REVIEW ARTICLE

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Pharmacotherapy and psychotherapy in depression – complementarity or exclusion?

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Abstract

Purpose: This article attempts to outline the dilemma regarding the use of pharmacotherapy and psychotherapy in the treatment of mental disorders with particular emphasis on depression. Depressive disorder is one of the most common mental disorders suffered by society; it affects from 5% to over 12% of the population [1]. It is also a growing problem as the number of diagnoses has increased over the last decades.

Views: The numerous organisations working to improve mental health have constructed guidelines focused on shaping preventive intervention and therapeutic procedures. However, the method of selecting a procedure remains unclear, with the choice between pharmacotherapy and psychotherapy being particularly troublesome. This begs the question of whether these forms of interaction are complementary or exclusive. The article provides an overview of the current discussion on the legitimacy of using multiple forms of interactions when treating depression. Currently, the treatment of depression is based primarily on pharmacotherapy using antidepressants and psychotherapy as well as combined treatment.

Conclusions: Although a diverse range of psychotherapeutic approaches are used to treat depression, research indicates that all leading approaches are similarly effective. Pharmacotherapy and psychotherapy offer comparable effectiveness in reducing depressive symptoms and demonstrate similar effects on neuronal activity. Combined treatment may offer optimal effectiveness, especially with moderate and severe symptoms of depression.

Key words: depression, effectiveness of psychotherapy, effectiveness of pharmacotherapy.

INTRODUCTION

The increasingly dynamic development of medicine, including new diagnostic and therapeutic methods, offers hope for the improvement of human mental health. However, while data obtained by the World Health Organization (WHO) or the Centers for Disease Control and Prevention (CDC) indicate that the general level of health in society has improved over the last several years, the opposite effect has been observed in the area of mental health. The National Comorbidity Survey covering the years 2001-2003 estimates that 57.4% of 9,282 participants had experienced mental disorders in the past, while 32.4% had suffered from them in the year preceding the survey. The WHO also estimates the percentage of people suffering from depression to be around 5%. However, this number may be slightly higher because many people who meet the criteria for clinical depression are never diagnosed: the lifetime prevalence is believed to be around 14.4-18.0% [1]. In the Polish EZOP II study, it was estimated that 25% of the Polish population exhibited mental disorders, with 3.85% having experienced an episode of depression.

The WHO and numerous organisations working for mental health have constructed guidelines focused on shaping preventive intervention and therapeutic procedures. However, the method of selecting a treatment procedure remains unclear, particularly the choice between pharmacotherapy and psychotherapy; this begs the question of whether these forms of interaction are complementary or exclusive.

In order to fully understand the essence of this dilemma, it is necessary to examine not only the range of available treatment procedures and the data regarding their effectiveness, but also the issues related to the way of understanding mental disorders, expressed in various concepts of constructing diagnostic classes and etiopathological models. It seems that the question of whether

pharmacotherapy and psychotherapy are complementarity or exclusive may stray into ontological issues. It may also address the classic split between Cartesian dualism and a more holistic understanding of the biopsychosocial nature of man, i.e., does psychotherapy affect only the mind, and pharmacotherapy only affect the brain?

MODELS OF MENTAL DISORDERS CONCEPTUALISATION

Numerous attempts have been made over the years to catalogue mental disorders with the aim of improving diagnosis and therapy; indeed, recognition demands classification and *vice versa* [2]. Classification systems provide an empirically grounded framework of practical and theoretical importance that guides the diagnostic process and, above all, the selection of appropriate therapeutic procedures. Thus, classification allows the distinguishing of a certain fragment of reality, which in this case is the phenomenon of human mental life. Furthermore, by separating clinically significant facts from others and ordering symptom classes according to an adopted criterion, it also outlines the boundaries of the norm [3].

Separating nosological units seems to be particularly problematic in psychiatry, especially due to the certain ambiguity of etiopathological mechanisms and the overlapping of symptoms of particular mental disorders [4]. It is assumed that the nosological position, i.e., the disease, should be characterised by a homogeneous aetiology and the resulting pathomechanism sustaining the symptoms; however, mental disorders exist as a syndromic constellation of symptoms related to each other at the empirical level, for which a common etiopathomechanism often remains elusive [5].Therefore, it can be concluded that mental disorders do not actually meet the criteria of a disease. This fact is important because it is associated with a specific perspective for perceiving the essence of these disorders. The concept of a *disease* assumes certain biological conditions and also determines the pharmacological treatment paradigm, while the term *mental disorders* emphasises the importance of psychosocial conditions and psychotherapeutic interactions as a treatment [3, 6].

