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EVALUATION OF DIFFERENTIATED NEUROTHERAPY PROGRAMS FOR PATIENTS RECOVERING FROM SEVERE TBI AND LONG TERM COMA

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SUMMARY

Background:

The purpose of this study was to evaluate the effectiveness of two different neurotherapy programs in patients aroused from prolonged coma after a severe traumatic brain injury. The assumption was that relative beta training would not have a significant impact on outcomes, while rTMS would support improved outcome.

Material/ Methods:

We examined 40 patients who had suffered a severe TBI and prolonged coma and were undergoing long-term rehabilitation according to a standard phased program. The patients were assigned to two numerically even groups: an experimental group in which rTMS was used, and a control group, in which relative beta training was used. The research tools included analysis of documentation, a structured clinical interview, and the Rehabilitation Effectiveness Scale for TBI Patients.

Results:

As hypothesized, the experimental group showed significantly greater improvement in health related quality of life, whereas in the control group, the improvement was slight and statistically nonsignificant.

Conclusions:

The patients from the experimental group, who were given rTMS, obtained a significantly greater improvement in the effectiveness of rehabilitation, especially mental and physical comfort, than did the patients from the control group, who received relative beta training.

Key words: relative beta training, rTMS, rehabilitation outcome, mental and physical comfort, quality of life

INTRODUCTION

Traumatic brain injury (TBI) occurs when the brain experiences an insult caused by the operation of an external force (WHO, 2004). These injuries can be classified in terms of the severity of the damage, the mechanism of their formation (closed, e.g. caused by a blow, or open, e.g. a gunshot wound), or other factors (such as the localization of the injury or the area damaged). The expression “head injury” is often used as a synonym for TBI, but the former is a much broader term, since it includes also injuries to organs other than the brain (e.g. the scalp or skull; Moskala et al., 2000, 2007; Pachalska, 2007).

TBI is one of the leading causes of death and disability around the world, especially among children and adolescents (WHO, 2004). Among the causes are falls, motor vehicle accidents, and violence (Pachalska, 2007). The number of cases could be reduced by applying safety measures in motor vehicles (such as seat belts and helmets) and enforcing traffic and safety regulations. Public education campaigns intended to prevent injuries and social dependency in persons who have already had an injury are also useful (WHO, 2004).

A TBI can be caused by a direct blow or by sudden acceleration and deceleration. The primary damage is accompanied by diverse secondary brain injuries, which can appear in the first minutes or even days after the original injury. These include especially injuries to the circulatory system and increased intracranial pressure, which contribute to increasing the extent of the primary damage (Moskala et al., 2007; Rehman et al, 2008).

The victims of TBI, especially those caused by motor vehicle accidents, are often young people, active in personal and professional life, intending to study, start a family, or begin a career (Ducrocq et al., 2006). After the patient has regained consciousness, the long-term effects of the TBI begin to be apparent. These can be divided into:

- physical problems, involving locomotion and/or the sense organs;
- cognitive disturbances, involving especially memory and concentration;
- changes in emotional functioning, behavior control, motivation, etc.

The particular profile of disturbances depends not only on the size of the injury to the brain, but also on the setting in which rehabilitation is conducted; the best outcomes are achieved by patients treated in rehabilitation centers with many different specializations (Talar et al., 2003; Tepas et al., 2013); it also depends on how early effective neurorehabilitation is commenced (Pachalska et al., 2010, 2012).

After the period of spontaneous improvement, further treatment of TBI patients can be effective; it is often difficult to anticipate precisely, however, how quickly and to what extent improvement will occur (Ducrocq et al., 2006; Agraval et al., 2012).

Many authors have suggested that one of the main obstacles to improvement is the presence of emotional and behavioral disorders, which are closely inter-related and take on many diverse forms (Mauritz et al., 2006; Ducrocq et al.,

2006). One of the most typical changes is loss of emotional control, that is, emotional lability. The patient's emotional state changes more quickly than normal; for example, a sudden leap from sadness to joy (or the other way around) or a sudden transition from laughter to weeping or from calmness to anger. These states constitute one of the major difficulties in effective communication between patients and therapists or family members, which in turn is a major obstacle in rehabilitation (Benedictus et al., 2012).

