

# Pregled istraživanja o primjeni i učinkovitosti *neurofeedback* metode u liječenju depresivnog poremećaja

## */ A Review of Research on the Application and Effectiveness of the Neurofeedback Method in the Treatment of Depressive Disorder*

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Depresivni poremećaj jedna je od najranije opisanih bolesti u povijesti medicine, s dubokim utjecajem na pojedince i društvo u cjelini. Prema predviđanjima, depresija će do 2030. godine uzrokovati najveći porast troškova i opterećenja za zdravstveni sustav, tj. oni će premašiti troškove i opterećenja svih drugih bolesti i poremećaja. Standardni pristupi liječenju depresije uključuju farmakološku terapiju i psihoterapijske tehnike, dok sve više pažnje dobivaju i komplementarne metode poput *neurofeedbacka*. *Neurofeedback* je računalno podržana metoda koja prati i analizira moždanu električnu aktivnost (EEG) sa ciljem regulacije disfunkcionalnih moždanih obrazaca povezanih s depresijom. Rezultati dosadašnjih istraživanja ukazuju na značajne prednosti *neurofeedbacka*. Osobe s depresivnim poremećajem koje su bile uključene u *neurofeedback* trening pokazale su statistički značajna poboljšanja u usporedbi s kontrolnim skupinama, što ukazuje na njegovu potencijalnu učinkovitost kao dopunske terapije. Ipak, iako preliminarni rezultati obećavaju, potreban je daljnji razvoj znanstvenih studija kako bi se osigurala jasnija metodologija i bolje razumijevanje mehanizama djelovanja *neurofeedbacka*. U radu se analiziraju dosadašnja istraživanja i raspravlja o mogućnostima implementacije *neurofeedbacka* u liječenju depresije naglašavajući njegov potencijalni doprinos smanjenju simptoma depresivnog poremećaja. Iznesen je kritički osvrt na metodološka ograničenja i zaključke istraživanja te su pružene smjernice za buduća istraživanja.

*/ Depressive disorder is one of the earliest illnesses to be described in the history of medicine, with profound effects on individuals and the society as a whole. By 2030, depression is projected to cause the largest increase in health care costs and burdens, thus exceeding the costs and burdens of all other diseases and disorders. Standard approaches to the treatment of depression include pharmacological therapy and psychotherapeutic techniques, while complementary methods such as neurofeedback are also gaining increasing attention. Neurofeedback is a computer-assisted method that monitors and analyzes the electrical activity of the brain (EEG) with the aim of regulating dysfunctional brain patterns associated with depression. The results of the studies conducted so far indicate significant advantages of neurofeedback. Individuals with depressive disorder who were included in neurofeedback training showed statistically significant improvements compared to the control groups, which points to its potential effectiveness as a form of supplementary therapy. Nevertheless, although the preliminary results are promising, further scientific studies are necessary in order to provide a clearer methodology and better understanding of the mechanisms of action of neurofeedback. An analysis of the previous studies and a discussion of the possibilities for implementing neurofeedback in the treatment of depression are provided in this study, with a special emphasis on its potential contribution to reducing the symptoms of depressive disorder. A critical review of the methodological limitations and study conclusions is provided, as well as some guidelines for future research.*

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**UVOD**

Mentalno zdravlje sastavnica je općeg zdravlja i važan resurs za pojedinca, njegovu obitelj i društvenu zajednicu (1), a razina mentalnog zdravlja pojedinca pod utjecajem je brojnih psiholoških, socijalnih i bioloških čimbenika. Depresivni poremećaj ili depresija (lat. *deprimere* – potištenost, bezvoljnost), jedna od najranije opisanih bolesti u povijesti medicine (2), bolest je za koju se danas procjenjuje da će do 2030. godine uzrokovati najveći porast troškova i opterećenja za zdravstveni sustav u odnosu na sve druge bolesti (3, 4). Depresija je rezultat složene interakcije psiholoških i bioloških čimbenika te značajno utječe na radnu sposobnost i kvalitetu života žena i muškaraca neovisno o ekonomskom stupnju razvoja društvene zajednice. Može se javiti u bilo kojem životnom razdoblju, no najčešća je između dvadeset i pete i četrdesete godine života (2). Najznačajnije važeće klasifikacije koje se koriste za sistemsko prikazivanje depresivnog poremećaja jesu Međunarodna klasifikacija bolesti MKB-10 i Dijagnostički i statistički priručnik za mentalne poremećaje DSM-5 (5-7). Dijagnoza depresivnog poremećaja postavlja se na osnovi raspoloživih podataka (anamneza, heteroanamneza i dr.), koji između ostalog uključuju i broj simptoma, trajanje poremećaja, utjecaj poremećaja na socijalno, obiteljsko i radno funkcioniranje, diferencijalne

**INTRODUCTION**

Mental health is a component of general health and an important resource for an individual, their family and the social community (1), while the level of an individual's mental health is influenced by a number of psychological, social and biological factors. Depressive disorder or depression (lat. *deprimere* – low mood, listlessness), is one of the earliest illnesses to be described in the history of medicine (2), projected to cause the largest increase in health care costs and burdens by 2030, thus exceeding all other diseases (3, 4). Depression is the result of a complex interaction of psychological and biological factors, and has a significant effect on the work capacity and quality of life of both women and men, regardless of the economic level of development of the community. It can occur at any age, but is most common between the ages of twenty-five and forty (2). The most important classifications used to systematically portray depressive disorder are the International Classification of Diseases (ICD-10) and the Diagnostic and Statistical Manual of Mental Disorders (DSM-5) (5-7). Depressive disorder is diagnosed based on the available data (medical history, collateral history etc.), including, among other things, the number of symptoms, duration of the disorder, its effect on the social, family and occupational functioning, differential diagnostic criteria and the circumstances in which depressive symptoms occurred (5). Despite the contem-

dijagnostičke kriterije i okolnosti pojave depresivnih simptoma (5). Unatoč suvremenim spoznajama i rastućem broju znanstvenih dokaza mehanizam nastanka depresivnog poremećaja do danas nije u potpunosti razjašnjen, ali je jasno da se radi o složenoj kliničkoj pojavi u čijoj je podlozi složeno međudjelovanje bioloških i psihosocijalnih čimbenika. Postoji nekoliko prihvaćenih teorija koje možemo svrstati u dvije skupine: biološke i psihosocijalne teorije. Biološke teorije nude značajne doprinose u etiologiji depresivnog poremećaja, ističući čimbenike poput genetske predispozicije (8), disfunkcije neurotransmitera (9), smanjene razine moždanog neurotrofnog čimbenika (BDNF) (10,11), poremećaji u regulaciji neuropeptida poput tvari P, neuropeptida Y, kortikotropina i vazopresina (12), nedostatka vitamina B12 (13) i folata (14), disfunkcije hipotalamičko-hipofizno-adrenalne (HHA) osi (15), smanjene razine tireotropnog hormona (TSH) (16) te prisutnosti neurodegenerativnih procesa (17).

U okviru psihosocijalnih teorija ključni su sljedeći uzroci: psihodinamski čimbenici (nesvjesni konflikti, osjećaj gubitka, nisko samopoštovanje), bihevioralni čimbenici (naučena bespomoćnost), kognitivni čimbenici (negativna uvjerenja, pesimizam, iskrivljena percepcija stvarnosti), socijalni čimbenici (stresni životni događaji, gubitak bliskih osoba, nepovoljni socijalni odnosi) (18-21). Važno je naglasiti da se socijalni gubitak prepoznaje kao jedan od ključnih čimbenika u razvoju i održavanju depresivnog poremećaja.

U liječenju depresivnog poremećaja danas koristimo farmakoterapiju te različite psihoterapijske tehnike kao i elektrokonvulzivnu terapiju za rezistentnu depresiju. U okviru psihoterapije različiti psihoterapijski modaliteti jesu psihodinamska, kognitivno-bihevioralna, ekspresivna (art) terapija i dr. Iz svega navedenog jasno je da postoji potreba za istraživanjem učinaka različitih terapijskih metoda kod osoba koje boluju od depresije što će osigurati znanstve-

porary knowledge and the increasing amount of scientific evidence, the mechanism of the onset of depressive disorder has not yet been completely clarified, however, it is clearly a multifaceted clinical phenomenon resulting from the complex interaction of biological and psychosocial factors. There are several accepted theories, which can be classified into two groups: biological and psychosocial theories. Biological theories offer significant contributions to the etiology of depressive disorder, highlighting the factors such as genetic predisposition (8), neurotransmitter dysfunction (9), lower levels of brain-derived neurotrophic factor (BDNF) (10, 11), dysregulation of neuropeptides such as substance P, neuropeptide Y, corticotropin and vasopressin (12), vitamin B12 (13) and folate (14) deficiency, dysfunction of the hypothalamic-pituitary-adrenal (HPA) axis (15), low thyrotropic hormone (TSH) levels (16), and the presence of neurodegenerative processes (17).

