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COMMUNICATION IN PATIENTS WITH DISORDERS OF CONSCIOUSNESS – LESSONS LEARNED FROM INTERDOCTOR PROJECT

KOMUNIKACJA W GRUPIE PACJENTÓW Z ZABURZENIAMI ŚWIADOMOŚCI – WNIOSKI Z PROJEKTU INTERDOCTOR

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Summary

Thanks to recent advances in health care an increased number of patients may recover from severe brain injuries, but some of them are still assessed as non-responsive. Reliance on behavioural measures in communication with DoC patients seems be too prone to errors. There is need for solutions providing more objective attempts of bidirectional communication (intentional questions/commands and adequate related responses) in patients with DoC using significant processed by the patient stimuli and novel technologies (EEG-, fMRI-, BCI-based, etc.) based on recent scientific and clinical evidences. Such communication may be fulfilled even in the absence of behavior.

This article aims at assessment the extent to which current possibilities in the area of devices for extended communication has been exploited, including own experiences within InteRDoCTor project.

Streszczenie

Dzięki najnowszym osiągnięciom w opiece zdrowotnej coraz większa liczba pacjentów może powrócić do zdrowia z poważnych urazów mózgu, lecz część z nich jest ciągle diagnozowana jako niereagujący na bodźce. Poleganie jedynie na miarach behawioralnych w komunikacji z pacjentami z zaburzeniami świadomości wydaje się zbyt podatne na błędy. Istnieje zapotrzebowanie na rozwiązania zapewniające bardziej obiektywne próby komunikacji dwukierunkowej (celowe pytania/polecenia i odpowiadające im reakcje)u pacjentów z zaburzeniami świadomości, z wykorzystaniem bodźców znaczących dla pacjenta i przetwarzanych przez niego oraz nowych technologii (opartych na EEG, fMRI, BCI, itd.) w oparciu o najnowsze dowody naukowe i kliniczne. Ww. komunikacja może być realizowana nawet w przypadku braku obserwowalnych zmian zachowania pacjenta.

Artykuł ma na celu ocenę, w jakim zakresie wykorzystuje się możliwości w tym obszarze, w tym w oparciu o doświadczenia własne z projektu InteRDoCTor.

Key words: assessment, communication, brain injury, disorders of consciousness, assistive technology
Słowa kluczowe: ocena, komunikacja, uraz mózgu, zaburzenia świadomości, technologia wspomagająca

INTRODUCTION

Communication abilities, both purely linguistic, multimodal, or artificially supported, are essential for a proper human development, everyday functioning, and social participation, in both healthy people and patients. Such defined communication cannot be reduced to the interactive transfer of information between people. Key feature of communication is its efficiency, fidelity, and reliability, which requires such complex communication-related processes as context-awareness, empathy, and lowest possible sensitivity to possible errors of transmission. Developmentally communication abilities depend on competence covered by umbrella-term “intersubjectivity” including five basic elements: sharing of emotion, sharing of attention, sharing of intention, sharing of beliefs and sharing of knowledge. What more aforementioned sharing may act (simultaneously or not) at three diverse levels: motor, mental, and cultural [1]. Communication disorders may negatively influence patients' communicative activities and daily life, even years following trauma. Thus maintaining of communication abilities and (if lost) recovery seem be one of the most important part of the therapy and rehabilitation [2, 3]. Cognitive deteriorations are commonly observed in patients with neurodegenerative diseases, after traumatic brain injury (TBI) or in post-stroke survivors [4]. They are key elements of the patient’s health status, undergoing diagnosis, therapy, and rehabilitation. Sometimes preserved natural abilities are not enough. Extended communication may provide artificial extension of human cognitive abilities [1] at diverse levels of its functional compensation: strengthening of weak signals, replenishment of partial functional deficits or and replacement of lost functions [5].