In recent years considerable hope has been associated with neurotherapy. Many authors believe that neurotraining can effect the mental state directly or indirectly, or even the effectiveness of rehabilitation of TBI patients (Pachalska et al., 2011). The question then arises whether or not neurotherapy can help patients aroused from prolonged coma.

The goal of the present study was to evaluate the effectiveness of two different neurotherapy programs in patients aroused from prolonged coma after a severe traumatic brain injury. The hypothesis was that relative beta training would not have a significant impact on outcomes, while rTMS would support improved outcome.

MATERIAL AND METHODS

Our research included 40 patients aroused from prolonged coma, all of whom were under treatment at the Rehabilitation Clinic of the Jurasz Hospital in Bydgoszcz, Poland, or in the Department of Medical Rehabilitation at the Cracow Rehabilitation Center, according to a standard, phased rehabilitation program (Pachalska et al., 2003). The patients were divided into two numerically equal groups: an experimental group, in which rTMS was used, and a control group, in which relative beta training was used.

The exclusion criteria for this experiment included the following:

- Aphasia or dysarthria, confirmed in neuropsychological testing;
- Severe disturbances of memory or attention;
- Severe emotional or motivational disturbances;
- Any other serious clinical condition that would make it difficult or impossible to participate in the experiment (such as serious cardiovascular disease, respiratory disorders, decubitus ulcers, poorly healed wounds or skin lesions).

Neurotherapy programs

Program A: Relative beta training

Training in HRV biofeedback was applied for a period of 10 minutes, while EEG feedback (neurofeedback) was applied for 20 minutes in a two-pole set-up with electrodes at points C3 and C4, on a Thought Technology apparatus, an 8-channel PROCOM Infiniti by BIOMED Neurotechnology. The training was conducted by a psychologist with an international certificate in neurotherapy at the Center for Reintegration and Training of the Polish Neuropsychological Society.

The training protocol was developed based on the results obtained by the QEEG method. The electrodes were placed in accordance with the 10-20 international system for electrode placement. The patients were prepared for the training in the standard way, with an electrode impedance below 5 kilo-ohms.

During the training the frequency of 9-13 Hz was reinforced. The patient sat in a relaxation chair (NEEDO) with foot support, providing a comfortable position with particular regard for the foot being treated. The head was supported on a headrest, while the arms were arranged comfortably on the armrests of the chair. The monitor displaying the stimuli was placed below the line of sight on a separate stand.

Program B: magnetic stimulation

In this method, as the name indicates, magnetic fields were used for stimulation. For this purpose an electromagnet was placed next to the head (Fig. 1), which at the specified moment creates a brief magnetic impulse. The changing magnetic fields induce a flow of current within the brain. In order for this current to stimulate neurons, the change of magnetic field must be not only large, but also very fast.

The stimulus directly simulates the nerve tissue, the flow of which creates tension in the circuit of the TMS nozzle; the magnetic field only mediates between the electrical circuits. This mediation, however, plays a key role, since magnetic fields penetrate the skull with no difficulty, in contrast to electrical fields.

Despite the relatively large penetrability of the magnetic field, its intensity gradually fades with distance from the nozzles of the electromagnet. The depth of stimulation thus remains an important question. The answer depends on sev-