Psychosocial theories highlight the following key causes: psychodynamic factors (subconscious conflicts, sense of loss, low self-esteem), behavioral factors (learned helplessness), cognitive factors (negative beliefs, pessimism, distorted perception of reality), social factors (stressful life events, loss of loved ones, unfavorable social relationships) (18-21). It should be emphasized that social loss is recognized as one of the key factors in the development and maintenance of depressive disorder.

Pharmacotherapy and various psychotherapeutic techniques are nowadays used in the treatment of depressive disorder, including electroconvulsive therapy (ECT) for resistant depression. Psychotherapy includes different psychotherapeutic modalities, such as psychodynamic, cognitive-behavioral, expressive (art) therapy, and others. It is clear from all of the above that the effects of different therapeutic methods should be studied in individuals with depression, which would ensure a scientifically-based approach to their treatment. Since this illness is becoming a growing public health issue, newer methods are also being explored. One of these methods is neurofeedback.

no utemeljen pristup njihovu liječenju. Budući da ova bolest postaje sve veći javnozdravstveni problem, istražuju se i novije metode. Jedna od tih metoda je *neurofeedback*.

*Neurofeedback* je terapijska neinvazivna metoda temeljena na praćenju električne aktivnosti mozga metodom elektroencefalografije (EEG) koja pomaže da osoba nauči modificirati moždane valove uz pomoć računalne tehnologije (22). Hammond definira *neurofeedback* kao vrstu *biofeedbacka*, odnosno kao trening moždanih valova (23). Zapravo, elektroencefalografija (EEG) u stvarnom vremenu bilježi informacije o moždanoj aktivnosti koje računalo zatim pretvara u povratne signale (vidne i/ili zvučne prikaze na ekranu). Moždani su valovi odraz specifičnih mentalnih stanja, a pojedini obrasci moždanih valova mogu biti manje ili više poželjni za određene mentalne aktivnosti pa *neurofeedbackom* učimo mozak kako da proizvede optimalne obrasce moždanih valova.

Za razumijevanje specifičnih mehanizama koji su temelj *neurofeedback* učenja prvo treba razumjeti opće teorijske i eksperimentalne osnove učenja. Dvije glavne vrste asocijativnog učenja klasično su i operantno (instrumentalno) uvjetovane. Među teorijama i modelima koji su bili predloženi kako bi objasnili učenje pomoću *neurofeedbacka* i njegove pozadinske mehanizme postoji preklapanje i kompatibilnost: npr. može se vidjeti da teorija instrumentalnog učenja djelomično oblikuje gledište koje odgovara teoriji dualnog procesa. Teorija motoričkog učenja i teorija učenja vještina također imaju neke zajedničke značajke, dok se teorija globalnog radnog prostora, koja pretpostavlja svijest o potkrepljenju (*feedback*) za učenje čini kompatibilnom s nekim oblicima teorije svijesti. Budući eksperimenti trebali bi pružiti nove uvide u valjanost navedenih teorija u *neurofeedback* učenju i izvedbi (24-27).

Početkom 2001. godine dvije stručne organizacije: *Association for Applied Psychophysiology and Biofeedback (AAPB)* i *International Society for Ne-*

*urofeedback* is a therapeutic, noninvasive method based on monitoring the electrical activity in the brain using electroencephalography (EEG), thus helping an individual learn how to modify the brain waves using computer technology (22). Hammond defines neurofeedback as a type of biofeedback, i.e. training of brain waves (23). In fact, electroencephalography (EEG) records information on brain activity in real time, which the computer then converts into feedback signals (visual and/or audio representations on the screen). Brain waves are a reflection of specific mental states, and individual brain wave patterns can be more or less desirable for specific mental activities, therefore neurofeedback teaches the brain how to produce the optimal brain wave patterns.

In order to understand the specific mechanisms underlying neurofeedback learning, we must first understand the general theoretical and experimental bases of learning. The two main types of associative learning are explained by classical and operant (instrumental) conditioning. There is an overlap and compatibility among the theories and models proposed for the purpose of explaining learning through neurofeedback and its underlying mechanisms, i.e. it is observable that the instrumental learning theory partially shapes the viewpoint corresponding to the dual process theory. The motor learning theory and skill acquisition theory also share some characteristics, while the global workspace theory, which assumes an awareness of feedback for learning, seems compatible with some forms of the theory of consciousness. Future experiments should provide new insights into the validity of the aforementioned theories in terms of neurofeedback learning and performance (24-27).

In early 2001, two professional organizations: *Association for Applied Psychophysiology and Biofeedback (AAPB)* and *International Society for Neuronal Regulation (ISNR)*, formed a working body tasked with developing the official standards for the methodology of research, at the same time developing the necessary conditions and forms of research for each of the 5 levels of neurofeed-

uronal Regulation (ISNR) osnovala su radno tijelo s ciljem razvoja službenih standarda za metodologiju istraživanja razvijajući pritom potrebne uvjete i oblike istraživanja za svaki od 5 stupnjeva učinkovitosti *neurofeedback* terapije (koje rangiraju od najniže, prve razine – nedovoljno empirijskih dokaza, sve do najviše pete razine – učinkovito i specifično). Najniže rangirani treninzi ne odražavaju slabu učinkovitost terapije, već je riječ o područjima nedovoljno istraženim da bi se izveli primjereni empirijski zaključci. Rigorozni standardi koje su donijeli AAPB i ISNR mnogo su stroži i oprezniji u zaključivanju o učinkovitosti nego mnoge dobro prihvaćene medicinske intervencije. *Neurofeedback* koji je posebno usmjeren na depresiju umjereno je podržan postojećim studijama (sve odgovaraju razini 2/5, „moguće učinkovito“) (28,29).

## METODOLOGIJA PRETRAŽIVANJA I ODABIRA LITERATURE

U cilju izrade preglednog rada o primjeni *neurofeedback* metode u liječenju depresivnog poremećaja provedena je detaljna i višefazna pretraga relevantnih znanstvenih baza podataka, stručnih časopisa i internetskih izvora. Pretraživane baze bile su: *PubMed*, *Scopus*, *Web of Science*, *PsychINFO*, *EBSCOhost*, *ScienceDirect*, *ProQuest Dissertations and Theses* te nacionalna baza Hrčak. Ove baze su odabrane zbog svoje reputacije u području biomedicine, psihologije i neuroznanosti, kao i dostupnosti recenziranih radova iz područja primjene *neurofeedbacka* u psihijatriji. Osim toga, ciljano su pretraženi i stručni časopisi s fokusom na *neurofeedback* poput: *Journal of Neurotherapy*, *Neuropsychobiology*, *Applied Psychophysiology and Biofeedback* i *Frontiers in Behavioral Neuroscience*.

Pretraživanje je provedeno u razdoblju od listopada do prosinca 2024. godine, a uključivalo je radove objavljene od 1997. do 2024. godine. Ključne riječi korištene pri pretraživa-

back therapy effectiveness (ranked from the lowest, Level 1 – “not empirically supported”, to the highest, Level 5 – “efficacious and specific”). The lowest ranking trainings do not indicate a low efficiency of the treatment, but represent areas that have not been explored enough to enable drawing appropriate empirical conclusions. The rigorous standards set by the AAPB and ISNR are much stricter and more cautious in their conclusions about efficacy than many other well-accepted medical interventions. Neurofeedback specifically focused on depression is moderately supported by the existing studies (all of which correspond to Level 2/5, “possibly efficacious”) (28, 29).

## SEARCH METHODOLOGY AND LITERATURE SELECTION

A detailed multiphase search of the relevant scientific databases, professional journals and internet sources was conducted for the purpose of preparing this review article on the application of the neurofeedback method in the treatment of depressive disorder. The following databases were searched: *PubMed*, *Scopus*, *Web of Science*, *PsycINFO*, *EBSCOhost*, *ScienceDirect*, *ProQuest Dissertations and Theses*, as well as the national database Hrčak. These databases were selected based on their reputation in the field of biomedicine, psychology and neuroscience, as well as the availability of reviewed papers in the field of neurofeedback application in psychiatry. In addition, a targeted search focusing on neurofeedback was conducted in the following professional journals: *Journal of Neurotherapy*, *Neuropsychobiology*, *Applied Psychophysiology and Biofeedback*, and *Frontiers in Behavioral Neuroscience*.

The search was conducted in the period from October to December 2024, and included papers published from 1997 to 2024. The key words used during the search included combinations in both Croatian and English: *elektroencefalogram*, *neurofeedback*, *depresivni poremećaj* (in English: *electroencephalogram*, *neurofeedback*, *depression*). The inclusion criteria involved the following: papers

nju uključivale su kombinacije na hrvatskom i engleskom jeziku: elektroencefalogram, *neurofeedback*, depresivni poremećaj (na engleskom jeziku: *electroencephalogram*, *neurofeedback*, *depression*). Kriteriji uključivanja obuhvaćali su: radove koji se bave primjenom EEG *neurofeedback* metode u liječenju depresivnog poremećaja, istraživanja provedena na ljudima (kliničke studije, prikazi slučajeva, probna istraživanja) te radove s dostupnim punim tekstom. Kriteriji isključivanja odnosili su se na: radove koji se primarno bave drugim poremećajima bez jasne poveznice s depresijom, te radove u kojima se *neurofeedback* spominje, ali nije primijenjen u terapijskom kontekstu liječenja depresije.

