Transcranial magnetic stimulation in the rehabilitation of motor deficits after ischemic stroke

Przezczaszkowa stymulacja magnetyczna w rehabilitacji osób z deficytami ruchowymi po udarze niedokrwiennym mózgu

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Key words
stroke, rehabilitation, plasticity, transcranial magnetic stimulation (TMS), repetitive transcranial magnetic stimulation (rTMS)

Abstract
Transcranial magnetic stimulation (TMS) was introduced to clinical practice in the 1980s and since that time has become more and more widely used. It is a noninvasive, painless brain stimulation technique that can modulate cortical excitability. It is possible to use single or paired TMS pulses, but the most promising method seems to be repetitive transcranial stimulation (rTMS) where magnetic pulses are repeated with a certain ferquency. Depending on the frequency of rTMS it is possible to activate or to inhibit the brain cortex. According to the latest research, the brain dysfunction after a stroke seems to be the matter of interhemispheric imbalance, most likely overactivation of the unaffected hemisphere. Based on this hypothesis, there are attempts to use TMS as a therapeutic tool after strokes. This review looks at the methods that use the TMS technique (rTMS – Repetitive Transcranial Magnetic Stimulation, TBS – Theta Burst Stimulation, PAS – Paired Associative Stimulation) to improve plasticity after a stroke. The effects encourage one to deepen research into TMS as a potential therapeutical tool in stroke rehabilitation. An issue of interest for future research is whether rTMS in conjunction with other stimulation parameters like standard physiotherapy could induce lasting changes in the nervous system, opening up new possibilities in rehabilitation.

Słowa kluczowe
udar, rehabilitacja, plastyczność, przezczaszkowa stymulacja magnetyczna (TMS), powtarzalna przezczaszkowa stymulacja magnetyczna (rTMS)

Streszczenie
Przezczaszkowa stymulacja magnetyczna (TMS – ang. *Transcranial Magnetic Stimulations*,) od momentu wprowadzenia jej do praktyki klinicznej w latach 80 tych XX wieku uzyskuje coraz więcej zastosowań. Jest nieinwazyjną, bezbolesną metodą stymulacji mózgu, która moduluje pobudliwość korową. Podstawowe schematy TMS obejmują pojedyncze impulsy lub ich pary, najbardziej jednak obiecująca wydaje się być powtarzalna przezczaszkowa stymulacja magnetyczna (rTMS – ang. *Repetitive Transcranial Magnetic Stimulation*), podczas której impulsy magnetyczne powtarzane są z określoną częstotliwością. W zależności od tej częstotliwości rTMS może albo pobudzać albo hamować korę mózgową. Bazując na hipotezie, że istotą zaburzeń funkcji mózgu po udarze jest zaburzenie równowagi międzypółkulowej, podejmuje się próby wykorzystania TMS również w rehabilitacji chorych po udarze. Niniejsza praca ma na celu przegląd metod wykorzystujących techniki TMS (rTMS, TBS – ang. *Theta Burst Stimulation*, PAS – ang. *Paired Associative Stimulation*) używanych po udarze niedokrwiennym w pobudzaniu procesów plastyczności w mózgu. Efekty cytowanych prac zachęcają do pogłębienia badań nad wykorzystaniem TMS w rehabilitacji chorych z poudarowym deficytem ruchowym. Pytaniem na przyszłość pozostaje, czy rTMS w połączeniu z innymi metodami stymulacji (takimi jak standardowa fizjoterapia) może wzbudzać trwałe zmiany w obrębie ośrodkowego układu nerwowego, otwierając nowe możliwości w rehabilitacji.