To understand communication problems in disorders of consciousness (DoCs, including i.e. vegetative state i.e. unresponsive wakefulness syndrome - VS/UWS, minimally conscious state – MCS, locked-in syndrome - LIS) there is need to define it, explain aetiologies and epidemiology and to describe underlying physiological and pathological mechanisms. Then both aims, stages, and principles of therapy and rehabilitation may be checked, during both the acute phase and long-term phase [6]. Aforementioned knowledge is still limited despite efforts of the clinicians and neuroscientists. We are aware, that VS/UWS, MCS and LIS are not the illnesses, but the sets of symptoms associated with many various diseases, cerebrovascular accidents and injuries, such as stroke, TBI, severe poisonings or metabolic diseases. Patients in VS/UWS shows only reflexive behaviour (spontaneous eye opening, breathing, etc.), but they are not aware of themselves or their environment. Prevalence of VS/UWS varies from 0.1 to 6.1 VS/UWS patients per 100 000 members of the population, but bias may be significant to the different methodologies of the related studies and possible misdiagnoses of VS/UWS and MCS [7, 8]. Study by Pisa et al. showed prevalence of VS/UWS ranging from 0.2 to 3.4 cases per 100,000 inhabitants and prevalence of MCS 1.5 cases per 100,000 inhabitants. The prevalence of trauma cases varied from 21.9% to 53.8% [9]. Current prevalence of LIS is unknown, but was established as much lower than prevalence of VS/UWS and MCS [10].

Understanding of the mechanisms of emergence, loss and recovery of consciousness following severe brain injury increases rapidly, but is still limited. Changed architecture of brain connectivity is main suspected to DoCs, similarly to outcomes in general anesthesia. Detailed mechanisms cover complex within-network dysfunctionality of the frontoparietal network and between-network hyperconnectivity of the insula, ventral tegmental area, and other brain regions [11]. We still do not known how DoCs are triggered, and how invert changes in central nervous systems (CNS) associated with DoCs. We still look for more efficient assessment tools and prognostic signs of recovery from DoCs. Traumatic brain injury (TBI) constitutes leading cause of long-term disability in people younger than 45 y.o. [2, 12]. Brain injury location and severity are predictors of cognitive function after trauma and partial or complete loss of the initial consciousness level. For example moderate and severe fronto-temporal lesion usually affects linguistic processing in the acute phase what may contribute to later cognitive-communication disorders [2]. Due to complexity of communication function variety of deficits and subcategories is huge, thus establishing of the rehabilitation plan and predictors of recovery is very complicated.

This article aims at assessment the extent to which current possibilities in the area of devices for extended communication has been exploited, including own experiences within InteRDoCTor project.

MANAGEMENT OF PATIENTS WITH DOC

Management of patient with DoC constitutes a difficult clinical, social, economic and ethical issue. It requires specific expertise of the interdisciplinary therapeutic team due difficulty of diagnosis and its interpretation, complex therapy, care and rehabilitation, and communication issues with the patient and the family. The last of aforementioned factors includes problem of lack of demonstration of consciousness (not always unconsciousness), difficult clinical assessment of the changes of the patient’s health status, everyday clinical management with total dependence of the patient, more sensitivity to responses and 24/7 involvement by the team, special attention to the communication with the patient and its training by experienced medical staff, and communication with the family of these patients [13].

DoC-associated neurological deficits cause such changes as loss of cellular integrity, altered/abnormal movements (e.g. flexor and extensor patterns), and alterations in cranial nerve function [14]. What more heath status of the patient with DoC may change significantly, e.g. hi/she can emerge from VS/UWS to MCS. Thus conventional investigation of a cognitive process in patients with DoC may be full of traps. Even so simple diagnostic task as detecting and monitoring pain in patients with DoC is difficult. Such patients are usually (apparently) non-communicative and unable to express perception of pain – only some patients in MCS can experience pain to some extent [15]. Pain location may be difficult or even impossible due to (apparent) absence of self- and environmental awareness, although elementary affective information may be processed [16]. We do not know exactly which central neural pathways involved in pain or emotion processing can be impaired in patients with DoC. But taking into consideration variety of the brain damages in such patients some of the preserved function may exist, individually shaped.

