Introduction

Until the mid-20th century, there were no specific medications with antipsychotic, antimanic and antidepressant effect. Some of psychiatric disorders, which are disabling and potentially lethal, were often treated using invasive methods, such as malaria pyrotherapy, hypoglycemic coma, electroconvulsive therapy and neurosurgery [1]. The first surgical attempts to treat psychotic patients, which had a limited success, date back to 1891. Back in 1937 scientists believed that abnormal models of functional and structural neuroanatomy of mood and regulation of behaviour were the consequences of dysfunctional thalamocortical communication, with the resulting introduction of methods of prefrontal leucotomy, and then lobotomy with numerous complications [2]. Prefrontal leucotomy was introduced by Prof. Dr. Slobodan Kostic, the head of the Department of Neurosurgery in Belgrade, Yugoslavia in 1947. By 1952, 339 surgical interventions had been performed. Kostic modified the classical Moniz’s procedure by making it significantly simpler. The majority (90%) of patients suf

DEEP BRAIN STIMULATION IN PSYCHIATRY

DUBOKA MOŽDANA STIMULACIJA U PSIHIJATRIJI

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Summary

Introduction. Deep brain stimulation is a stereotactic neurosurgical method used in the treatment of Parkinson’s disease and some other movement disorders. The application of deep brain stimulation in the treatment of certain psychiatric disorders has been intensively investigated taking into account the current knowledge of neurobiological basis of mood regulation, cognition, and behavior. This paper has been aimed at presenting the available data on experience in the application of deep brain stimulation in the treatment of psychiatric disorders. It gives an overview of scientific and professional literature, bearing in mind all the contemporary approaches in the treatment of certain psychiatric disorders. Research results available so far in the treatment of treatment-resistant depression, obsessive-compulsive disorder, Gilles de la Tourette syndrome, addiction and Alzheimer’s dementia, are affirmative concerning the efficacy of the method and low risk of adverse effects. Deep brain stimulation, as a relatively new neurosurgical method in the treatment of psychiatric disorders, is being intensively developed, and it is certainly going to be one of the treatments of choice, primarily of treatment-resistant disorders.

Key words: Deep Brain Stimulation; Psychiatry; Stereotaxic Techniques; Neurosurgical Procedures

Sažetak

Uvod. Duboka moždana stimulacija je stereotakšna neurohirurška metoda koja se koristi u terapiji Parkinsonove bolesti i drugih poremećaja pokreta. Uzimajući u obzir dosadašnja znanja o neurobiološkim osnovama regulacije raspoloženja, kognicije i ponašanja, primena duboke moždane stimulacije u lečenju nekih psihijatrijskih poremećaja intenzivno se istražuje. Cilj ovog rada je da prikaže raspoložive informacije o dosadašnjem iskustvu u primeni duboke moždane stimulacije u lečenju psihijatrijskih poremećaja. Dat je pregled naučne i stručne literature imajući u vidu sve savremene pristupe u lečenju pojedinih psihijatrijskih poremećaja. Do sada su dostupni rezultati istraživanja u lečenju teraporezistentne depresije, opsesivno-kom pulsivnog poremećaja, Žil de la Turetovog sindroma, bolesti zavisnosti i Alhajmerovu demenciju, koji ilustruju efikasnosti ove metode, uz prihvatljiv rizik od neželjenih dejstava. Duboka moždana stimulacija kao relativno nova neurohirurška metoda u lečenju psihijatrijskih bolesti intenzivno se razvija i u budućnosti će sigurno predstavljati jednu od dragocenih metoda u terapiji pre svega teraporezistentnih poremećaja.