The individual division on this paper was as follows: A – research work project; B – data collection; C – statistical analysis; D – data interpretation; E – manuscript compilation; F – publication search; G – grant and funding acquisition

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INTRODUCTION

Transcranial Magnetic Stimulations (TMS) is a diagnostic and therapeutic method which has been in use since the 1980s. This method employs the use of magnetic stimulators which contain two separate parts: a generator of high-current impulses as well as stimulating coils. The essence of TMS lies in the utilisation of the phenomenon of electromagnetic induction. The current generator sends through the induction coil, which is placed perpendicular to the head of the individual to be stimulated, an electical impulse of a high intensity lasting for 1 ms. The magnetic field created perpendicular to the coil passes through the skull and creates in the region of the brian a secondary current parallel to the coil. If the magnetic stimulant utilised is sufficiently high and the coil is positioned above the motor cortex then the stimulation reaches the corticospinal tract activating specific muscles[1]. TMS is a non-invasive painless method which is fairly easy in application and given the observance of clearly defined principles and contraindications is extremely safe[2,3], both for those under stimulation as for those conducting the treatment.

There exist three basic methods for the application of TMS: through single pulses, pairs of stimuli or through trains of stimuli (rTMS – Repetitive Transcranial Magnetic Stimulation). The application of single pulses allows one to conclude as to the sensitivity of cerebral cortex, the conductivity in longer efferent tracts (corticospinal) or through the corpus callosum. In pairs the stimuli test the inhibitive and stimulating interactions in the area of the cerebral cortex. In relation to rTMS there is shown the effectiveness in the field of the impact on the level of stimulation/inhibition of specific areas of the cerebral cortex as well as the induction of neuroplasticity. This became the basis for the application of this method both as a therapeutic method as equally in the field of psychiatric disturbances as well as its neurological application, chiefly in the rehabilitation of patients after suffering an ischemic stroke[4,5].

Besides the methods presented above there is also applied forms of stimulation of the nerve tissue which are combinations of the above mentioned TBS (Theta Burst Stimulation) as well as PAS (Paired Associative Stimulation).

THE ROLE OF TRANSCRANIAL MAGNETIC STIMULATION IN THE MODULATING OF BRAIN NEUROPLASTICITY FOLLOWING A STROKE – THE NEURO-REHABILITATION ASPECTS

Regenerative processes begin within the central nervous system immediately in the first minutes following the occurence of a cerebral stroke. The focal damage of one hemisphere of the brain has an influence on the reorganisational processes in the area of both hemispheres. The structures which participate in the reconstruction of the lost motor functions are located in the primary motor cortex (M1) in the areas belonging to those damaged; in additional motor systems responsible for the executive control of motor functions (ipsi- and contralateral to the damage) as well as in the undamaged brain hemisphere in the homologous centre M1[6]. In the first reaction to deafferentation - the separation of the elements of the functional system for a given activity leads to a loss of balance between the processes of mutual activation and inhibition amongst the undamaged neurons. On the level of the hemispheres one then speaks of a reduction in the trancallosal inhibition on the part of the damaged hemisphere (Interhemispheric Inhibition, IHI), which consequently leads to an over activation of intact hemisphere[7,8]. In tests using a pair of magnetic impulses (paired TMS) it was shown that in stroke patients who take longer to recover and who do so to a lesser degree, the activity of the healthy hemisphere increases. In patients making a recovery more quickly the activity of the intact hemisphere is significantly less, or equally not present[9,10]. This phenomenon has served as the theoretical basis for subsequent tests allowing the application of transcranial magnetic stimulation as an auxiliary instrument in the processes of brain plasticity.

Repetitive magnetic stimulation (rTMS) can strenghten or suppress the activity of particular regions of the cerebral cortex depending on the parameters applied: frequency, stimulation length, the shape of the coil used (cylindrical or figure of eight) and the intensity of the magnetic field. The intensity of the stimulation provided is strictly dependant on the individual rest threshold of the cerebral exciteability of the patient (RMT – Rest Motor Treshold), which is defined in literature as the lowest stimulation intensity required to bring about a responce from the muscles in question (MEP - Motor Evoke Potential) of an amplitude (peak-to-peak) of over 50 μV, in which at least 50% of the effective attempts in the muscles targetted are at rest[1,5]. The strength of the magnetic field used is expressed as a fraction (in percentage) of the maximum ejection of the stimulator where 100% corresponds with a magnetic field of an intensity of up to 2T in the case of the most often used stimulators. In the papers cited below, where the authors have highlighted the fact, Magstim 200 stimulators were used in stimulation through individual TMS pulses and Magstim Rapid or Magstim Super Rapid (Magstim, UK) in the stimulation by means of a series of magnetic impulses. The coils that were employed as standard were figures of eight with a diameter of 700-950 mm (Magstim).