In 2016, *Lancet Psychiatry* presented a list of key problems faced by contemporary psychiatry [7, 8]. Among these items, the article noted a fundamental issue – there was no comprehensive and precise explanation that could enhance our understanding of the aetiology of disorders or of our classification, diagnosis, and treatment strategies. Furthermore, it was neither possible to reveal the pathomechanisms of a specific phenomenon, nor could any existing classification integrate all levels of analysis, i.e., from the cellular level, via computational models of the mind, to interactions between genes and the environment.

The problem faced by the contemporary discussion on constructing a classification of diseases or disorders basically boils down to the discrepancy between the categorical and dimensional approaches. It derives from the multifaceted dispute about biological reductionism in psychiatry, and thus whether mental disorders should be strictly understood as diseases of the brain [9]. This approach is relatively strongly rooted in the categorical model of understanding mental disorders; this model unfortunately does not meet the expectations placed on it, especially since biological markers are rare in psychiatry [7]. It should be emphasised that while the International Classification of Diseases (ICD-10) was designed on the basis of the categorical model, its eleventh revision seeks consensus between the categorical and dimensional approaches, thus constructing a hybrid model of mental disorders.

The categorical model of mental disorders assumes that it is possible to distinguish separate group of symptoms constituting disorders [10]. The disadvantage of this model is the fact that the symptoms characterising a particular disorder may overlap with those of another. It is also possible that various mental disorders may coexist [11, 12]. It should be emphasised, however, that it is not always possible to allocate disorders into separate categories. Assuming that all mental phenomena, ranging from unconscious phenomena to very complex mental processes, arise in the brain, disorders cannot be regarded as separate disease entities.

An alternative approach is to assume that mental disorders have an internal structure that can be described in the form of dimensions, i.e., the dimensional model [4]. It assumes that symptoms exist as a continuum which blurs their distinct nature and prevents their rigid grouping within diagnostic classes. The disadvantage of this approach is that there is no agreement on the number of dimensions needed. In addition, for each dimension, it is necessary to define the point at which the benefits of the treatment appear, which would require blurring the edges of the defined dimensions. The dimensional approach opens up new horizons in understanding and diagnosing mental disorders, suggesting that there are more general mechanisms of psychopathology that go deeper than the groups of symptoms constituting the categorical model. This facilitates better understanding of the high comorbidity of mental disorders, which is problematic for categorical classifications. However, when taking a dimensional approach, the lack of a non-categorical diagnosis makes it more complicated to select an appropriate therapeutic procedure [8].

The latest revision of the diagnostic classifications uses a hybrid model, enriching the existing categorical approach with elements of dimensional understanding of mental disorders [13, 14]. The use of designations based on distinct nosological units is still largely justified

in many respects, e.g., when granting certain social security benefits, such as sick leave and disability benefits.

ETIOPATHOLOGICAL FACTORS OF MENTAL DISORDERS

Nowadays, it is assumed that while certain specific cases may be influenced by a particular factor, the concepts of etiopathogenesis indicate that mental illness generally arises as a product of various biological, psychological, and social factors [3].

However, it should be emphasised that within psychopathology, there is a predilection for exploring the biological and psychological determinants of mental disorders separately. In biological terms, factors related to genes, hormones, brain structures, and functions are primarily considered. In contrast, from the psychological perspective, the key roles are played by inhibited development or deficits in certain mental structures and processes, such as internal conflicts, unconscious processes, and irrational beliefs. Thanks to research in psychoneuroendocrinology and psychoimmunology, biological and psychological approaches are no longer perceived as competitive – intense emotional states are associated with both changes in central nervous system (CNS) neurotransmission and structure through neuroendocrine and immunological mechanisms [15].

The tendency towards multifactorial conceptualisation of the etiopathology of mental disorders is illustrated in the "vulnerability-stress" model, which emphasises the importance of interactions between internal predispositions and the influence of external factors [16]. Mental disorders are understood to arise by the activation of vulnerability (*diathesis*) under the influence of psychosocial stress.

Stress is the basis of physiology; "in its essence, stress is the measure of all the hardships and adversities of life", i.e., that it manifests from situations that disturb the mechanism that maintains the physiological, emotional, and cognitive stability of an individual [17, 18]. Vulnerability, in turn, is conceptualised as an individual's sensitivity to stressors [18]. The genetic and constitutional characteristics of the organism (e.g., temperament) and psychological variables (e.g., negative cognitive styles) serve as predisposing factors.