Ključne reči: Duboka moždana stimulacija; Psihijatrija; Stereotakšne tehnike; Neurohirurške procedure
Deep brain stimulation developed as a less invasive alternative to ablative neurosurgery in addition to the relatively well-accepted method of transcranial magnetic stimulation over the last decade. It is important both for studying the mechanism of occurrence and in the treatment of depressive episodes in Parkinson's disease [19,20]. In addition to the desired inhibitory mode of action in the grey matter, its stimulating effect was observed as well. The complex mechanism of action of this method depends on both the localization and distribution of bodies of neurons and white matter, which pervades the field of localization, and the parameters of stimulation. Besides the effect at the cellular level, DBS is believed to have a systemic effect on the behaviour through the modulatory activity of neural networks. Assumptions about the development of a number of psychiatric disorders are based on observations of altered activity in certain neural networks and those that connect different brain regions. Beneficial effects of DBS are believed to result from the changing of this activity and the mutual communication of certain neural networks [21].

Deep brain stimulation is applied by implanting one or more electric leads into certain regions of the brain through the skull using neuroimaging-guided stereotaxic techniques. Each lead usually has several electrodes at the depth of 10-20 mm. They are connected via subcutaneous extensions to the battery-powered pulse generator implanted under the skin and a device that generates stimulation. The whole system is internalized into the patient's body. Parameters such as frequency, wavelength and voltage are adjusted non-invasively and adapted by computer control [22].

Serious risks and side effects associated with DBS are rare: intracranial haemorrhage, infection, epileptic seizure and complications associated with anaesthesia [22, 23]. The literature hereby reviewed also mentions symptoms which are not directly associated with the application of DBS, but may occur later as adverse events: vegetative symptoms, headache, transient anxiety, irritability, worsening of mood as well as suicide attempt and suicide [21]. According to the available literature, cognitive impairment is not associated with DBS, although it is mentioned with other invasive methods of treatment. Malfunctioning or failure of the system for DBS is possible as well, which would require replacement of one or more components. Acute and chronic effects of deep brain stimulation depend on the indication [23].

After 25 years of application and development of this method, there are some other restrictions in addition to the aforementioned, which are not so common but potentially serious side effects for an individual. The execution of the procedure and good previous diagnostics, a potential pharmacological or other non-invasive therapy, as well as the subsequent rehabilitation and further treatment require the cooperation of a neurosurgeon, neurologist and psychiatrist, who should share a common goal, that being the welfare of the patient [24].

### Obsessive-Compulsive Disorder

Although the prevalence of about 2% in the general population classifies this psychiatric disorder between depressive disorder and schizophrenia, it is still insufficiently recognized. It significantly affects the quality of life and disability of the patient. Evidence-based treatment involves administration of antidepressants with a dominant influence on the monoamine neurotransmitter systems, antipsychotics with anxioytics as well as cognitive behavioural psychotherapy [25]. However, up to 60% of patients do not respond satisfactorily to the treatment, which makes treatment-resistant OCD a serious public health problem. Target areas for DBS are the frontal part of the internal capsule and ventral striatum, i.e. nucleus accumbens, subthalamic nucleus and lower thalamic peduncle. So far, a significant number of small case studies with few people have been published [26-30]. Compared to other non-pharmacological treatments, DBS did not have a significant impact on cognitive impairment.
Treatment-Resistant Depression