Konačan broj radova uključenih u analizu iznosio je 34, a obuhvaćaju znanstvene članke, poglavljia iz stručnih knjiga i specijalistički rad.

## NEUROFEEDBACK I DEPRESIVNI POREMEĆAJ

Baehr, Rosenfeld i Baehr među prvima su prikazali dvije studije slučaja na depresivnim pacijentima. U navedenim prikazima slučaja navode da prethodno trogodišnje liječenje medikamentnom terapijom i psihoterapijom kod pacijenata nije dovelo do poboljšanja. U procesu liječenja uz medikamentnu terapiju i psihoterapiju autori uvode i *neurofeedback* trening alfa asimetrije u kojem pokušavaju povećati razliku u aktivaciji lijevog i desnog frontalnog režnja. Elektrode su bile smještene na F3 i F4 položaje u odnosu na referentno smještenu Cz poziciju. Ovu (vlastitu) metodu nazivaju ALAY (od *alpha asymmetry*), a uvode i indeks alfa asimetrije (veći od nule ukazuje na višu zastupljenost desnostrane alfa frekvencije, odnosno nižu aktivaciju desnog u odnosu na lijevo frontalno moždano područje što se povezuje sa smanjenjem neugodnih emocija). Ispitanici su dolazili jednom do dva puta/tjedan na *neurofeedback* trening nakon čega su bili uključeni u pola sata psihoterapije. Tijekom *neurofeedbacka*

exploring the application of the EEG neurofeedback method in the treatment of depressive disorder, studies conducted on people (clinical studies, case studies, trial studies) and papers with full text available. The exclusion criteria were the following: papers primarily examining other disorders without a clear connection to depression; and papers mentioning neurofeedback, but without applying it in the therapeutic context of depression treatment.

The final number of papers included in the analysis was 34, and included scientific papers, chapters from expert books and a specialist paper.

## NEUROFEEDBACK AND DEPRESSIVE DISORDER

Baehr, Rosenfeld and Baehr were among the first to present two case studies on depressive patients. In these case studies, they reported that previous three-year treatments with medication therapy and psychotherapy did not lead to improvements in the patients. In the process of treatment with medication therapy and psychotherapy, the authors also introduced alpha asymmetry neurofeedback training in an attempt to increase the difference in the activation of the left and right frontal lobes. The electrodes were positioned at F3 and F4, relative to the reference position Cz. They called this (their own) method ALAY (alpha asymmetry), and also introduced the alpha asymmetry index (greater than zero indicates higher alpha frequency on the right side, i.e. lower activation of the right frontal brain area as opposed to the left, which is associated with fewer unpleasant emotions). The respondents underwent neurofeedback training one/two times per week, followed by a half hour of psychotherapy. In the course of neurofeedback, the goal was to learn how to increase the alpha asymmetry index above zero (when the alpha asymmetry index was above zero, the respondent would get a confirmation, i.e. a reinforcing sound, vibration or image change on the screen confirming that they managed to increase their alpha asymmetry index

cilj je bio naučiti povisiti indeks alfa asimetrije iznad nule (kada bi indeks alfa asimetrije bio iznad nule, ispitanik bi dobio potvrdu odnosno potkrepljenje zvukom, vibracijom ili promjenom slike na ekranu što bi bila potvrda da je uspio povisiti indeks alfa asimetrije iznad nule). *Neurofeedback* trening trajao je od 34 do 36 susreta tijekom razdoblja od dvije godine. Rezultati su pokazali nižu razinu depresije na svim kliničkim mjernim ljestvicama. Ponovno EEG mjerenje nakon pet mjeseci za jednu pacijenticu pokazalo je da su se naučene promjene u EEG frontalnoj asimetriji zadržale. Druga pacijentica nije bila dostupna. Autori su zaključili kako je *neurofeedback* tretman učinkovit dodatak psihoterapiji u liječenju depresije (30).

U svom su sljedećem radu Baehr i suradnici koristili *neurofeedback* kao dodatni tretman za depresiju uz prisutnost psihoterapije i medikamentne terapije. Izvijestili su da je četvero od šest ispitanika pokazalo poboljšanje na tri mjere Beckova upitnika depresije (BDI), Minnesota multifazičnom inventaru ličnosti (MMPI-2) te indeksu alfa asimetrije. Dva ispitanika nisu zadovoljila sve kriterije, jedan je ispitanik razvio nuspojave na lijekove, dok je kod drugoga bio prisutan trend smanjenja simptoma. Autori navode kako *neurofeedback* tretman nije uspješan kod svih sudionika te predlažu daljnja istraživanja s kontrolnim skupinama. *Neurofeedback* metodu autori predlažu kao dodatnu metodu liječenja, uz medikamentnu terapiju i psihoterapiju, a nikako ne kao jedini tretmanski izbor kod depresije (31).

Studija slučaja Hammonda uvodi novi postupak *neurofeedbacka* pod nazivom Roshi. Autor smatra da i drugi protokoli, osim ALAY-a, mogu mijenjati učinke alfa frontalne asimetrije i na taj način smanjiti simptome depresije. Postupak Roschi sastoji se od jačanja frekvencija beta valova te istovremenog inhibiranja alfa i *theta* frekvencija. Ispitanik je bio uključen u 12 *neurofeedback* treninga s elektrodama smještenim na F3 i F4 referentno u odnosu na Cz te 13 *neurofeedback* treninga s elektrodama smješte-

above zero). The neurofeedback training included 34 to 36 meetings over a period of two years. The results showed lower levels of depression on all clinical measurement scales. Repeated EEG measurements conducted on a female patient five months later showed that the learned changes in the EEG frontal asymmetry were maintained. The other patient was not available. The authors concluded that neurofeedback was an efficient addition to psychotherapy for the treatment of depression (30).

In their following paper, Baehr et al. used neurofeedback as a supplementary treatment for depression in addition to psychotherapy and medication. They reported that four out of the six respondents showed improvement on three items of the Beck Depression Inventory, the Minnesota Multiphasic Personality Inventory (MMPI-2) and the alpha asymmetry index. Two respondents did not meet all of the criteria, one developed side effects to medication, while another presented with a trend of symptom reduction. The authors stated that the neurofeedback treatment was not successful in all participants, and proposed further research which would include control groups. The authors suggested neurofeedback as a supplementary treatment method in addition to medication and psychotherapy, but certainly not as the only treatment for depression (31).

The case study conducted by Hammond introduced a new neurofeedback procedure, entitled Roshi. The author believed that other protocols, beside ALAY, could change the effects of frontal alpha asymmetry and thus reduce the symptoms of depression. The Roshi procedure consists of increasing the frequencies of beta brainwaves, while simultaneously inhibiting the alpha and theta frequencies. The respondent was included in 12 sessions of neurofeedback training, with electrodes positioned at F3 and F4, relative to the reference position Cz, and 13 sessions of neurofeedback training with electrodes positioned at C3 and C4. The results indicated reduced symptoms on the BDI depression scale, from 21 to 2 after four months of undergoing neurofeedback training. However, since the sample consisted of only one

nim na C3 i C4. Rezultati ukazuju na smanjenje pojave simptoma na BDI ljestvici za depresiju s 21 na 2 nakon četiri mjeseca *neurofeedback* treninga. Međutim, budući da je u uzorku bila samo 1 osoba, ti nalazi ne mogu reprezentativno predstavljati učinak metode (32).

Pet godina kasnije Hammond je koristio protokol korekcije alfa asimetrije za 9 Amerikanaca s teškom depresijom, ali nije prikazao srednje vrijednosti ili standardne devijacije, što znači da ovi nalazi također ne mogu reprezentativno predstavljati učinak metode. Sudionici s depresivnim poremećajem otpornim na medikamentnu terapiju bili su uključeni u *neurofeedback* terapiju tijekom 20 susreta po pola sata. Osam je pacijenata završilo trening bez druge psihoterapije. Sedam od osam pacijenata postiglo je značajna poboljšanja (na ljestvici depresije MMPI), a jedan je pacijent nakon pet susreta odustao. Autor zaključuje kako tretman depresije postupkom Roshi dovodi do smanjenja simptoma depresivnog poremećaja te predlaže daljnja kontrolirana eksperimentalna istraživanja (33).