As a therapeutic instrument rTMS can create long-lasting (plastic) changes in the scope of synaptic stimulation in the area of the motor cortex, and the consequent alleviation of the neurological symptoms.The influence of rTMS on the stimulation of the cerebral cortex can be maintained for even double the length than the period of stimulation itself. Low frequencies (≤1Hz) have an inhibiting influence on the stimulated cortical area, while the frequencies >1Hz stimulate the cerebral cortex. The mechanisms of modulation of cortex stimulation beyond the period of the duration of rTMS sequence are still unclear. It has been suggested that the possible mechanisms enabling one to explain the influence of rTMS of a large and small frequency are respectively: cortical long-term synaptic intensification (LTP – Long Term Potentiation) as well as the phenomenon of long lasting cortical depression (LTD – Long Term Depression)[11]. LTP and LTD are phenomena involving the constant intensification or weakening of the synaptic transmission as a result of a short but strong synaptic modulation[1,12] – in this case with the aid of TMS. Tests conducted on animals have shown that in these long term modulatory actions with the aid of rTMS modulation of neurotransmitters as well as the induction of genes can contribute[4,5,13].

The therapeutic application of a series of magnetic impulses (rTMS) in patients with paresis of an upper limb as a result of a cerebral stroke

A therapeutic effect can be obtained after a cerebral stroke by utilising principles based on the basis of a model of rivilization between the cortical motor areas in the damaged hemisphere and in the intact hemisphere. On the basis of this model motor deficits are caused by (1) a decrease of activity of the damaged hemisphere as a result of a stroke as well as (2) an increase in the process of inhibiting the damaged hemisphere potential as a result of overactivation of the healthy hemisphere. In such a case improvement may be obtained by an increase in the activation of the damaged hemisphere, or equally its reduction in the healthy hemisphere[1]. In other words, this may be obtained thanks to an increase in the exciteability of the damaged cortical structures or a reduction in the overactivity of the homological structures in the healthy hemisphere. This form of treatment may be conducted through the application of stimulation of set parameters (inhibiting or arousing).

To date there have been published only a few pieces of research on the effectiveness of using rTMS in rehabilitation following a cerebral stroke, even though the effects obtained have been extremely promising. The method of transcranial magnetic stimulation has been used in, among other things, tests into the improvement of cognitive deficits resulting from a cerebral stroke (aphasia, hemineglect syndrome), however the decisive majority of tests have been conducted with patients suffering from post-stroke paresis of an upper limb. Usually patients are included at a late stage following the stroke, and consequently in a period of the affliction longer than 3 months. This was dictated first and foremost by considerations of safety, particularly in relation to the potential possibility of causing an epileptic attack as a consequence of stimulation[34]. At present, however, the generally accepted principles for the application of this method allow for its application in patients already in an early stage of a cerebral stroke, consequently already two weeks from the moment of falling ill[2,3]. In many papers there has been observed an improvement within the tested motor functions in the upper limb touched by paresis as a result of a cerebral stroke. On the whole the primary motor cortex M1 (precentral gyrus) responsible for movement of the arm was stimulated. The stimulation of particularly this area is quite easy to carry out as a result of the large cortical representation. In one case[15] an attempt at the stimulation of the premotor cortex of the healthy hemisphere that was undertaken did not achieve any improvement in the functioning of the paretic upper limb. In the majority of experiements attention is drawn to the chief use of the inhibitive stimulation of rTMS on the undamaged brain hemisphere as well as the safe spectrum of the strength of the magnetic field used (90-120% at the level of RMT). In none of the works cited was there observed adverse events.