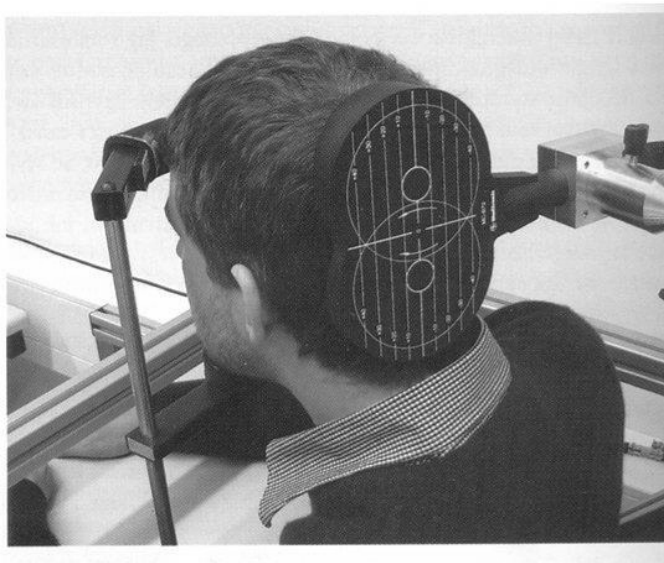


Fig. 1. Transcranial Magnetic Stimulation (rTMS)

eral factors: the size of the electromagnet, the maximum intensity of the field, or the thickness of the skull. For the typical apparatus the depth of stimulation comes to about two centimeters. This means that only the surface of the cortex can be stimulated (although the stimulation may of course spread to other structures), while many deep structures, such as the amygdala or the thalamus, lie beyond the range of TMS

It is also impossible to stimulate the ventral areas of the brain. This problem is not solved by using stronger electromagnets: to be sure, the field reaches somewhat deeper structures, but at the same time the tissue lying between the electromagnet and these structures is more strongly stimulated, which makes it practically impossible to interpret the results (Barker, 1999; Cowey, 2005).

Research methods

The following research instruments were used to evaluate rehabilitation outcome:

1. Analysis of patient's documentation (patient history and test results, including MRI and CT);
2. Clinical interview appropriately structured to focus on how the patient copes with the limitations resulting from the disease and the patient's attitude (especially self image and future orientation) hierarchy of values (especially life goals), and personality, including any available information about the premorbid personality;
3. The Quality of Life Evaluation Scale (Pachalska & MacQueen, 1998), including a subscale to evaluate the patients' mental and physical comfort, which involves dealing with pain and sleep disturbances, mood disorders (especially anxiety, sadness and excessive jocularity, and behavioral disturbances, especially aggressiveness. The evaluation involves three to five activities in terms of the approximate percentage of the patient's own participation in the activity. The level of help required by the patient is specified in points according to the following scale, which has been adapted from the widely used ASIA Scale, used to provide international standards for the neurological and functional classification of spinal injuries (ASIA, 1996; Baranowski, 2000):
 - 1 or 2 points: complete dependency (patient's own involvement: 0-25%);
 - 3 to 5 points: limited independence (patient's own participation: 50-75% or independent but under immediate supervision);
 - 6 to 7 points: independence (patient's own participation: 100% with or without adaptational equipment).

The evaluation was conducted by a physician specializing in rehabilitation on the basis of his own examination and a clinical interview. Points were assigned by three competent judges. Both the patients themselves and the local bioethics committee gave their consent to this experiment.

RESULTS

Our analysis of the results includes the evaluation of mental and physical comfort and an evaluation of communication skills in social situations.

Mental and physical comfort

The result of the combined evaluation of mental and physical comfort at baseline and followup in both research groups is presented in Table 1.

Table 1 shows that the greatest differences are observable at the extreme ends of the scale: that is in the lowest bracket (1 to 2 points) and the highest bracket (6 to 7 points). At baseline the experimental group had 28 scores in the lowest bracket, which constituted almost half of all the scores, while at followup this number had dropped to 1. In the highest bracket there were 6 scores at baseline, as compared to 32 scores at followup, an increase of more than 5 times. In the 4-5 point bracket there were differences of 4 and 5 scores respectively. A statistical analysis shows that the differences between groups at baseline and followup are statistically highly significant ($\chi^2 = 45.953$; $p = 0.0001$). Thus the rehabilitation program had a significant impact on improving the mental and physical comfort of these patients. The contingency factor C_{SK} was calculated at 0.644, indicating a strong association and significant dependency between the type of rehabilitation and the mental and physical comfort of the patients.