Behavioral assessment of DoC requires quasi-simultaneous application of the several different diagnostic tools to address different responses indicating possible awareness. Number and kind of stimuli and their variability in a particular patient is mainly experience-based then evidence-based. Huge number of factors influences complexity of presentation in such patients. The auditory stimuli are regarded as the most sensitive for detecting awareness in patients with DoCs, but measurement of auditory responsiveness (e.g. Music Therapy Assessment Tool for Awareness in Disorders of Consciousness - MATADOC principal subscale) may still be regarded as not exact [17]. There is often need to join various tools, e.g. Sensory Modality Assessment and Rehabilitation Technique (SMART, higher sensitivity in the motor domain, e.g. tactile response) and MATADOC (higher sensitivity within auditory and visual domains), to explore relationship between diagnosis and behavioral characteristics of the patients and fully understanding of a patient's level of awareness [18]. MATODOC subscales two and three is often used in patients with prolonged DoC (persisting for at least 4 weeks after brain damage), but there can be observed variations caused by diverse therapist’s clinical experience and training [17, 18, 19]. Administration and interpretation of tools for assessment of patients with DoC should be independent on influence of researcher-related features and variations.

Consciousness level is usually evaluated using the Glasgow Coma Scale (GCS) and Coma Recovery Scale-Revised (CRC-r), also functional imaging is applied, but the “gold standard” is still far from objective semi-automated assessment, and outcome still depend on the observation of clinical signs of responsiveness. According to the recent study by Cortese et al. probability for a VS/UWS patients of being classified as MCS at least once during the 13 weeks is 30% [20, 21]. Presence of caregivers may decrease misdiagnosis percentage [22]. Within-day variability of diagnosis was high: it may achieve 33% in the VS/UWS and 38% in MCS [23]. What important assessment using GCS do not provide predictor that a patient is emerging from VS/UWS to an MCS [14].

There is many rehabilitation methods, techniques and tools for patients with DoCs, but evidence regarding aforementioned interventions is weak and recommendations are limited [24]. There are many complex details, indications, and contraindications concerning e.g. physiotherapy in patients with DoCs undergoing mechanical ventilation [25, 26]. Moreover patients have poor access to rehabilitation. According to the study of van Erp et al. [8] even more than 50% of hospitalized and institutionalized patients with VS/UWS in Netherlands had not received rehabilitation services. There is also substantial risk for misdiagnosis and inadequate therapy and rehabilitation, despite life-prolonging treatment may last up to 25 years.

fMRI-measured intrinsic functional connectivity strength (FCS) in many CNS regions, including posterior cingulate cortex and precuneus, significantly correlated with consciousness level and recovery outcome measured using GCS and CRS-r. Aforementioned results were predictors of recovery form VS/UWS and come with an accuracy of 81.25% [27].