In describing the influence of rTMS on the return of lost functions on the basis of the cited literature it seems important to note the fact that in the majority research patients did not take part in kinesitherapy. It seems that the inclusion after rTMS treatment of standard physiotherapy with the aim of rebuilding the lost functions utilising through this the obtained post-stimulator effect (ceased or cortical stimulation) could bring with it improved results. An example could be the research conducted by Scheidtmann et al.[35] pointing to the positive influence of pharmacotherapy on the effects of getting better in connection with standard physiotherapy. There participated in this experiment 53 patients with paresis following first ischemic stroke. The patients received levodopa or placebo in a single dose, 30 minutes before exercises with a physiotherapist for a period of 6 weeks. The patients motor function was evaluated three times on the Rivermead Motor Assessment (RMA), at the start, after three and subsequently six weeks of therapy. The results revealed in both groups a statistically significant improvement althought this was greater in the group with levodopa. The patients from the group helped with medication started to walk independently earlier than those from the group with the placebo. A similar difference was confirmed following group division as a result of the degree of initial disability.

In research carried out to date into the application of rTMS in the rehabilitation of motor functions following a cerebral stroke (first and foremostly of the paresis of the upper limb) individual sessions were also employed after which the improvement in the functional ability of the paretic arm was evaluated, as well as the implementation of a series of sessions (up to 10 sessions) The application of a therapeutic process comprising a larger number of sessions turns out to be a more successful form of treatment in as far as the durabilty of the post-stimulatory effects is concerned[33].

The influence of individual rTMS sessions on the improved functioning of a paretic upper limb following a cerebral stroke

The influence of a single rTMS session on the motor functions following a cerebral stroke has been examined by a Korean research team[36]. The application in the research of stimulating parameters of a frequency of 10 Hz applied to the damaged hemisphere resulted in improvements in the precision and speed of finger movements in paretic hand in comparison with placebo stimulation. Mansur et al. in their experiment a low-frequency stimulation (1Hz) was utilised on the homological motor structures within a healthy hemisphere. An improvement was also obtained in the range of the variable measured motor functions (the time of reaction, as well as the results in the PPT test (Purdue Pegboard Test) registered a significant improvement in comparison with patients amongstwhom a placebo stimulation was administered). Similar results were obtained through the application of low frequency stimulation upon the motor areas of an undamaged hemisphere in the research conducted by Takeuchi[20] and Nowak[18]. The shortcoming of the majority of the researcg cited is the lack of an evaluation of the maintenance of improvement in a longer time perspective. It is only in the results of Takeuchi that it has been established that the improvement failed to maintain itself 30 minutes after stimulation (Table 1).

The influence of a series of rTMS sessions on therapeutic effects following a cerebral stroke

As has been mentioned above, the application of a series of rTMS sessions increases the post-stimulatory effect in the form of inhibition potentiation the cerebral cortex in the place of stimulation. In reality, however, there has been conducted to date only one research on healthy individuals which confirmed the said hypothesis. In this paper Baumer et al. [33] applied for 2 consecutive days rTMS stimulation lasting for 30 minutes (1800 impulses) of a low frequency of 1 Hz on the premotor cerebral cortex. It is shown that the post-stimulatory effect on the state of arousal of the motor cortex lasted for longer following the ending of stimulation on the second day than was the case after stimulation during the first day.

The data presented in Table 2 appear to confirm the premise advanced. Kedr et al.[17] applied stimulation for a ten day period at a frequency of 3Hz in a group of 52 patients in the acute phase following a cerebral stroke. Additionally patients participated in standard movement rehabilitation. No particular criteria were applied for the inclusion of patients in the test attempt, with the exception of those criteria essential to ensure safety for the individuals subjected to stimulation. In the experimental group, in comparison to the group of patients receiving placebo stimulation, there was noted a significantly better improvement in the motor functions of the arm (on the basis of an evaluation of the results on the Bartel Index and Scandinavian Stroke Scale) 10 days after the end of stimulaiton. There was not, however, noticed any effect in the case of patients with a large cortical lesions arising as a result of a massive stroke. Even though the effectiveness of rTMS in this test cannot be explicitely interpreted if only because of the short period of test follow-up (conducted 10 days after the end of procedures) this experiment does supply us with two important pieces of information: (1) rTMS used on a damaged hemisphere appears to be a safe method even in the acute phase following a stroke and that (2) cortical stimulation of the damaged hemisphere appears in the case of large cortical lesions to be ineffective.