In the control group no significant differences were found between the results at baseline and followup ($\chi^2 = 3.093$; $p = 0.797$). A detailed analysis of the data from the control group indicates that, in contrast to the experimental group, the number of scores in the highest and lowest brackets changed only slightly: there was one less score in the lower bracket and one more score in the highest bracket at followup. The greatest change in this group took place in the middle

Table 1. Test results for mental and physical comfort in both research groups

Group	Exam	Scores							Total	Significance
		1	2	3	4	5	6	7		
Experimental	I	18	10	6	15	5	5	1	60	$\chi^2 = 45.953$
	II	0	1	6	11	10	20	12	60	$p = 0.0001$
Difference	×	-18	-9	0	-4	5	15	11	×	×
Control	I	7	7	10	15	14	5	2	60	$\chi^2 = 3.093$
	II	6	9	7	20	13	2	3	60	$p = 0.797$
Difference	×	-1	2	-3	5	-1	-3	1	×	×

*This analysis is based on the number of questions in the evaluation of mental and physical comfort (4) multiplied by the number of subjects.

bracket, which had five more scores at followup, i.e. a 30% increase. There was a surprising change in the number of 6-point scores, which went down from 5 at baseline to 2 at followup, which may suggest that some patients subjectively evaluated their own mental and physical comfort at a lower level. The circumstances (apart from the χ^2 results) demonstrate either a lack of association between mental and physical comfort and the type of rehabilitation or increased criticism and a more realistic evaluation by the patients of their own situation.

DISCUSSION

One of the main problems in the rehabilitation of TBI patients is emotional disturbance, including aggressiveness. A certain explanation of this problem is given by Gainotti (2003), who maintains that the emotional disturbances observed in TBI patients are caused by two types of factors:

1. Neurological factors. In patients involved in a typical motor vehicle accident with acceleration and deceleration the axial structures of the brain are most often damaged, along with the basal and medial parts of the frontal and temporal lobes. Thus the cortical and subcortical structures that are most often damaged are those which play an essential role in various emotional processes. The primary clinical proof of this statement is the well known prevalence of emotional and neurobehavioral disturbances over motor, sensory or aphasic disturbances in TBI patients as compared to stroke patients. These disturbances can be divided into four categories namely:
 - A deep apathy syndrome, characterized by a lack of emotional reaction to pleasant or unpleasant events and a lack of goal-directed behavior.
 - Lability, i.e. the inability to control social unacceptable emotional reactions (for example an outburst of aggressiveness in frustrating situations).
 - Nonspecific anxiety or depression, manifesting in a feeling of significant threat or sadness without any obvious cause, which may be accompanied by vegetative symptoms.
 - Impulsiveness and aggressiveness, which should be attributed to the instability of the nervous system caused by the injury and the lack of control of behavior by the frontal lobes.
2. Mental or psychodynamic factors. These result from the process of evaluation performed by the patient in respect to:
 - The importance of the consequences of the brain damage in the patient's personal and professional life.
 - The patient's actual and perceived ability to cope with these consequences in various social situations.

A critical factor in this individual process of evaluation is the patient's awareness concerning the damage and its consequences (Pachalska, 2007; Tepas, 2013). If the patient is fully aware of the painful truth regarding their changed situation, the emotional reaction may take the form of a catastrophic reaction, that is, a difficult to control attack of anxiety bordering on panic and despair. The pa-

tient may also display a more stable syndrome of anxiety and depression (Gainotti, 2003).

When the patient's level of awareness of their actual situation is low, as for example in a patient with frontal lobe damage, or generally right hemisphere damage, a pathological lack of interest, or even apathy, can be observed (Prigatano, 2003). The patient's behavior is then classified as "lack of motivation," which can be the cause of considerable problems in communication with the patient. In such cases further rehabilitation is often interrupted (Pachalska et al., 2001; Lefebvre et al., 2007).