Analysis of the therapy in patients with DOCs emphasizes necessity for integrated technology for evaluation of brain function and neural plasticity. Such plasticity affects developing, adult, and (partly) aging brain thanks to shaping by environmental inputs. It works in both healthy people and patients after a brain lesion. True may be hypothesis that after lesion (mainly within sensorimotor cortical areas) its neural networks aggregates neuronal areas adjacent to a lesion. Such overmapping (reorganization) may provide taking over the function previously played by the damaged neurons. Such reorganization may be natural or be intentionally shaped during the rehabilitation processes (by long-term directed overstimulation), causing complete or partial recovery of the function associated with damaged areas. Of course associated novel activation patterns may be different from natural, and thus reorganization may be marked in behavior, but usually tends to achieve normal pattern/range. Brain functional imaging (fMRI, PET, EEG, TMS or combined) show that this mechanism works in hemiplegic patients, despite lever of cortical remodeling and recovery of function varies depend on the patient. Individual neuroanatomic variability causes both original and novel patterns remarkable, but this individualization is natural. Function should be as close to the natural as possible - improper compensational patterns have to be avoided if possible. Of course monohemispheric reorganization is easier and more exact due to higher asymmetric between hemispheres. Also activation of the brain areas normally not engaged in the particular tasks is normal. We do not know limits of the aforementioned activation. Thus is hard to oversee if brain damage due to lesion causing DoC cay be replaced by remapping of the function by adjacent (or another) brain area due to rehabilitation-induced overstimulation (traditional in motor function) or artificial devices giving direct deep brain stimulation (DBS, artificial signals supporting the natural work of the certain brain areas or deactivating redundant brain areas). Understanding of the complex mechanisms underlying partial or complete recovery of several sensorimotor functions, need for recovery form DoC, can be beyond our possibilities now. Although some devices affecting spared perilesional neural networks or intacted deafferented cortex exist and are still dynamically developed. Time is need for further case studies on various types of the plastic neural reorganization, including training strategies, its limits concerning size of shaped neural areas or their maladaptation to the too complex functions [28]. Moreover, there is limited evidence concerning plastic abilities of the natural networks in non-cortical brain areas involved in consciousness emergence and recovery, including sub-cortical areas and brainstem [29, 30, 31]. Diverse localization, functional hierarchy, neural organization (e.g. nuclei vs. columns, lack of large neural areas, poor interconnection), extension, excitability, and morphological factors may influence their plastic abilities. Associated recovery may be also much longer than usually due to more complex function to re-learn. Thus in the cases of DoC, even with use of sophisticated artificial stimulation, only certain compensatory cognitive strategies may be possible, even partial. It seems only integrated approach to complex brain function at different level (genes, proteins, single neuron, neural networks, brain areas, cognitive and motor function) may help achieve success.

Functional neuroimaging may significantly help in this process. Brain processes understanding was shifted from basic stages of perception, language, and motor functions to more advanced cognitive, personality, and affective functions, including patients with DoCs [32].

MUCH EASIER EXAMPLE: APHASIA

Scale of difficulties in recovery of communication skills in patients with DoCs we illustrate using much mild and well known example: aphasia. It is regarded as a common neurological condition (one-third of stroke survivors experience aphasia), diagnostic procedure is rather well established, and treatment is not always complicated, but the results may be diverse. Aphasia, acquired language impairment following brain damage, may affects various modalities: expression and understanding of speech, reading and writing. Interindividual differences are so huge that predictive factors may significantly depend. on e.g. damage circumstances, preserved language, perception, and sensory-motor functions, etc. Despite knowledge and experience, neuroimaging techniques show elusive relationship between lesion localization and symptoms of aphasia. High intensity, high dose, long period of the peach and language therapy (SLT) for people with aphasia is usually beneficial and result in improved functional communication, but not always as good as before the brain damage, and usually after 4 months after cerebrovascular accident. Early therapy of the aphasia is difficult beyond attention control. Alternatively low frequency repetitive transcranial magnetic stimulation rTMS may be beneficial. Lack of randomized controlled trials (RCT), particularly with respect to chronic aphasia (lasting for >6 months after initial stroke) is observed [33-39]. What more patients with aphasia still experience various problems, e.g. mobile phone use can be problematic [40], some of them still need printed education materials in formats preferred by patients with aphasia [41, 42, 43].

Aforementioned problems with preserved communication skills assessment, planning the therapy, their execution and re-assessment toward successful outcomes (i.e. the best possible in the particular patient, not always full health) are nothing compared with similar problems in people with DoC. Residual communicative abilities are much worse, their assessment is complex due to both weak understanding and lack of commonly accepted and affective tools, and ways of the therapy are not standardized.

APPROACHES TO COMMUNICATION DISORDERS IN DOC

The most important challenge in recovery of the communication abilities in patients with DOC is the continuous assessment of the current cognitive functioning of the patient, spectrum of possibilities of development of successful extended communication through the use of the novel technical solutions, and establishing goals and program of the therapy and rehabilitation carried by various members of the interdisciplinary therapeutic team. We should take into consideration that health status of the patients may change thus both plan of the rehabilitation, and methods/tools used can be re-assessed and significantly modified taking into consideration an EBM paradigm. Collaborative support of the patient's family is usually precious.