CLINICAL IMPROVEMENT ASSESSMENT INDICATORS

The effectiveness of a particular intervention (pharmacotherapy, psychotherapy) should be considered in terms of its resulting changes occurring in the most important areas of patient functioning. Therefore, it is necessary to analyse in particular:

- its impact on neurobiology, e.g., inflammatory markers, BDNF, IGF;
- its impact on functioning, e.g., assuming social roles, coping with stress, level of adaptation;
- its impact on clinical parameters, e.g., improvement or deterioration measured with diagnostic tools (e.g., PANSS, MADRS and other tools for psychological and neuropsychological assessment), assessment of relapse, rehospitalisation.

Clinical trials usually assess the effect of treatment with regard to a single function and examine only a single therapeutic method, which complicates the choice of optimal treatment for an individual patient. A certain dualism emerges here, and one which reflects the essence of the discussion on whether pharmacological and psychotherapeutic effects are combined or exclusive. Recent research, however, emphasises the value of taking a holistic perspective to understanding mental disorders and the indicators of improvement in treatment. So, it can be contradictory to say that "psychotherapy causes changes in the functioning of the brain, and pharmacotherapy affects the state of mind" [19].

The recent development of neuroimaging methods (fMRI, SPEC, PET) has extended the scope for monitoring the effectiveness of psychotherapeutic interactions [20] on functioning and clinical parameters. It has long been known that psychological and psychotherapeutic interactions can contribute to changes in thinking patterns, beliefs, attitudes, emotional states, and behaviours. An extremely interesting area of exploration, however, remains the neural activity behind these observed effects. Studies conducted among patients diagnosed with depressive disorder indicate that the reduction of symptoms following psychotherapeutic intervention in various approaches may be related to, *inter alia*, increased cerebral metabolism [21] or decreased activity in certain areas, such as the cingulate cortex and the left anterior hippocampus/amygdala [22].

Deciding on the optimal treatment strategy and interventions often presents a challenge for clinicians. Many patients demonstrate an ambivalent attitude towards pharmacotherapy, fearing the side effects of treatment, their impact on the personality or the potential for addiction. Of course, most of these doubts are the result of drug resistance and are not based on science. It also happens in practice that patients expect a "miracle" from a drug and perceive pharmacotherapy as a remedy for all of life's problems. Resistance to psychotherapy also turns out to be problematic, which may result from fears related to the therapy itself and a belief in the low value of interactions, as well as social stigmatisation and a reluctance to reveal oneself and experience difficult emotions [23].

DEPRESSION – A GROWING PROBLEM

The WHO, CDC, Blue Cross Blue Shield (BCBS), and official reports of the European Union indicate an increase

in the number of diagnosed cases of depressive disorder over the last few years. While data from 2001-2016 show that this increase was relatively small, reports from subsequent years show significant changes.

The recent global pandemic has had a particular impact on the increase in depression and anxiety disorders: various studies from different counties suggest a very large increase in the number of cases since 2019 [24, 25]. A study conducted by the Lancet Group [26] identified a 27.6% global increase in cases of depressive disorder since the outbreak of the pandemic. However, the origins of this disturbing trend can be traced back much earlier. According to the BCBS report, the number of diagnosed cases of major depressive disorder in the US increased by 33% between 2013 and 2016.

Particularly worrying data from recent years, however, concern adolescents and young adults, among whom the greatest increase in diagnosed cases of depression was noted. According to the BCBS, among teenagers in the USA aged 12-17 between 2013 and 2016, the number of diagnosed cases of major depressive disorder increased by as much as 63%. Another study for the Pew Research Center (2017) found that 13% of US teens aged 12-17 had experienced a major depressive disorder at least once in the past year. This is a significant increase as compared to the data from 2007, where the corresponding indicator was 8%. The same trend was also noted by Mojtabai *et al.* [27] in 2005-2014. Although the above data is limited to the USA, similar trends can be expected in Europe and the rest of the world. Growing tendencies towards mental health problems among adolescents have also been indicated in Europe. For example, the WHO report, "Adolescent mental health in the European Region", found the percentage of mental health problems among children and adolescents aged 10–19 years to be high and steadily increasing.

These findings highlight that depression is a current issue and a future challenge for both public health and the economy. The epidemiology of mental disorders, particularly depression, should be considered not only in the clinical context, but also in the socio-economic conditions. It might seem that medication, psychiatrist visits, psychotherapy sessions, and hospitalization constitute the true economic burden of depression; however, in reality, the burden of mental disorders far outweighs the costs associated with direct diagnosis and treatment [28-30]. It also incurs a number of indirect or, "invisible costs", associated with losses in income due to mortality, disability, and care seeking, as well as lost production due to absence from work or early retirement. For the EU, a region with highly developed healthcare systems, the direct and indirect costs together were estimated at €798 billion [31], and these are expected to double by 2030 compared to 2010 [28]. It should be emphasised in this context that the availability of treatment, and the selection of appropriate intervention strategies as either monotherapy or combined pharmacotherapy and psychotherapy, are largely dependent on economic conditions.

