excitability. At 3 Hz stimulation, an increase in the excitability of the hemisphere affected by the ischemic lesion was observed and only a slight effect in the opposite structures. On the basis of the results, the authors indicated that the improvement in the swallowing function correlated with the motor potential evoked by the mylohyoid muscles of the hemisphere affected by the stroke in all patients after 3 months. The study showed an improvement in the functioning of patients covered by rTMS compared to the sham stimulation group, based on the Barthel Index and the modified Rnakin Scale [10].

The results of the study conducted by the second team showed that patients undergoing anodic stimulation obtained a statistically significant result, indicating an improvement in the swallowing function as measured by the Dysphagia Score and Severity Scale. 86% (6/7) of patients in the anodic stimulation group obtained 2 or more points in the DOSS, while in the sham group it was only 43% (3/7) of the patients [9].

In both studies, information about approval by an ethics committee or an audit committee was provided [9, 10]. Group allocation was randomized. In the case of the pilot studies, the size of the group participating in the study was small, which did not allow for taking into account all significant variables. The patients qualified for the study were within the time frame of 1–7 days from the onset of stroke symptoms, the duration of stimulation was 5 days. Overall, 6–12 days passed from the onset of

Table 1. Comparison of studies using stimulation rTMS and tDCS

	rTMS	tDCS
Number of patients	40	14
Tools and scales for the assessment of dysphagia and the patient's functioning status after a stroke and its severity	• physical examination, • Standardized Swallowing Assessment (SSA), • water swallow test , • degree of dysphagia (DD), • The National Institutes of Health Stroke Scale (NIHSS), • Barthel Index (BI), • modified Rankin Scale.	• Dysphagia Outcome and Severity Scale (DOSS) • Videofluoroscopy
Dysphagia assessment specialist	Neurologist	Speech therapist specializing in dysphagia
Time frame from onset of stroke symptoms to qualification for research	less than 2 months	24–168 hours

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	rTMS			tDCS	
	3 Hz high frequency group	1 Hz low frequency group	Control group	Anode brain stimulation group	Control group
Number of patients	15	13	12	7	7
Men	13	7	6	3	3
Women	2	6	6	4	4
Age	58.2 ± 2.78	57.92 ± 2.47	58.83 ± 3.35	64–92	50–83

symptoms till the end of the study. The study did not take into account that in 90% of patients the symptoms of dysphagia disappear within 2 weeks. The effects of deferred therapies have also not been investigated [10,4]. The large age range from 50 to 92 years with a small group of study participants is also noteworthy.

Conclusion

Findings from the studies analysed for the purposes of this study indicate that non-invasive brain stimulation with the use of tDCS and rTMS in the treatment of dysphagia is associated with the improvement of the swallowing function. However, the small amount of studies conducted in this area does not allow for extrapolation of their results. Undoubtedly, however, the obtained results suggest the need for further research to assess the effects of these therapies, including those deferred in time, and to develop effective and safe procedures for their use.

Effective and adequately early implemented therapy of dysphagia could counteract its complications. The scale of the incidence of strokes and dysphagia indicates the need for research into methods of its therapy.

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