Decision concerning use of certain diagnostic method for identifying awareness in patient with DoC should be careful and reasonable. Despite auditory modality is currently perceived the most sensitive, lack of standardization causes challenging monitoring, measurement, interpretation, and compartment of auditory responses [17, 18, 19]. Even preserved specific EEG features may be useful [44].

Extended communication constitutes objective attempts of bidirectional communication (intentional questions/commands and adequate related responses) in patients with DoC using significant processed by the patient stimuli and novel technologies (EEG, fMRI, BCI, etc.) based on recent scientific and clinical evidences. Such communication may be fulfilled even in the absence of behavior.

Patients with DoC, despite behaviorally non-responsive, can follow commands by modulating their brain activity. Aforementioned communication can be fulfilled i.e. by so called motor imagery (MI) tasks allowing for similar-to-binary communication in the severe cases of DoC patients. The problem lies in answer to several questions:

- how many patients have preserved modal (e.g. auditory) processing and associated cognitive function,
- how many alternative stimuli can be tested,
- what we can do if attention is absent permanently or temporary (if patients sleeps or cannot focus on the particular stimulus),
- how many patients can understand commands or questions,
- how many patients want to response,
- how many patients have preserved neural function providing them ability to intentionally change of e.g. imagined two different types of arm movements,
- how errors, misunderstanding, low communication pace, etc. are perceived by the patient and research team,
- how to assess and compare an experimental, individually-shaped communication to provide general paradigm [45],
- what factors may influence MI response, e.g. limb position [46].

Reliance on behavioral measures (externally observable signs of consciousness and cognition) in communication with DoC patients seems be too prone to errors since it is influenced by motor, sensory and cognitive deficits of the patient [47, 48]. Detecting awareness, assessing cognition, and interpretation of command-response activity requires more complicated and exact procedures. Functional magnetic resonance imaging (fMRI), electroencephalography (EEG), and magnetoencephalography (MEG) seem be better natural signals to explore the neural possibilities (and neural possible answers) in patients with DoC, but heterogeneity of patients, preserved neural areas, and cognitive functions may shape whole communication. Initial behavioral assessment is usually made using CRS-r. Some evidences supporting such approach has been recently showed by Gibsoen et al. [49].

Etiology of MCS may influence ability to successfully complete MI tasks: 33% of traumatic patients possess high-level cognitive functions, but none of non-traumatic patients with MCS returned similar result [50]. Quantitative EEG (qEEG) for patients with MCS is so diverse that allows for differentiation of MCS VS/UWS in patients with DoC [51].

Patients in VS/UWS remaining nonresponsive behaviorally can show preserved covert motor behavior despite absent intentional motor behavior. They are able to follow command(s) by modulating their neural responses in motor imagery (MI) tasks reflected in fMRI findings. Study by Fernadez-espejo et al. showed, that they have intacted thalamus, but damaged excitatory coupling between the thalamus and primary motor cortex [52]. But role of certain brain areas (bilateral occipital areas, left parahippocampus, other temporal and frontal areas, etc.) in MI is still discussed. Outcomes may very depend on tasks, instruction types, provided training, and way of neuroimaging (fMRI, MEG) [53]. In selected patients MI may be replaced by visual imagery (VI) or more complex tasks, if such cognitive functions are available [54].

Some results can signalize that procedure is at least threefold. The first stage is individual assessment of the functional status of (apparently) unresponsive patient. Key is specificity of the influence of the particular brain injury thus results of the functional imaging cannot be grouped across patients with DoCs, as in healthy volunteers. The outcomes should preserved communication abilities: language, perception, and sensory-motor functions in each individual patient. The second stage is paradigm selection, stimulation choice, and (as an option) planning of neurosurgical intervention to enhance hidden communication abilities. We have to bring out the preserved communication possibilities [32].

Improved accuracy of consciousness assessment offers also transcranial magnetic stimulation combined with high-density electroencephalography (TMS-EEG). Its value in extended communication have been not established yet [55].

Diagnostic error rate in this patients with VS/UWS seems be higher than previously assumed [55, 56]. Relatively other approach, fMRI and EEG active paradigms, suggests that unavoidable false positive and false negative outcomes are natural risk and can be influenced by different statistical methods used in patient data analysis [55, 56].