It may be useful to recall at this point that these symptoms often occur in young persons, even very young persons, and are accompanied by major memory deficits and attendant disturbances in social communication. They are, then, not only a barrier to effective rehabilitation but also to a possible return to social life or work, and constitute a significant burden for the family. Thus, it is necessary to cope with emotional lability, childish behavior, a lack of initiative, a low frustration threshold, and impulsive or aggressive reactions (Prigatano, 2003; Lefebvre et al., 2007).

Although several methods exist for the pharmacological, behavioral, or psychological treatment of these symptoms, it must be confessed that in many cases the prognosis is not favorable, and a return to normal productive life very often proves to be impossible. Often the only realistic goal for rehabilitation is to increase the patient's independence and to improve their mental and physical comfort and a quality of life (Gainotti, 2003; Lefebvre et al., 2007; Pachalska, 2003, 2008).

The results obtained here indicate that, as hypothesized, the experimental group showed significantly better rehabilitation outcomes, especially as regards mental and physical comfort, and thus health related quality of life, whereas in the control group the improvement was slight and statistically nonsignificant.

These results have considerable significance for the further progress of these patients. The problem raised in this article has proven to be particularly important in the process of the comprehensive rehabilitation of TBI patients, and accordingly should be further explored in future research.

CONCLUSIONS

As hypothesized, the patients from the experimental group, who received rTMS, obtained significantly greater improvement in rehabilitation outcome, especially in terms of mental and physical comfort, than did the patients from the control group, who received relative beta training.

REFERENCES

- Agrawal, A., Galwankar, S., Kapil, V., Coronado, V., Basavaraju, S.V., McGuire, L.C., Joshi, R., Quazi, S.Z. & Dwivedi, S. (2012). Epidemiology and clinical characteristics of traumatic brain injuries in a rural setting in Maharashtra, India. 2007-2009. *International Journal of Critical Illness & Injury Science*, 3, 167-71.