Prvi kvantitativni EEG (*quantitative EEG*, qEEG) kao smjernicu u *neurofeedback* treningu kod depresije opisali su Walker, Lawson i Kozlowski u prikazu dvije studije slučaja. U prvom prikazu ispitanica je bila uključena u 16 *neurofeedback* treninga trenirajući beta 12 – 15Hz i snižavajući *theta* vrijednosti na C3 lokaciji. Nakon završenog treninga i poslije dvije godine ispitanica više nije imala depresivne simptome. U drugom prikazu slučaja ispitaniku koji se liječio od bipolarnog afektivnog poremećaja mijenjali su nekoliko *neurofeedback* protokola. Nakon treninga autor navodi kako su se kod ispitanika smanjili simptomi anksioznosti, iritabilnosti, ljutnje i depresivnosti, no ne navodi na koji način su promjene izmjerene. Pacijentov QEEG zapis nakon *neurofeedback* tretmana pokazao je promjene. Autor zaključuje kako QEEG može pomoći u određivanju individualnih protokola te na taj način ubrzati oporavak od depresivnog poremećaja (34).

individual, these results cannot represent the effect of the method (32).

Five years later, Hammond used the alpha asymmetry correction protocol on a sample of 9 Americans with severe depression, but did not present medium values or standard deviations, meaning that these findings could not represent the effect of the method either. Participants with treatment-resistant depression were included in neurofeedback therapy encompassing 20 half-hour sessions. Eight patients completed the training without other psychotherapy. Seven out of eight patients experienced significant improvement (on the MMPI depression scale), while one patient dropped out after five sessions. The author concluded that depression treatment with the Roshi procedure leads to a reduction of depressive symptoms, and suggested further controlled experimental research to be conducted (33).

The first quantitative EEG (qEEG) as a guideline for neurofeedback training in depression was described by Walker, Lawson and Kozlowski in their two case studies. In the first study, the female respondent underwent 16 sessions of neurofeedback training, training beta at 12 – 15Hz and lowering theta values at C3 location. After completing the training and after two years, the respondent no longer exhibited depressive symptoms. In the second case study, several different neurofeedback protocols were applied on a patient who was treated for bipolar affective disorder. After training, the author stated that the patient experienced fewer symptoms of anxiety, irritability, anger and depression, but he did not state in which manner the changes were measured. Changes were observable on the patient's QEEG report after the neurofeedback treatment. The author concluded that QEEG could assist in determining the individual protocols, and in this way accelerate recovery in depressive disorder (34).

Dias and van Deusen provided an overview of the neurofeedback protocols for depression, with a suggestion of a new, their own, protocol. The protocol focused on the symptoms presented by the

Pregled *neurofeedback* protokola za depresiju, uz prijedlog novog vlastitog protokola prikazuju Dias i van Deusen. Protokol je bio usmjeren na simptome koje je ispitanik pokazivao s obzirom na QEEG mjerenje. Autori predlažu spajanje dosadašnjih protokola alfa asimetrije te *theta* – beta omjer na lijevom prefrontalnom korteksu. Povećavali su desnostranu alfa asimetriju (koja je bila usmjerena na povećanje pozitivnog ponašanja) i lijevostrani prefrontalni beta – *theta* omjer (koji je usmjeren na poboljšanje kognitivnih i motivacijskih funkcija), a smanjivali su visoku betu u prefrontalnom korteksu (usmjerenu na smanjivanje anksioznosti). Istraživanje je provedeno tijekom 10 *neurofeedback* treninga u trajanju od sat vremena, a istovremeno su se primjenjivala sva tri *neurofeedback* kriterija na F3 i F4 smještaju elektroda. Potkrepljujući zvuk čuo se kada su bila zadovoljena sva tri kriterija. Upitnik samoprocjene depresivnog stanja ispitanik je ispunjavao nakon svakog *neurofeedback* treninga. Novi protokol, prema riječima autora, bio je djelomično uspješan: uspjeh da se zadrže sva tri *neurofeedback* kriterija porastao je s početnih 15 % na 26 % na kraju tretmana, dok je smanjenje simptoma u odgovorima na upitnik samoprocjene iznosilo 43 %. Rezultat u upitniku samoprocjene zadržao se jedan mjesec nakon istraživanja. Autori predlažu povećanje broja *neurofeedback* tretmana (35).

Ghosh, Jahan i Singh prikazali su primjenu *neurofeedback* tretmana kod 39-godišnjeg ispitanika iz Indije koji se liječio od ovisnosti o alkoholu, anksioznosti i depresivnosti. Prije uključivanja u *neurofeedback* trening ispitanik je podučan o progresivnom treningu opuštanja kako bi se naučio samostalno opustiti bez podrške terapeuta. Ispitanik je bio uključen u 10 *neurofeedback* treninga u trajanju od 40 minuta. Sam protokol *neurofeedback* treninga u radu nije bio opisan. Autori primjećuju trend smanjenja simptoma na upitnicima anksioznosti i depresivnosti (BDI je inicijalno iznosio 23, finalno 19) te poboljšanje rezultata na kogni-

respondent in regard to the QEEG measurement. The authors suggested merging the previous alpha asymmetry protocols and the theta-beta ratio in the left prefrontal cortex. They increased the alpha asymmetry on the right side (which aimed at increasing positive behavior) and the theta-beta ratio in the left prefrontal cortex (aimed at improving the cognitive and motivational functions), and decreased the high beta activity in the prefrontal cortex (aimed at reducing anxiety). The study was conducted over 10 one-hour neurofeedback training sessions, and all three neurofeedback criteria were simultaneously applied at F3 and F4 electrode positions. A reinforcing sound was played when all three criteria were met. The patient filled out the depression self-assessment questionnaire after every neurofeedback training session. According to the authors, the new protocol, was a partial success: the success rate in maintaining all three neurofeedback criteria increased from the starting 15% to 26% at the end of the treatment, while the self-assessment questionnaire showed a 43% symptom decrease. The self-assessment questionnaire results were maintained for one month after the study. The authors suggested increasing the number of neurofeedback treatments (35).

Ghosh, Jahan and Singh observed the application of neurofeedback treatment on a 39-year-old patient from India, who was being treated for alcohol addiction, anxiety and depression. Before starting the neurofeedback training sessions, the respondent was taught progressive relaxation training in order to learn how to relax on his own, without support from the therapist. The respondent underwent ten 40-minute neurofeedback training sessions. The neurofeedback training protocol was not described in the paper. The authors observed a trend of symptom reduction on the anxiety and depression questionnaires (BDI initially amounted to 23, and finally to 19), as well as an improvement in the cognitive test results. The respondent also significantly reduced his alcohol consumption. Based on the graphs of the arithmetic means of alpha, theta, and beta frequencies, the authors observed lower frequen-

tivnim testovima. Ispitanik je također značajno smanjio konzumaciju alkohola. Na temelju grafova aritmetičkih sredina alfa, *theta* i beta frekvencija autori su primijetili snižavanje frekvencija tijekom 10 susreta pa zaključuju kako je *neurofeedback* tretman imao važnu ulogu u pacijentovu oporavku i predlažu daljnja istraživanja na većem uzorku i s pacijentima koji pate od drugih psihijatrijskih poremećaja (36).

Posljedice alfa frontalnog *neurofeedbacka* na depresiju ispitala je Nazarian u svojoj doktorskoj disertaciji. Istraživanje je na početku uključivalo 19 sudionika. Ispitanici su trebali biti uključeni u 36 *neurofeedback* treninga triput/tjedan u trajanju od pola sata (elektrode su bile postavljene na F3 i F4, a referentno na Cz). Zadatak ispitanika bio je povisiti glasnoću tona tijekom tretmana, a ton se javljao kada su ispitanici uspjeli povisiti desnostranu alfa aktivnost, što bi podrazumijevalo jaču lijevostranu frontalnu aktivaciju (s obzirom da su alfa snaga i kortikalna aktivnost obrnuto povezane). U studiju je bilo uključeno 19 ispitanika. Autorica navodi kako je 12 ispitanika odustalo unutar prvih 12 susreta, ostali ispitanici prošli su *neurofeedback* trening, ali je odustanje ispitanika značajno utjecalo na izvorni nacrt istraživanja. Mjerni instrumenti, Beckov upitnik depresije (BDI), Hamiltonova ljestvica depresivnosti (HAM-D), Penn State upitnik zabrinutosti (*Penn State Worry Questionnaire*) te *Inventar depresivne simptomatologije*, primjenjivali su se svaka dva tjedna. Ni kod jednog od 7 sudionika nije dobivena statistički značajna povezanost frontalne EEG asimetrije i rezultata na mjernim instrumentima ( $r$  nije prelazio 0.38,  $p > 0.05$ ). *Inventar depresivne simptomatologije* nije pokazao značajno smanjenje simptoma ( $F(6,30) = 2,11$ ,  $p > 0,05$ ), dok je BDI pokazao statistički značajno smanjenje simptoma ( $F(5,25) = 6,95$ ,  $p < 0,05$ ). Autorica je provjeravala utjecaj *neurofeedback* treninga na promjenu u frontalnoj asimetriji, no nisu dobiveni statistički značajni rezultati (svi  $p > 0,05$ ).

cies over 10 sessions, and therefore concluded that the neurofeedback treatment had a significant role in the patient's recovery, suggesting further research to be conducted on a larger sample and with patients suffering from other psychiatric disorders (36).