Depression is the fourth leading cause of disability in the world according to the World Health Organization, and there are predictions that it will be the second one by 2020 [31]. Treatment of patients with depressive disorder, according to the guidelines, involves antidepressant pharmacotherapy, psychotherapy and electroconvulsive therapy. Despite the aforementioned possibilities of treatment, about two-thirds of patients do not respond to the initial antidepressant treatment, the combined pharmacotherapy gets no response in about one-third of the patients and regardless of the therapeutic approach, symptoms persist in about one-fifth of patients, i.e. they never reach full remission. Depressive disorder is often recurrent in about 60% of patients who have a good therapeutic response [22]. In recent decades, progress has been achieved in the imaging of neuroanatomical structures associated with depressive disorder and response to antidepressant therapy. In our country, the treatment of depression included the method of transcranial magnetic stimulation, both in patients suffering from Parkinson’s disease and depression, and in patients with mild depressive episodes [20, 32]. Mayberg and Hamani apply DBS of the white matter cingulum and describe neuroanatomical changes similar to the effects of a favourable response to the treatment with antidepressants [9, 33]. Nucleus accumbens, which is involved in the neural pathways associated with reward and motivation, may also be the target of DBS due to its favourable effect on anhedonia as a key symptom of Treatment-Resistant Depression (TRD) [34]. Sartorius described the case of a female patient with TRD undergoing electroconvulsive therapy, in which remission was achieved by additional DBS of medullary stria of thalamus. This is a relatively new target location, which is normally involved in the coordination of monoamine neurotransmission [35]. There are more and more reports stating favourable results achieved in patients having treatment-resistant depressive disorder who were treated by DBS [36,37].

Gilles de la Tourette syndrome

This disorder, whose prevalence amounts to about 1% [12], is characterized by disabling vocal and motor tics, as well as symptoms similar to OCD. Its frequent association with OCD suggests a common etiologic significance of the basal ganglia dysfunction in the development of motor symptoms [21]. In smaller studies, bilateral DBS of the globus pallidus, centromedian thalamic nuclei and anterior complex of thalamic nuclei yielded favourable results in patients with this syndrome [38].

Antipsychotic-induced tardive dystonia and dyskinesia

Late extrapyramidal side effects of antipsychotic therapy are not rare, and their treatment by replacing antipsychotics with anticholinergics, anxiolytics, levodopa, botulinum toxin and physical therapy is often unsuccessful [39]. DBS proved to be a very effective and long-term solution for the treatment of primary localized or generalized dystonia and dyskinesia. Bilateral DBS of the globus pallidus is a potentially important treatment of secondary, antipsychotic-induced tardive dystonia and dyskinesia as well, which are often disabling and pharmacotherapy-resistant [13, 15, 40].

Addiction

Case reports of smokers having OCD who were treated with DBS of nucleus accumbens, also mention a favourable response in nicotine addiction [41]. In three patients unsuccessfully treated for alcoholism, Muller shows good effects of the nucleus accumbens DBS [16], which could be explained by a qualitative change of the experience of the reward associated with the intake of substance or regulation of behaviour related to the addictive behaviour, which indirectly reduces the likelihood of relapse.

Alzheimer disease

About 8% of population over 65 years of age suffer from this neurodegenerative and neuropsychiatric disease. Pharmacological therapy involves slowing down, but not prevention of further cognitive decline within disease progression. Acetylcholinesterase inhibitors and N-methyl-D-aspartate (NMDA) receptor antagonists as well as antipsychotics are used for the regulation of altered behaviour [22, 25]. A potentially modulating neurophysiological effect of DBS of fornix and hypothalamus on the activity in these pathological regions is being intensively studied [17, 18].

Conclusion

Neurosurgical treatment approach in psychiatry has a long history. Previous attempts were limited by the occurrence of a number of complications. Taking into account the development of neuroanatomical, neurophysiological and neurobiochemical models of mood, thinking and behaviour on one hand and technological advances regarding the increased safety of application of deep brain stimulation on the other, opens up possibilities of relieving symptoms and improving psychosocial functioning with its application. Current results regarding efficacy and safety of this method are encouraging, but larger, randomized, placebo-controlled studies are required. More precise defining of specific effects on clearly determined brain structures in patients with different psychiatric disorders, as well as the adjustment of all variable parameter values of the technical part of the deep brain stimulation system are a part of clearly set goals for further studies of the application of deep
brain stimulation. Modern therapeutic approach to most psychiatric disorders involves a combination of pharmacotherapy, psychotherapy, as well as the application of electroconvulsive therapy. Neurosurgical approach followed by proper psychiatric rehabilitation should definitely be considered for patients who fail to respond to the aforementioned treatment options and who become disabled.

References