- Benedictus, M.R., Spikman, J.M. & van der Naalt, J. (2010). Cognitive and behavioral impairment in traumatic brain injury related to outcome and return to work. *Archives of Physical Medicine & Rehabilitation*, 91(9), 1436-41.
- Gainotti, G. (2003). Assessment and treatment of emotional disorders. In: P.W. Halligan, U. Kischka & J.C. Marshall (eds.), *Handbook of clinical neuropsychology* (pp. 368-386). Oxford: Oxford University Press.
- Ducrocq, S.C., Meyer, P.G., Orliaguet, G.A., Blanot, S., Laurent-Vannier, A., Renier, D., & Carli, P.A. (2006). Epidemiology and early predictive factors of mortality and outcome in children with traumatic severe brain injury: experience of a French pediatric trauma center. *Pediatric Critical Care Medicine*, 7(5), 461-7.
- Kaczmarek, B.L.J., Code, C. & Wallesch, C.-W. (2003). Brain damage from the inside: Luria's study of Lieutenant Zasetzky. In: C. Code, Y. Joanette, A.R. Lecours (eds.), *Classic cases in neuropsychology*, vol. 2 (pp. 131-144). Hove & New York: Psychology Press.
- Kądziaława, D. (2003). Zaburzenia językowe po urazach czaszkowo-mózgowych. In: A. Herzyk, B. Daniłuk, M. Pąchalska & B.D. MacQueen (eds.), *Neuropsychologiczne konsekwencje urazów głowy: Jakość życia pacjentów* (pp. 17-24). Lublin: Wydawnictwo UMCS.
- Kolb, B. & Whishaw, I.Q. (2003). *Fundamentals of Human Neuropsychology*. New York: V. Worth Publishers.
- Lefebvre, H., Pelchat, D. & Levert, M.J. (2007). Interdisciplinary family intervention program: a partnership among health professionals, traumatic brain injury patients, and caregiving relatives. *Journal of Trauma Nursing*, 14(2), 100-13.
- Mauritz, W., Wilbacher, I., Majdan, M., Leitgeb, J., Janciak, I., Brazinova, A. & Rusnak, M. (2008). Epidemiology, treatment and outcome of patients after severe traumatic brain injury in European regions with different economic status. *European Journal of Public Health*, 18(6), 575-80.
- Moskała, M., Gościński, I., Krupa, M. et al. (2000). Pourazowe krwiaki śródczaszkowe. *Neurotraumatologia*, 1, 28-31.
- Pąchalska, M. (2003). Neuropsychological rehabilitation for post-traumatic frontal syndrome in patients recovering from prolonged coma: A preliminary report. *Acta Neuropsychologica*, 1(2), 194-227.
- Pąchalska, M. (2007). *Neuropsychologia kliniczna: Urazy mózgu*. Warsaw: Wydawnictwo Naukowe PWN.
- Pąchalska, M. (2008). *Rehabilitacja neuropsychologiczna: Procesy poznawcze i emocjonalne*. Lublin: Wydawnictwo UMCS.
- Pachalska, M. & Kaczmarek, B.L.J. (2013). *Neuropsychologia kliniczna. Ujęcie procesowe*. Warsaw: Wydawnictwo Naukowe PWN.
- Pąchalska, M. & MacQueen, B.D. (1998). *Skale Oceny Efektywności Rehabilitacji Pacjentów po Urazach Czaszkowo-Mózgowych*. Kraków: Fundacja na Rzecz Osób z Dysfunkcjami Mózgu.
- Pąchalska, M., Talar, J., MacQueen, B.D. & Baranowski, P. (2001). Ocena efektywności komunikacji lekarz-pacjent po urazie czaszkowo-mózgowym. *Ortopedia Traumatologia Rehabilitacja*, 3(5), 109-120.
- Pachalska, M., Łukowicz, M., Kropotov, I.D., Herman Sucharska, I. & Talar, J. (2011) Evaluation of differentiated neurotherapy programs for a patient after severe TBI and long term coma using event-related potentials. *Medical Science Monitor*, 17(10), CS120-128.
- Pachalska, M., Moskała, M., MacQueen, B.D., Polak, J., Wilk-Frańczuk, M. (2010). Early neurorehabilitation in a patient with severe traumatic brain injury to the frontal lobes. *Medical Science Monitor*, 16(12), CS157-67.
- Pachalska M., Mańko G., Kropotov I.D., Mirski A., Łukowicz M., Jedwabińska A., Talar J. (2012) Evaluation of neurotherapy for a patient with chronic impaired self-awareness and secondary ADHD after severe TBI and long term coma using event-related potentials. *Acta Neuropsychologica* 10(3):399-417.
- Prigatano, G.P. (2003). Assessment and rehabilitation of anosognosia and syndromes of impaired awareness. In: P.W. Halligan, U. Kischka & J.C. Marshall (eds.), *Handbook of clinical neuropsychology* (pp. 387-397). Oxford: Oxford University Press.

- Rehman, T., Ali, R., Tawil, I. & Yonas, H. (2008). Rapid progression of traumatic bifrontal contusions to transtentorial herniation: A case report. *Cases Journal*, 1 (1), 203.
- Talar, J., ed. (2003). *Neurorehabilitacja u progu XXI wieku*. Bydgoszcz: Katedra i Klinika Rehabilitacji AM w Bydgoszczy.
- Tepas, J.J. 3rd, Pracht, E.E., Orban, B.L. & Flint, L.M. (2013). High-volume trauma centers have better outcomes treating traumatic brain injury. *Journal of Trauma & Acute Care Surgery*, 74(1), 143-8
- World Health Organization. (2004). *Annex Table 2: Deaths by cause, sex and mortality stratum in WHO regions, estimates for 2002*. In: *The World Health Report 2004 – changing history* [online]. 2004. [d.o.i. 2008-11-01].

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