A different research procedure in comparison to the one cited above was undertaken by Fregi et. al[16], in utilising rTMS parameters of stimulation of a low frequency of 1 Hz with the aim of suppressing the hyperactivity of the

Table 1

Single-sessions studies using rTMS protocols to improve the function of the upper limb after ischemic in stroke patients and in healthy individuals

Author	Tested individuals profile	Time since stroke	Scheme of rTMS stimulation	Effects after stimulation	Follow - up effects
Mansur, C.G. et al. (2005)	10 patients and 6 healthy volunteers (control group)	< 1 year	1Hz, 100% RMT, 600 impulses, session on the motor cortex of the undamaged hemisphere (real and placebo), 1 session on the pre-motor cortex of a healthy hemisphere	1.shorter sRT (p=0.014) 2.shorter cRT (p=0.013) 3.Better result in PPT (p=0.002) 4. Without effect in the finger tapping test No statistical improvement after stimulation of the pre-motor cortex was obtained in any of the tests	Not tested
Takeuchi, N. et al. (2005)	20 patients	> 6 months (average 26.95)	1Hz, 90%RMT 1500 impulses on M1 undamaged hemisphere, placebo control	Shortening of the time for task realisation (p<0.01), rTMS without influence on pinch grip in the tested hand	The effect was not sustained 30 minutes after rTMS
Kim, Y-H. et al. (2006)	10 patients	6 – 21 months	M1 damaged hemisphere, 8x20s batches of 10 Hz , 58s break between subsequent impulse batches, 80% RMT, placebo control	Increase in the precision of movements undertaken with finger (p<0.01), increase in the speed of finger movements (p<0.01)	Not tested
Nowak, D. et al (2008)	15 patients	4 weeks - 4 months	M1 undamaged hemisphere 1Hz, 100%RMT, 600 pulses, placebo control	Increase in the frequency of finger movements undertaken (p<0.001) , increase in speed of finger movements (p<0.2), increase in speed of wrist movements (p<0.001), shortening of time for fist opening (p<0.001)	Not tested

M1 – motor cortex, JTT – Jebsen-Taylor Hand Function Test, sRT – time for individual motor reacton, cRT – four-choice time reaction ,PPT- Purdue Pegboard Test, ADM –finger adductor muscle V hands, SSS – Scandanavian Stroke Scale, NIHSS – NIH scale, BI – Bartel Index, MAUEF – Melbourne assessment of upper extremity function.

Table 2

Multiple-sessions studies using rTMS protocols to improve the function of the upper limb after a ischemic stroke in patients and in healthy individuals

Author	Tested individuals profile	Time since stroke	Scheme of rTMS stimulation	Effects after stimulation	Follow - up effects
Kobayashi, M. et al. (2004)	16 healthy individuals	Not applicable	90%RMT, 600 pulses, 1 Hz, subsequently for three days over the ipsilateral region M1 to the tested kg, over the contralateral M1 as well as over the apex of the skull (control)	Shortening of motor task completion time for the left arm after ipsilateral stimulation M1 (p<0.05)	After 10 minutes shortening of the task realisation time for both hands after M1 ipsilateral stimulation for each hand
Khedr, E.M. et al. (2005)	52 patients	5-10 days after the stroke	M1 region of the undamaged hemisphere, 10 sessions, 120%RMT, 10x10s batches of 3Hz, 50s interval between them, placebo control	Improvement of functioning measured in scales: SSS, NIHSS, BI (p<0.0001), better effects in patients with small disability than in those with a large disability	The effects remain after 10 days
Fregni, F. et al. (2006)	15 patients	>1 year (average 3.97 years)	5 sessions over M1 of the undamaged hemisphere, 100% RMT, 1Hz, 1200 impulses; placebo control	1.Shorter sRT (P<0.0001) 2.Improvement of motor functions kg measured acording to JTT (P=0.0024)	The effects remain after 2 months 1.P<0.0001 2. P = 0.09 result statistically insignificant
Kirton, A. et al. (2008)	10 patients (children 7-21, average 13.25 years old)	> 2 years after the stroke (average 6.33)	M1 of the undamaged hemisphere, 1 Hz, 100% RMT, 1200 pulses, 8 sessons, placebo control	1.Greater force in hand grip (p=0.009) 2.Improvement of result in the MAUEF scale (p=0.002)	After 7 days 1.effect still visible (p=0.01) 2. without effect (p=0.32)