METHODS OF TREATING DEPRESSION

Mental health organisations provide a range of institutional and individual-level guidelines intended to shape therapeutic procedures. There are many methods and approaches to treating depression, but the gold standard of modern psychiatry is pharmacotherapy and psychotherapy.

In patients with mild to moderate depression, American Psychiatric Association [32] standards recommend the implementation of antidepressant treatment alone in the initial phase. As antidepressant medications are characterised by generally similar effectiveness, the initial selection of an antidepressant medication should be based on its anticipated side effects, the safety or tolerability of these side effects and the pharmacological properties of the medication. It also indicates the possibility of using psychotherapy alone (cognitive-behavioural therapy [CBT], interpersonal therapy, psychodynamic therapy, problem-solving therapy in individual or group setting) in the initial phase, in the case of mild to moderate depression.

During the continuation phase of treatment, to reduce the risk of relapse, patients who have been treated successfully with antidepressant medications in the acute phase should continue treatment with these agents with the same dose for four to nine months. It is also recommended to continue psychotherapy by the cognitive-behavioural approach. During the maintenance phase, the current pharmacotherapy should be continued, assuming it turned out to be effective in the initial and continuation phase. Psychotherapy conducted in the initial phase and continuation may be continued, but with reduced session frequency.

Moreover, directions given by institutions, such as the American Psychiatric Association, British Association for Psychopharmacology, or World Federation of Societies for Biological Psychiatry, emphasise that conjunction of pharmacotherapy and psychotherapy is superior to single-modality treatments, especially for patients with moderate-to-severe major depressive disorder, as well as in case of mild depression associated with psychosocial or interpersonal problems, personality disorder, or intrapsychic conflict [32-35]. It is also indicated that combination treatment with psychotherapy and antidepressant medication can be applied during the acute phase as well as in the continuation and maintenance phases, either in parallel or sequentially [36].

In the latter case, sequential treatment requires the selection of a single treatment modality in the first phase, which may be guided by both patient preference and

other practical considerations. The form of additional therapy is selected based on various considerations, including the patient's condition and the effects obtained in monotherapy, particularly a lack of response to the initial treatment, the presence of residual symptoms after improvement with initial therapy, or prevention of relapse and recurrence [36, 37].

In many cases, such as mild depressive episodes, psychotherapy alone is sufficient. Alternatively, recurrent depression may respond best to permanent treatment with antidepressants, even during remission or in the case of a mild episode. In addition, in exceptionally severe cases of depressive episodes, pharmacotherapy is necessary, while psychotherapy may be inadvisable until partial alleviation of symptoms [38]. Each choice of treatment depends on the individual case and the context of the situation.

The validity of combined treatment and its advantage over monotherapy can be justified based on two models [36]. The additive model reflects the potential for a patient to respond to only one form of treatment (i.e., psychotherapy or pharmacotherapy). However, the parallel use of both forms of treatment can elicit synergic effects. For example, the quick effect of using an antidepressant may enable the patient to become more involved in the psychotherapy process or, conversely, psychotherapy may contribute to an increase in medication adherence [36, 37]. A meta-analysis of the interaction between pharmacotherapy and psychotherapy conducted by Cuijpers *et al.* [39] found no association between the use of antidepressants and the effects of psychotherapies, and that the former probably does not interfere with the latter.

Currently, psychiatrists have a fairly wide range of pharmacological agents with proven effectiveness in the treatment of depression; however, the most commonly used are SSRIs (selective serotonin reuptake inhibitors), which are currently considered the first-line drugs in the treatment of major depressive disorder [1, 40]. Another frequently used group of pharmacological agents are those from the SNRI drugs (selective serotonin and norepinephrine reuptake inhibitors); together with SSRI drugs, these constitute the vast majority of drugs used in the treatment of major depressive disorder [41, 42]. Depending on the context, especially drug-resistant depression, other drugs can also be used in various combinations.

Psychotherapy offers many more potential options. It comprises a multiplicity of diverse trends that, despite sharing common foundations, conceptualise depression differently, and thus have different therapeutic assumptions. It should be emphasised that each of these approaches can be helpful and effective in the right situation. The choice of therapy depends on many factors, such as the course and intensity of the disorder, its history and causes, the patient's time, material resources and personality, and the history of other disorders or the patient's personal preferences. Nevertheless, regardless of the chosen approach, the relationship between the patient and the psychotherapist is of fundamental importance [43]. While advocates of various therapeutic approaches may differ in their assessment of the importance and impact of the therapeutic relationship on the psychotherapy process, in extreme approaches, it is assumed that all techniques and interventions only serve as a pretext to establish and maintain this specific bond [44].