The effects of frontal alpha neurofeedback on depression were studied by Nazarian in her doctoral dissertation. The study initially involved 19 participants. They were intended to undergo 36 neurofeedback training sessions three times a week, each lasting half an hour (the electrodes were positioned at F3 and F4, relative to the reference position Cz). The respondents' task was to increase the sound volume during the treatment, and the sound was played when the respondents managed to increase the alpha activity on the right side, which would imply a stronger left frontal activation (given that alpha power and cortical activity are inversely related). A total of 19 respondents took part in the study. The author stated that 12 respondents dropped out during the first 12 sessions, while the other respondents underwent neurofeedback training. However, the withdrawal of respondents had a significant impact on the original research design. The measuring instruments, the Beck Depression Inventory (BDI), Hamilton Depression Rating Scale (HAM-D), Penn State Worry Questionnaire and the Inventory for Depressive Symptomatology were applied every two weeks. No statistically significant association between frontal EEG asymmetry and psychometric results was obtained in any of the 7 participants ( $r$  never exceeded 0.38,  $p > 0.05$ ). The Inventory for Depressive Symptomatology showed no significant symptom reduction ( $F(6.30) = 2.11$ ,  $p > 0.05$ ), while the BDI showed statistically significant symptom reduction ( $F(5.25) = 6.95$ ,  $p < 0.05$ ). The author examined the effect of neurofeedback training on the change in frontal asymmetry, however no statistically significant results were obtained (all at  $p > 0.05$ ). The assumption is that statistically significant results were not obtained due to a small number of respondents, while the significant reduction in BDI can be explained by other factors, and not only by

Pretpostavka je da je uzrok rezultata koji nisu statistički značajni bio mali broj ispitanika, a značajno smanjenje na BDI može se objasniti i drugim čimbenicima, a ne samo *neurofeedback* treningom. Na primjer, ispitanici su navodili kako se tijekom *neurofeedback* treninga osjećaju opušteno te da im se sviđa podržavajući pristup tijekom istraživanja. Zapaženo je da nakon 18 *neurofeedback* treninga krivulja pozitivno potkrepljujućih zvukova nije došla do kritične vrijednosti odnosno ispitanici nisu naučili što povisuje ton (svi  $p > 0.05$ ), što kod depresivnih sudionika može biti obeshrabrujuće. Rezultati ovog istraživanja ne podupiru povezanost promjena raspoloženja ispitanika i promjena u alfa frontalnoj asimetriji (37).

Choi i suradnici primijenili su protokol korekcije alfa asimetrije kako bi izmjerili učinke *neurofeedbacka* na depresiju. Istraživanje su proveli na 24 ispitanika koja su bila podijeljena u kontrolnu i eksperimentalnu skupinu. Tijekom pet tjedana u eksperimentalnoj skupini primjenjivan je *neurofeedback* trening dva puta/tjedan, dok je u kontrolnoj skupini primjenjivan trening placebo psihoterapije. Cilj je *neurofeedback* treninga bio da ispitanici održavaju kontinuitet klasične glazbe koja se javljala kada bi individualni indeks frontalne alfa asimetrije bio veći od nule, što označava smanjenje neugodnih emocija. Elektrodamama su mjerili frontalnu alfa asimetriju na lokacijama F3 i F4 te referentno na Cz. Koristili su upitnike samoprocjene i procjenu kognitivnog funkcioniranja. U eksperimentalnoj skupini dobivena je statistički značajna razlika u indeksu alfa frontalne asimetrije prije i poslije treninga, tj. povećanju desnostrane frontalne alfa snage. Prosječna razina depresivnih simptoma prije primjene *neurofeedbacka* u ovoj studiji bila je 22,75 (SD = 12,35), a nakon primjene *neurofeedbacka* razina simptoma pala je na prosjek od 9,08 (SD = 6,92). Veličina učinka ovog smanjenja bila je  $d = -1,32$  što je pokazatelj vrlo velikog učinka, a smanjenje je bilo statistički značajno pri  $p < 0,001$ . U kontrolnoj

*neurofeedback* training. For example, the respondents stated that they felt relaxed during *neurofeedback* training sessions, and that they liked the supportive approach provided in the course of the research. It was observed that after 18 *neurofeedback* training sessions the curve of positive reinforcing sounds did not reach a critical value, i.e. the respondents did not learn what raised the tone (all at  $p > 0.05$ ), which can be discouraging in depressed participants. The results of this study did not support a connection between the respondents' mood changes and changes in the frontal alpha asymmetry (37).

Choi et al. applied the alpha asymmetry correction protocol in order to measure the effects of *neurofeedback* on depression. The study was conducted on 24 respondents, divided into a control and an experimental group. In the course of five weeks, *neurofeedback* training was applied in the experimental group two times a week, while placebo psychotherapy training was conducted in the control group. The goal of *neurofeedback* training was for the respondents to maintain the continuity of classical music which played when the individual frontal alpha asymmetry index was greater than zero, signifying reduced unpleasant emotions. Electrodes were used to measure the frontal alpha asymmetry on locations F3 and F4, and relative to Cz. They used self-assessment questionnaires and cognitive functioning assessment. A statistically significant difference was obtained in the experimental group in terms of the frontal alpha asymmetry index before and after training sessions, i.e. an increase of alpha power in the right frontal region. The average level of depressive symptoms before *neurofeedback* application in this study amounted to 22.75 (SD = 12.35), while after *neurofeedback* application the symptom level decreased to an average 9.08 (SD = 6.92). The size of the effect of this reduction amounted to  $d = -1.32$ , indicating a very high effect, and the reduction was statistically relevant at  $p < 0.001$ . No statistically significant differences were found in the control group before and after training sessions, and the authors did not provide any specific data. Furthermore,

skupini nisu pronađene statistički značajne razlike prije i poslije treninga, a autori u radu ne iznose konkretne podatke. Također, u retestiranju nakon mjesec dana nije došlo do promjena fizioloških, kliničkih i kognitivnih mjera u odnosu na rezultate poslije tretmana, što autori smatraju pokazateljem da su se nastale promjene zadržale. Ova studija ukazuje na mogućnost da bi EEG *biofeedback* mogao biti obećavajući alternativni tretman za depresivne pacijente kod kojih je zbog nuspojava otežano standardno farmakološko liječenje. Autori naglašavaju da bi studija s dovoljno velikim uzorkom i placebo kontroliranim dizajnom te ponovljenim ispitivanjima potvrdila valjanost asimetričnog *neurofeedback* treninga (38).

Peeters i suradnici proveli su istraživanje na devet ispitanika s teškim depresivnim poremećajem (*major depressive disorder*). Ispitanici su bili uključeni u 30 *neurofeedback* treninga s ciljem smanjivanja frontalne alfa asimetrije, a elektrode su bile smještene na položaje F3 i F4. Prije svakog treninga primijenjen je *Kratki upitnik depresivnosti* (QIDS-SR16). Upitnik QIDS-SR16 (*Quick Inventory of Depressive Symptomatology – Self-Report*, 16) alat je za samoprocjenu depresije. Razvili su ga John Rush i suradnici, a koristi se za brzo mjerenje težine depresivnih simptoma. Za analizu frontalne alfa asimetrije korištena je višerazinska regresijska analiza kojom je utvrđeno značajno sniženje prosječnih rezultata u frontalnoj alfa asimetriji tijekom 30 tretmana ( $p < 0,01$ ). Prosječni rezultati u upitniku depresivnosti QIDS-SR16 bili su značajno sniženi ( $p < 0,05$ ) nakon 30 tretmana te su bili povezani s padom u alfa asimetriji ( $p < 0,001$ ). Autori su ispitali i promjene u alfa asimetriji tijekom jednog *neurofeedback* tretmana i prikazali kako alfa asimetrija ima značajan linearni i kvadratični učinak, tj. pada do pete minute treninga (od ukupno osam minuta) nakon čega ponovno počinje polagano rasti. Na kraju svih *neurofeedback* tretmana jedan sudionik izvijestio je o pozitivnom odgovoru na *neurofeedback*

in retesting after a month, there were no changes to the physiological, clinical and cognitive measures in relation to the results obtained after the treatment, which the authors considered to be an indication that the changes were maintained. This study points to the possibility that EEG *biofeedback* could be a promising alternative treatment for depressed patients who due to side effects experience difficulty when receiving standard pharmacological treatment. The authors highlighted that a study with a large enough sample and a placebo-controlled design and repeated testing would confirm the validity of asymmetry *neurofeedback* training (38).