M1 – motor cortex, JTT – Jebsen-Taylor Hand Function Test, sRT – time for individual motor reaction, cRT – four-choice time reaction ,PPT- Purdue Pegboard Test, ADM –finger adductor muscle V hands, SSS – Scandanavian Stroke Scale, NIHSS – NIH scale, BI – Bartel Index, MAUEF – Melbourne assessment of upper extremity function.

homological motor areas in the healthy hemisphere. 15 patients in the chronic phase following a cerebral stroke, a year after the stroke, were incorporated into the research. 5 therapeutic sessions were applied comprising 1200 impulses. There was noted an improvement both during the time of reaction as equally in the scope of the motor functions (evaluated on the basis of the JTT scale - Jebsen-Taylor Hand Function Test). The effects of improvement in the field of reaction time for task complition were mainteined for 2 months following the termination of the stimulatory procedure.

Equally the positive effect of rTMS on the motor cortex of healthy individuals was shown. In the tests conducted by Kobayashi et al.[19] similar effects were obtained to those conducted on sick individuals – after stimulation with a rTMS inhibiting frequency of the M1 area of the hemisphere on the side of the tested upper limb (i.e. as if it related to the conditions following the stroke – the hemisphere corresponding to the healthy hemisphere) obtained a shortened time for the fulfillment of the motor task by the given limb.

In another work there was also applied a similar protocol to that mentioned above with the aim of evaluating whether 1 Hz of rTMS has an influence on the level of spasticity in the paretic upper limb as a result of a stroke. Mally et al.[21] tested 64 patients 5 years and upwards after a stroke. They observed a reduction, pathologically increased as a result of the cerebral stroke, in muscle tone, amongst all the patients regardless of which of the cerebral hemispheres had been stimulated. The therapeutic effect was maintained for three months following stimulation but did not, however, go together in all cases with an improvement in the motor functions of the limb.

The influence of rTMS on other regions of the cerebal cortex was also researched, attempting in this way to predict the influence of rTMS on the return of other functions than paresis lost as a result of the stroke. In Knecht's research[22], in which 59 healthy volunteers took part, rTMS (1 Hz, 110% RMT) was applied to the primary somatosensory cortex of both hemispheres and obtained a weakening of the discrimination of sensation in the upper limb only after the contralateral stimulation of the sensory cortex. The time during which this effect was observed correlated with the time of the stimulation applied. Taking into consideration the fact that in the previously cited research the effects obtained in healthy individuals translated into the results of patients after focal damage to the cerebral hemisphere, then we may, in this case, expect that through the aid of rTMS they could influence the function of tactile sensation.

The weak side of all the research cited are the relatively small groups of tested patients as well as the fact that in the majority of cases there is a lack of research measuring the results obtained at larger time distances from the ending of stimulatory procedures, something which would allow one to answer the question as to how lasting the therapeutic effects of rTMS are.

This is not the subject of the present work but it follows equally to remember about the attempts to utilise rTMS in the rehabilitaiton of aphatic problems[23,24] and functions of attention disturbances[25,26], as a result of a cerebral stroke. It has been re-seached how TMS influences the withdrawl of neglect syndrome, or the level of post-stroke aphasia with the obtainment, as in the case of motor functions, of encouraging results.