Despite quick development number of traditional brain-computer interfaces (BCI) is limited to:

- EEG-based (P300, SSVEP, ERP/ERS and hybrid),
- fMRI-based,
- fNIRS-based,
- mixed,
- others not mentioned above.

Aforementioned approaches are only a small part of D-C-related devices. Unfortunately many of them are prototypes or scientific devices, not always achievable in everyday clinical practice.

There may be discussion if command following is really interactive communication. Patient with DOC shows limited ability to interact and shape way of communication, if any. Command following Thus we should differentiate natural interactive communication from extended (artificial) communication and their variations individual for each patient with DoC. In the other not all levels of communication competence (competence to intersubjectivity) are achievable. If reduced it still may serve as component to build even partial communication competence. But such acquired competence may play key role in further rehabilitation and recovery thus is very precious and worth every effort.

COMPUTATIONAL MODELS OF DOC

Understanding of the neurobiological mechanisms underlying emergence and loss of consciousness may lead to the new therapeutic strategies, more accurate diagnosis and prognostic prediction, and increased efficiency of rehabilitation interventions. Computational models may make easier better understanding of the physiological and pathological processes in patients with DoCs joining knowledge-based hypotheses and experimental outcomes. Many of models go out far beyond our current knowledge e.g. in the area of brainstem models and their role in DoCs, especially role of the *ascending reticular activation* *system* (ARAS) [29, 30, 31, 57]. Despite efforts aforementioned models are not complete now, and underlying knowledge is also incomplete. There is e.g. still no consensus, activity of which brain areas can act as predictors for consciousness level and possible recovery outcome [27].

DISCUSSION

Limitations of other scientists' concepts include both weak theoretical basement of CNS pathologies associated with DoCs and limited experimental evidences including randomized controlled trials (RCTs) on bigger samples. Novel biomarkers are needed for more accurate clinical diagnosis, prediction of recovery outcome, and decision making for treatment strategies for patients with DoC.

Limitations of own concepts lies in lack of standardization of BCI approaches, limited amount of the BCI systems available for commercial clinical purposes (not as scientific solutions), and significant individualization of the communication in patients with DoC, making studies on bigger samples long-term, and their results hard to replicate or compare with results of another scientists due to e.g. population heterogeneity.

Directions for further research include:

- integration of the current approaches to the physiology and pathology of DoC,
- integration of the current knowledge and experimental results through the more detailed multi-level computational models of DoC,
- advanced studies on communication with patients with DoC and associated chances of stimulation, recovery and use of the neuroprosheses and other technical solutions,
- looking at communication with (apparently) unresponsive patient end re-definition of this term,
- looking for alternative stimuli in MI or other advanced techniques.

We should be aware that bilateral communication, even if unimodal, may be influenced by many diverse factors, even not known. Moreover it may be not achievable when health status of the patient with DoC is worsening, or due to natural processes associated with aging. Thus we always try to provide redundant ways of extended communication. We are sure that technical development should provide more advanced devices, but the issue of ethical and cultural factors (e.g. family acceptability) may outweigh possible advantages [58, 59, 60].

CONCLUSIONS

Current knowledge, experience, and estimates show high variability of communication aids used in patients with DoCs, thus could not be pooled. Future studies on much bigger samples (especially RCTs) require common and comparable definitions, valid and reliable methods and tools for the assessment (including automated were able devices or in-bed devices), and confirmation of the diagnosis cases to avoid misdiagnoses. Devices and systems designed for extended communication, despite individualized, should be standardized (or even sold as the ready-to-use modules) to provide possibility of compartmental studies. Such strengthen evidence meets requirements of the evidence-based medicine paradigm, and increase efficiency of the extended communication devices in everyday clinical practice in patients with DoCs. Despite relatively low incidence of the DoCs dedicated skilled multidisciplinary therapeutic teams are needed to cyclic re-assessment of patients' skills, recognition of the new technologies possibilities, and to see e.g. whether particular patient needs more assistance to adapt to the alternative means of communication.

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