Peeters et al. conducted a study on nine respondents suffering from major depressive disorder. The respondents underwent 30 *neurofeedback* training sessions with the aim of reducing frontal alpha asymmetry, and the electrodes were positioned at F3 and F4. The Quick Inventory of Depressive Symptomatology – Self-Report, 16 (QIDS-SR16) was applied before every training session. The QIDS-SR16 is a tool used for the self-assessment of depression. It was developed by John Rush et al., with the aim to quickly assess the severity of depressive symptoms. A multilevel regression analysis was used to analyze the frontal alpha asymmetry, determining a significant reduction of average frontal alpha asymmetry scores in the course of 30 treatments ( $p < 0.01$ ). The average scores in the QIDS-SR16 depression questionnaire were significantly lower ( $p < 0.05$ ) after 30 treatments, and were associated with a decrease in alpha asymmetry ( $p < 0.001$ ). The authors also examined the changes in alpha asymmetry during one *neurofeedback* treatment, and presented that alpha asymmetry has a significant linear and quadratic effect, i.e. it decreases until the fifth minute of training (out of eight minutes in total), after which it starts to slowly increase again. Upon the completion of all *neurofeedback* treatments, one participant reported having a positive response to the *neurofeedback* treatment, four experienced a remission of depressive symptoms, two had dropped out during the treatment, and the remaining two did not

tretman, četvero ih je izvijestilo o remisiji depresivnih simptoma, dvoje ih je odustalo tijekom tretmana, dok preostalih dvoje nisu imali nikakav pomak u razini depresivnih simptoma. Autori zaključuju kako je *neurofeedback* bio djelomično uspješan tretman depresivnosti. Kako je istraživanje bilo ograničeno malim brojem sudionika te nekontroliranim metodološkim čimbenicima, predlažu provođenje novog istraživanja s većim brojem sudionika raspoređenih slučajnom raspodjelom u eksperimentalnu i kontrolnu skupinu (39).

Temeljna ideja treninga asimetrije korištena je i u istraživanju Cheona i suradnika. Autori su proveli istraživanje s ciljem ispitivanja utjecaja *neurofeedback* tretmana na promjene u izraženošću depresivnih simptoma i EEG pokazatelja kod pacijenata s depresivnim poremećajem. U istraživanju je sudjelovalo dvadeset ispitanika koji su *neurofeedback* trening provodili dva do tri puta/tjedan tijekom razdoblja od dva mjeseca. Protokol tretmana obuhvaćao je 30-minutni trening beta aktivnosti na F3 lokaciji te regulaciju alfa/*theta* omjera na Pz lokaciji u istom trajanju. Za procjenu učinkovitosti tretmana korišteni su *Globalni indeks težine kliničkog stanja* (*Clinical Global Impression-Severity*, CGI-S) te Hamiltonova i Beckova ljestvica za procjenu anksioznosti i depresije. Mjere su prikupljene prije početka tretmana, nakon četiri tjedna te nakon završetka intervencije. Rezultati su pokazali statistički značajno smanjenje simptoma depresije i anksioznosti na svim upitničkim ljestvicama već nakon četiri tjedna, a poboljšanje se nastavilo do kraja tretmana. Navode ograničenja provedenog istraživanja: mali broj ispitanika, izostanak kontrolne skupine i izostanak dugoročnog praćenja ispitanika (40).

Mennella i suradnici primijenili su Alpha protokol korekcije asimetrije kako bi izmjerili učinke *neurofeedbacka* na smanjenje depresije u uzorku od 16 odraslih osoba koristeći BDI mjeru depresije. Srednja vrijednost depresije prije primjene *neurofeedbacka* u ovoj studiji bila je 9,75

experience any shift in the depressive symptom levels. The authors concluded that neurofeedback was partially successful in treating depression. Since the study was limited by a small number of participants and uncontrolled methodological factors, they proposed conducting a new study with a larger number of participants who would be placed into experimental and control groups by random assignment (39).

The fundamental idea of asymmetry training was also used in a study conducted by Cheon et al. The authors conducted the study in order to examine the effects of neurofeedback treatments on the changes in the severity of depressive symptoms and EEG indicators in patients with depressive disorder. A total of 20 respondents took part in the study, and they underwent feedback training sessions two to three times a week over a period of two months. The treatment protocol encompassed 30-minute training of beta activity at F3, and regulation of the alpha/*theta* ratio at Pz location in the same duration. The Clinical Global Impression-Severity (CGI-S) scale and Hamilton and Beck's scales for anxiety and depression assessment were used to verify the effectiveness of the treatment. The measures were collected before the treatment started, then after four weeks, and finally after the intervention had ended. The results showed a statistically significant reduction of depression and anxiety symptoms in all questionnaire scales after four weeks already, while the improvement continued until the end of the treatment. They listed the following limitations of the conducted study: a small number of respondents, lack of control group and lack of long-term follow-ups of the respondents (40).

Manella et al. applied the alpha asymmetry correction protocol in order to measure the effects of neurofeedback on the reduction of depressive symptoms on a sample of 16 adults by using the BDI depression measure. The mean value of depressive symptoms before neurofeedback application in this study amounted to 9.75 (SD = 12.38); while after neurofeedback application the symptom level decreased to an average 6.00 (SD = 7.90). The size of the effect of this drop

(SD = 12,38); nakon primjene *neurofeedbacka* depresija je pala na prosjek od 6,00 (SD = 7,90). Veličina učinka ovog pada bila je  $d = -0,35$ , što ukazuje na mali učinak, a pad je bio statistički značajan pri  $p < 0,05$ . Studija Mennella i sur. stoga je poduprla tvrdnju da *neurofeedback* smanjuje depresiju (41). Sažetci istraživanja zadnjih pet godina prikazani su u tablici 1.

Grin-Yatsenko i suradnici predstavili su tri studije slučaja u kojima su procijenili učinke infra-niskog *neurofeedbacka* na depresiju. Jedna sudionica i dva sudionika pokazivali su simptome depresivnog poremećaja; nitko se nije obratio liječniku niti je uzimao lijekove protiv depresije. Osnovno istraživanje sastojalo se od ljestvica za ocjenjivanje depresije: Montgomery-Åsbergova ljestvica za ocjenjivanje depresije (MADRS), Hamiltonova ljestvica depresije (HAM-D) i Beckov upitnik depresije (BDI). ILF-*Neurofeedback* korišten je pozicioniranjem elektrode na T4 – P4 i T4 – Fp2 tijekom prvih susreta; naknadno su dodane elektrode na T4 –

amounted to  $d = -0.35$ , indicating a very small effect, and the drop was statistically relevant at  $p < 0.05$ . The study by Mennella et al., therefore, confirmed the hypothesis that the use of neurofeedback reduces depression (41). Summaries of the studies conducted in the last five years are presented in Table 1.

Grin-Yatsenko et al. presented three case studies in which they estimated the effects of infra-low neurofeedback on depression. One female and two male participants presented symptoms of depressive disorder; none had gone to a doctor or taken antidepressant medications. The basic research consisted of the following depression assessment scales: the Montgomery-Asberg Depression Rating Scale (MADRS), the Hamilton Depression Rating Scale (HAM-D) and the Beck Depression Inventory (BDI). ILF-neurofeedback was used by positioning the electrodes at T4 – P4 and T4 – Fp2 in the first sessions; electrodes were additionally added at T4 – T3 and T3 – Fp1. After 20 neurofeedback training sessions, each lasting between 30 to 45 minutes, all three pa-

**TABLICA 1.** Prikaz sažetaka istraživanja (ukupno 6 studija) o učinkovitosti *neurofeedback* tretmana kod depresivnog poremećaja objavljenih unutar posljednjih 10 godina (2019-2021).

**TABLE 1.** Summaries of the studies (6 studies in total) on the effectiveness of neurofeedback treatment in depressive disorder, published within the last 10 years (2019-2021).

Autor / Author	NF protokol / NF protocol	Uzorak / Sample	Mjerni instrument / Measuring instrument	Inicijalno NF / Initial NF M (SD)	Finalno NF / Final NF M (SD)
Wang et al. (42)	Alfa asimetrija / Alpha asymmetry	24	BDI	30.25 (8.39)	19.83 (12.02)
Takamura et al. (43)	rftMRI-NF	6	BDI	28.70 (8.57)	17.20 (6.12)
Yu et al. (44)	10-11 Hz povećanje aktivnosti na Fp1 i Fp2 / 10-11 Hz activity increase at Fp1 and Fp2	14	BDI	24.90 (8.25)	16.80 (9.24)
Zotev et al. (45)	rtfMRI-EEG-NF	E = 18 K = 8	POMS	15.40 (14.00)	7.75 (10.10)
Hariss et al. (46)	Nespecifični <i>neurofeedback</i> / Nonspecific neurofeedback	11	BDI	10.55 (9.66)	5.64 (6.86)
Hou et al. (47)	Alfa asimetrija / Alpha asymmetry Lijevi parijetalni režanj / Left parietal lobe	13	BDI	20.23 (0.47)	12.08 (7.33)
Hou et al. (47)	Alfa asimetrija / Alpha asymmetry Desni parijetalni režanj / Right parietal lobe	13	BDI	17.69 (7.24)	10.31 (5.98)

Legenda: rtfMRI-EEG-NF (*real-time fMRI and EEG neurofeedback*) – *neurofeedback* u stvarnom vremenu temeljen na istodobnom snimanju funkcionalne magnetske rezonancije i elektroencefalografije. POMS (*Profile of Mood States*) – Profil stanja raspoloženja.  
/ Legend: rtfMRI-EEG-NF (*real-time fMRI and EEG neurofeedback*) – *neurofeedback* in real time, based on a simultaneous recording of functional magnetic resonance imaging (fMRI) and electroencephalogram (EEG). POMS – Profile of Mood States