OTHER METHODS OF TRANSCRANIAL CEREBRAL STIMULATION

There has been attempted in certain tests, besides the standard rTMS, the utiliation of TMS in different protocols. As an example may serve TBS - Theta Burst Stimulation. This is a form of rTMS whereby a series of magnetic impulses are applied with a theta frequency (i.e. 407 Hz). The stimulation lasts for a mere 20 – 190 seconds, yet the post-stimulatory effect on the modulation of the motor cortex is maintained even 20 minutes after the end of the application.[27] The obtained effects through the aid of theta beams are visible for significantly longer, for a period of up to twice as long than the period of stimulation itself. In Talelli's research[28] a series of three impulses were employed, transmitted with a frequency of 50 Hz, repeated with a frequency of 5 Hz (at a level of 80% of the Active Motor Threshold (AMT)). Six patients with a case history of cerebral strokes took part in the test (at least a year after the stroke, on average 31 months). Five experiments with the use of the so-called cTBS (continuous TBS – an uninterupped sequence of 100 impulse series) were conducted, which had an inhibitive effect on the exciteability of the cerebral cortex as well as so-called iTBS (intermittent TBS – where every 20 series of 10 impulses there occurred an 8 second break) intensifying exciteability. In accordance with the results obtained the iTBS used on the hemisphere which had been damaged by the stroke influenced the improvement in the functioning of the motor deficits of the upper limb. However, on the other hand – despite encouraging theoretical bases pointing to the superority of this method over 'classic rTMS' in a comparative test, out of both of these methods there was not shown to be any superiority of TBS over rTMS amongst healthy volunteers[29].

Another idea for the application of transcranial magnetic stimulation in rehabilitation was the utilisation of PAS methods (Paired Associative Stimulation) combining TMS with the stimulation of peripheral nerves. It was discovered that such a procedure induces permanent changes in the exciteability of the motor cortex both in healthy volunteers and patients who have suffered an ischemic stroke[30,31]. In the experiment by Stefan et al.[30] 22 healthy volunteers took part. The test procedure involved the stimulation of the central nerve at the level of the wrist by a single electric impulse of a duration of 200µs, and subsequently at intervals of 25 ms of a single impulse of TMS above the motor cortex of the hand muscle (abductor pollicis brevis muscle). The intensity of the applied magnetic field for the TMS stimulation was defined individually for each patient and it also matched that value of the ejection of the TMS stimulator which caused a response from the muscle at an amplitude of 1 mV. 90 such pairs of impulses were applied at an interval of 20 seconds, one after the other. The research idea was the synchronised stimulating of the motor cortex by two independent paths: an electrical impulse and a magnetic impulse – the gap used between the two types of impulse resulted from the time in which each stimulation was able to achieve the motor cortex. The effect constituted an arousal of the processes of plasticity of the cerebral cortex, defined as the growth in amplitude of the motor potentials aroused and an extension in the silent period. The observed changes were present for 30-60 minutes after the termination of the stimulation.

SUMMING UP

In summing up the results of the works cited above one may say that rTMS (and all its variations) is a method capable of finding its place in the rehabilitation of patients with post-stroke deficits in the upper limb. It does not seem, however, in basing oneself on the results obtained to date, that it could be a method employed in isolation. The results of the majority of tests though statistically significant are not, however, sufficiently convincing to allow one to limit rehabilitation exclusively to rTMS. The tests employed by the majority of authors to evaluate the functional improvement of the upper limb (PPT, sRT, cRT) are tests exploring extremely precise and isolated functions. To a large degree they do not have a clinical significance and subsequently do not influence in an important way the functioning of a patient after a cerebral stroke. Experiments conducted merely prove processes of plasticity and it is necessary to conduct a greater number of tests in which rTMS will be conducted together with standard physiotherapy. This element was absent from the works cited (only Khedr's patients[17] were actively rehabilitated during the course of the rTMS session). The questons as to what stage of stroke recovery rTMS stimulation is the most effective and rather at which stages it should not be applied remain without answers. The conducting of a greater number of tests with the application of rTMS in neuro-rehabilitation will equally certainly allow one to establish the most effective stimulation parameters in the treatment of cerebral stroke patients. The question also arises as to whether a greater number of rTMS series employed in the course of therapeutical procedure would not extend the duration time of clinical effects as was observed in the tests in psychiatry[32].

The research conducted to date into the use of rTMS in post-stroke rehabiliation should be treated as a starting point for further experiments, which would allow one to utilise this promising method in its optimal way.

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