T3 i T3 – Fp1. Nakon 20 *neurofeedback* treninga, svakog u trajanju od 30 do 45 minuta, sva tri pacijenta pokazala su poboljšanje raspoloženja i vještina samoorganizacije, smanjenu anksioznost, kao i povećanu emocionalnu stabilnost i otpornost. Posebno se promijenio rezultat profila depresije slučajeva A i B tijekom drugog testiranja pri čemu su se sve ljestvice poboljšale za najmanje 90 %, a slučaj C pokazao je poboljšanje od najmanje 70 %. Rezultat profila depresije za sva tri sudionika nije ukazivao na depresiju i poboljšanja su bila stabilna godinu dana nakon početka ILF *neurofeedback* terapije. Prema autorima, ova je studija također pokazala da je trening doveo do promjene u moždanoj aktivnosti, posebno do smanjenja *theta* aktivnosti u frontalnim i središnjim područjima u pasivnim stanjima (48). I drugi rad Grin-Yatsenka i suradnika pokazao je pozitivne učinke ILF-treninga na 8 ispitanika sa širokim popisom simptoma (umor, depresivno raspoloženje, simptomi unutarnje napetosti, promjene raspoloženja, glavobolja, problemi sa spavanjem, smanjena pozornost i slabo radno pamćenje). Elektrode su postavljene na T4 – P4, T4 – T3 i, naknadno, T4 – Fp2 i T3 – Fp1. Nakon 20 ILF-*neurofeedback* treninga svi su sudionici prijavili poboljšanje svog stanja: smanjenje unutarnje napetosti, reaktivnosti na stresne čimbenike, stabilnost raspoloženja, poboljšanu svijest o tijelu i prostoru, povećanje razine energije i kognitivnih performansi (49). Na temelju prikazanih studija moguće je sagledati glavne prednosti, ali i metodološka ograničenja primjene *neurofeedback* metode kod depresije.

## RASPRAVA

*Neurofeedback* je relativno nova metoda koja se sve češće primjenjuje u liječenju psihičkih poremećaja. Ovu je metodu putem znanstvenih istraživanja važno približiti stručnoj, ali i široj javnosti. Cilj ove rasprave jest pružiti novi doprinos razumijevanju i primjeni *neurofeedback* metode u kliničkom kontekstu.

tients showed improvements in terms of their moods and self-organization skills, as well as reduced anxiety and improved emotional stability and resilience. The results of depression profiles in the A and B cases particularly changed in the second testing, whereby all scales showed an improvement of at least 90%, while case C showed an improvement of at least 70%. The depression profile results in all three participants did not indicate depression, and the improvements were stable a year after starting the ILF *neurofeedback* therapy. According to the authors, this study also showed that the training led to changes in the brain activity, particularly to a reduction of *theta* activity in the frontal and central areas of the brain in passive states (48). Another paper written by Grin-Yatsenka et al. presented positive effects of the ILF training on eight respondents with a wide range of symptoms (fatigue, depressive mood, internal tension symptoms, mood changes, headaches, difficulty sleeping, reduced attention and poor working memory). The electrodes were positioned at T4 – P4, T4 – T3, and subsequently at T4 – Fp2 and T3 – Fp1. After 20 ILF-*neurofeedback* training sessions, all the participants reported improvements in their conditions: lower internal tension, reactivity to stressors, mood stability, improved body and spatial awareness, increased energy levels and cognitive performances (49). Based on the presented studies, it is possible to review the main advantages, as well as the methodological limitations, of applying the *neurofeedback* method in depression treatment.

## DISCUSSION

*Neurofeedback* is a relatively new method, which is increasingly being used in the treatment of mental disorders. It is important to present this method to the professional, but also wider public, through scientific research. The aim of this discussion is to provide a new contribution to the understanding and application of the *neurofeedback* method in the clinical context.

Jedan od glavnih problema s kojim se istraživači suočavaju jest osipanje sudionika u istraživačkom uzorku. U svojoj doktorskoj disertaciji Nazarian detaljno opisuje ovu pojavu. Od planiranih 138 ispitanika samo ih je 19 započelo *neurofeedback* trening, dok je svega 6 ispitanika dovršilo eksperiment. *Neurofeedback* zahtijeva visoku razinu motivacije, redovitost i ustrajnost, što je izazov i razlog osipanja ispitanika. U konkretnom istraživanju, uzorak od 60 ispitanika skupljao se tijekom pet godina. Kako navodi Nazarian, mnogi su sudionici odustali jer nisu razumjeli kako metoda djeluje, a zahtijevala je znatan vremenski angažman.

Pojednostavljenje terminologije i jasnija komunikacija mogli bi pomoći u povećanju zadržavanja sudionika tijekom tretmana. Uz obrazovanje, i dob sudionika može imati ulogu – mlađe osobe, sklonije tehnologiji, potencijalno su motiviranije i rjeđe odustaju od tretmana.

Prva istraživanja o *neurofeedbacku* bila su uglavnom prikazi slučajeva. Premda ograničena metodološki, pružila su vrijedan kvalitativni uvid u iskustva korisnika. Sudionici su najčešće imali depresivni poremećaj, često u komorbiditetu s drugim stanjima, poput anksioznosti, bipolarnog poremećaja, alkoholizma ili posljedica moždanog udara. Takvi slučajevi otežavaju donošenje zaključaka o učinkovitosti metode kod izolirane depresije.

Escolano i sur. navode da čak 80 % osoba s depresijom ima i anksiozni poremećaj, dok drugi autori uopće ne navode podatke o komorbiditetima ili navode da su ih isključili. Zbog toga je u istraživanjima nužno sustavno ispitivati i jasno prikazivati komorbiditete.

U literaturi se uočava velika raznolikost u kriterijima uključivanja i isključivanja sudionika. Neki autori isključuju sudionike zbog lijevo-rukosti, prisutnosti organskih oštećenja, istodobne farmakoterapije ili uključivanja u psihoterapiju što otežava međusobnu usporedbu

One of the main problems for researchers is the dropout of participants in the research sample. In her doctoral dissertation, Nazarian describes this phenomenon in detail. Out of the planned 138 respondents, only 19 started their neurofeedback training, while a mere 6 of them finished the experiment. Neurofeedback requires a high level of motivation, regularity and persistence, which represents a challenge and is the reason for the participant dropouts. In this specific study, a sample of 60 respondents was collected over a period of five years. According to Nazarian, many participants dropped out because they did not understand the functioning of the method, and it required a significant time commitment.

Simplifying the terminology and ensuring clearer communication could help increase participants' retention during the treatment. In addition to education, the participants' age could also play a role – younger individuals, more inclined to technology, are potentially more motivated and less likely to give up on the treatment.

The first neurofeedback studies were mainly case studies. Although they were methodologically limited, they offered a valuable qualitative insight into the users' experiences. The participants most often suffered from depressive disorder, often in comorbidity with other conditions such as anxiety, bipolar disorder, alcoholism or consequences of a stroke. Such cases make it difficult to draw conclusions in regard to the effectiveness of the method in isolated depression.

Escolano et al. observed that as many as 80% of patients with depression also suffered from anxiety disorder, while other authors did not present any data on comorbidities or stated that they had excluded them. Due to the aforementioned, it is necessary to conduct systemic research and provide a clear presentation of comorbidities in the studies.

There is a great variety of inclusion and exclusion criteria for the participants in the literature. Some authors exclude participants due to left-handedness, presence of organic defects, concomitant pharmacotherapy or inclusion in psychotherapy,

rezultata. Broj *neurofeedback* treninga varira od 5 do 30, a trajanje se kreće od 15 do 60 minuta. U prosjeku, istraživanja uključuju 15 tretmana, a Peeters i suradnici među rijetkima su koristili maksimalnih 30 tretmana. U ovom istraživanju sudionici su prošli 15 treninga u trajanju od 20 minuta. Postavlja se pitanje optimalnog broja i trajanja tretmana kako bi se postigli značajni učinci. Iako neka istraživanja ukazuju da je potrebno barem 20 seansi, ovo područje ostaje nedovoljno istraženo.

Gotovo sva istraživanja koriste samoprocjenske mjere poput ljestvica BDI i MADRS. Iako korisne, one su podložne subjektivnosti i nedostatku objektivizacije.

Primijenjeni *neurofeedback* protokoli međusobno se značajno razlikuju – od protokola temeljenih na frontalnoj alfa asimetriji, preko funkcionalne magnetske rezonancije u stvarnom vremenu (fMRI *neurofeedback*) do treninga u infra-niskim frekvencijama (ILF). Ova raznolikost otežava sistemsku analizu učinkovitosti metode. Zbog toga APA i dalje navodi da je razina učinkovitosti *neurofeedbacka* u tretmanu depresije od 2 do 5 („možda učinkovito“). To ne znači da *neurofeedback* nije učinkovit, već da su potrebna dodatna istraživanja s kontrolnim skupinama.

Batail i suradnici ističu kako većina istraživanja ne izvještava o procesima koji dovode do kliničke učinkovitosti niti o učenju koje se odvija tijekom treninga. Gaume i suradnici predlažu sveobuhvatan, transdisciplinarni model istraživanja mehanizama *neurofeedbacka* uključujući biomedicinsku, inženjersku, psihološku i neuroznanstvenu perspektivu.

Određena istraživanja ukazuju na potencijalnu učinkovitost *neurofeedbacka* u kombinaciji s psihoterapijom, no za takve tvrdnje nedostaje dovoljno znanstvenih dokaza.

U Hrvatskoj se *neurofeedback* trening može provoditi u zdravstvenim ustanovama i brojnim privatnim praksama. Na tržištu postoji

which makes it difficult to compare results. The number of neurofeedback training sessions varies from 5 to 30, and the duration spans from 15 to 60 minutes. The studies, on average, include 15 treatments, and Peeters et al. were among the rare ones who used the maximum 30 treatments. In this study, the participants underwent 15 training sessions, each lasting 20 minutes. The question arises as to the optimal number and duration of treatments necessary to achieve significant effects. Although some studies indicate that at least 20 sessions are necessary, this area remains underexplored.

Almost all studies use self-assessment measures such as the BDI and MADRS scales. Although useful, they are often subjective and lack objectivization.

The applied neurofeedback protocols differ significantly – from protocols based on frontal alpha asymmetry, through functional magnetic resonance imaging in real time (fMRI neurofeedback) to infra-low frequency training. This diversity makes it difficult to systematically analyze the effectiveness of the method. For this reason, APA still states that the effectiveness level of neurofeedback in depression treatment ranges from 2 to 5 (“possibly efficacious”). This does not mean that neurofeedback is not effective, but that additional research that would include control groups is necessary.

Batail et al. emphasized that most studies report neither on the processes leading to clinical effectiveness, nor on the learning processes that develop during the training. Gaume et al. proposed a comprehensive, transdisciplinary model for neurofeedback mechanism research, including biomedical, engineering, psychological and neuroscientific perspectives.

Certain studies pointed to a potential effectiveness of neurofeedback in combination with psychotherapy, however there is insufficient evidence for such claims.

In Croatia, neurofeedback training can be conducted in medical institutions and numerous

više od 15 različitih softverskih rješenja. Istraživači koriste različite uređaje – od komercijalno dostupnih, jednostavnih za korištenje, ali s lošijom kvalitetom signala – do sofisticiranijih koji zahtijevaju dodatnu kalibraciju. Ramirez i suradnici preporučuju upotrebu naprednijih uređaja u budućim istraživanjima. Do danas nije provedena komparativna studija u kojoj bi se usporedila kvaliteta tih uređaja.

Pitanje postavljanja kriterija za kritične vrijednosti povratnih informacija također je važno. Upute koje sudionici dobivaju tijekom tretmana značajno se razlikuju – od preciznih zadataka (npr. „podignite stupac“) do sugestivnih uputa („opustite se“). Peeters i suradnici zaključuju da mentalne strategije poput opuštanja nisu učinkovite u povećanju željene moždane aktivnosti. Ovo područje ostaje nedovoljno istraženo i zaslužuje veću pažnju u budućim istraživanjima. Autori također opisuju da su se sudionici, ovisno i izvedbi, tijekom tretmana osjećali istovremeno kompetentno i frustrirano.

## ZAKLJUČAK

*Neurofeedback* se čini obećavajućom metodom u liječenju depresivnog poremećaja, no postoje značajne metodološke prepreke koje otežavaju generalizaciju rezultata i precizno određivanje njegove učinkovitosti. Glavni izazovi u istraživanju *neurofeedback* metode uključuju visoku stopu osipanja sudionika, različite kriterije uključivanja i isključivanja ispitanika te heterogenost *neurofeedback* protokola i uređaja. Unatoč sve većem broju istraživanja i dalje nisu jasno definirani optimalni parametri poput broja i trajanja *neurofeedback* treninga, što otežava formuliranje jasnih smjernica za kliničku primjenu.

Buduća istraživanja trebala bi se usmjeriti na poboljšanje eksperimentalnog dizajna, povećanje reprezentativnosti uzoraka, standardizaciju protokola i objektivizaciju mjernih instrume-

ntal private practices. There are more than 15 different software solutions in the market. The researchers use various devices – from commercially available, simple to use devices which, however, have poorer signal quality – to more sophisticated ones that require additional calibration. Ramirez et al. recommended the use of more advanced devices in future research. No comparative studies have been conducted so far to compare the quality of these devices.

The issue of setting the criteria for the critical values of feedback is also important. The instructions that the participants receive during treatment also significantly vary – from precise tasks (e.g. “raise the column”) to suggestive instructions (“relax”). Peeters et al. concluded that mental strategies such as relaxation were not effective in increasing the desired brain activity. This area remains insufficiently researched and deserves more attention in future research. The authors also described that, depending on their performance, the participants felt both competent and frustrated during the treatment.

## CONCLUSION

Neurofeedback appears to be a promising method in the treatment of depressive disorder, however there are significant methodological obstacles that hinder the generalization of results and a precise determination of its effectiveness. The main challenges in researching the neurofeedback method include high participant dropout rates, different inclusion and exclusion criteria for the respondents, and a heterogeneity of neurofeedback protocols and devices. Despite an increasing number of studies, the optimal parameters such as the number and duration of neurofeedback training sessions have still not been defined, which makes it difficult to formulate clear guidelines for clinical application.

Future studies should focus on improving the experimental design, increasing the representativeness of the samples, standardizing the protocols, and objectivizing the measuring instruments.

nata. Također, važno je dublje istražiti učinkovitost mentalnih strategija koje ispitanici koriste tijekom *neurofeedback* treninga te njihov utjecaj na terapijske ishode. Konačno, iako postoje preliminarni dokazi o učinkovitosti *neurofeedback* metode u kombinaciji s drugim terapijama, potrebno je daljnje istraživanje kako bi se razvili optimalni tretmanski modeli temeljeni na znanstvenim dokazima.

Unatoč opisanim ograničenjima, rezultati znanstvenih studija ukazuju da *neurofeedback* predstavlja perspektivnu metodu koja može utjecati na smanjenje depresivne simptomatologije. S obzirom na tehnološki napredak *neurofeedback* uređaja (biosenzori) u bliskoj budućnosti može se očekivati i veliki napredak u razvoju ove metode te bi se intervencije mogle dosljednije integrirati u dosadašnje metode liječenja depresivnog poremećaja. Daljnji razvoj sofisticiranijih sustava za obradu neuroloških signala, primjena umjetne inteligencije u analizi podataka te optimizacija personaliziranih *neurofeedback* protokola mogli bi značajno povećati efikasnost i preciznost ove metode. Osim toga, povećana dostupnost *neurofeedback* tehnologije u kliničkim i istraživačkim postavkama mogla bi olakšati provođenje longitudinalnih studija, što bi doprinijelo boljem razumijevanju dugoročnih ishoda primjene *neurofeedbacka* u liječenju depresivnog poremećaja. Integracija *neurofeedbacka* s drugim terapijskim modalitetima, poput kognitivno-bihevioralne terapije ili farmakoterapije, mogla bi dovesti do sinergijskog učinka i poboljšanja terapijskih rezultata kod pacijenata s depresijom.

Ovaj rad doprinosi boljem razumijevanju trenutnog stanja istraživanja te može poslužiti kao temelj za buduća istraživanja usmjerena na standardizaciju i kliničku primjenu *neurofeedbacka* u cilju smanjenja simptoma depresivnog poremećaja.

Furthermore, it is important to further investigate the effectiveness of mental strategies used by the respondents in the course of neurofeedback training, as well as their influence on the therapeutic outcomes. Finally, although there is preliminary evidence on the effectiveness of the neurofeedback method in combination with other therapies, further research is required in order to develop the optimal treatment models based on scientific evidence.

Despite the described limitations, the results of scientific studies indicate that neurofeedback represents a perspective method that could have an effect on reducing depressive symptomatology. Considering the technological improvements of neurofeedback devices (biosensors), great developments to this method can be expected in the future, and interventions could thus be integrated more consistently into the current methods of depressive disorder treatment. Further developments of more sophisticated neurological signal processing systems, application of artificial intelligence in data analysis and optimization of personalized neurofeedback protocols, could significantly increase the effectiveness and precision of this method. In addition, increased availability of neurofeedback technology in clinical and research settings could facilitate the implementation of longitudinal studies, thus contributing to a better understanding of the long-term outcomes of neurofeedback application in the treatment of depressive disorder. An integration of neurofeedback with other therapeutic modalities, such as cognitive-behavioral therapy or pharmacotherapy, could lead to synergistic effects and improved therapeutic outcomes in patients with depression.

This paper contributes to a better understanding of the current state of research and can serve as a basis for future research aimed at the standardization and clinical application of neurofeedback for the purpose of reducing the symptoms of depressive disorder.

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