THE EFFECTIVENESS OF MONOTHERAPY AND COMBINED TREATMENT OF DEPRESSION

Over the years, the effectiveness of various psychotherapeutic approaches in the treatment of depression have been assessed by both individual studies and meta-analyses. A 2016 meta-analysis of 198 independent studies by Barth *et al.* [45] found all included psychotherapy approaches to be effective and yield positive effects, with no statistically significant differences observed between particular modalities. Similar conclusions were reached by Cuijpers *et al.* [46] in a meta-analysis conducted in 2021, who report that while psychotherapy exhibited significant effectiveness in the treatment of depression, no significant differences in effectiveness were found between different psychotherapeutic approaches. These studies may therefore suggest that while psychotherapy is certainly an effective form of treating depression, the approach to psychotherapy is a very individual and case-dependent matter.

The most widely examined form of psychological treatment for depression, and the most strongly recommended in most treatment guidelines, is CBT. A meta-analysis by Cuijpers *et al.* [47] in 2023 found CBT to have moderate to large effects compared to control conditions, such as care as usual and waitlist. CBT was significantly more effective than other psychotherapies, but the difference was small. The effects of CBT did not differ significantly from those of pharmacotherapies at the short term but were significantly larger at 6-12-month follow-up.

Another commonly used psychotherapeutic modality in the treatment of depression is psychodynamic therapy. Meta-analysis findings confirm short-term psychodynamic psychotherapy (STPP) to be superior to no intervention [48]. In addition, STPP has been found to demonstrate slight superiority over cognitive-behavioural psychotherapy (CBT).

Depression is often treated using an interpersonal approach. Meta-analyses indicate that the difference in effectiveness between interpersonal therapy (IPT) and CBT is small and not significant [49, 50]. However, another study found IPT to demonstrate an insignificantly

greater differential effect size over other psychological treatments, while pharmacotherapy turned out to be more effective than IPT [51].

While, generally speaking, all psychotherapeutic modalities have similar effectiveness, studies indicate small differences between them, which may be associated with the diverse impact of mediating factors. It is also worth mentioning that although psychotherapies for depression may be effective as compared with control conditions, more than half of patients receiving psychotherapy do not respond, and only one third went into remission [52].

The meta-analyses evaluating the effectiveness of antidepressants do not indicate clear conclusions. Available evidence shows that while antidepressants have significant effects on depressive symptoms, their effect size is too little to have any clinical relevance [53-55]. Advocates of antidepressant therapy highlight the significant effect size of acute phase pharmacotherapy, the ability to continue and maintain antidepressants to reduce risk of relapse or recurrence in those who remit, and the reduced suicide risk. On the other hand, there are doubts whether antidepressants have clinically significant surplus value over and above placebo [56]. The efficacy of selective serotonin reuptake inhibitors (SSRIs), which are the most widely-prescribed psychiatric drugs for the treatment of depression, was variable and incomplete, i.e., 60-70% of the patients do not experience remission, while 30-40% do not show a significant response [57]. A meta-analysis conducted by Yuan *et al.* [57] compared the efficacy of seven first-line antidepressants (fluoxetine, paroxetine, escitalopram, sertraline, fluvoxamine, venlafaxine, duloxetine), three kinds of anti-inflammatory drugs (NASIDs, cytokine-inhibitor, pioglitazone), and ketamine. It was found that NASID, venlafaxine, and ketamine demonstrated the highest OR value in response, and NASID, ketamine, and venlafaxine – in remission.

However, studies performed to date have many methodological limitations [58]. There is a risk that the results overestimate the advantageous result and underestimate the harmful effects, such as dependence, withdrawal, sexual dysfunction, tardive dysphoria [59-61], and increased risk of relapse due to their iatrogenic effect [62].

Meta-analyses based on various indicators show that pharmacotherapy and short-term psychotherapy exhibit similar effectiveness in reducing depression symptoms, while long-term psychotherapy appears to be more effective, especially in preventing relapse [62-66]. Pharmacotherapy and psychotherapy also elicit comparable changes in neurotransmission in the CNS [67]. Although patients using pharmacological treatment were more likely to refuse treatment and end it prematurely [68, 69], the two approaches have similar remission rates, with a slight advantage of psychotherapeutic interventions, while pharmacotherapy demonstrated a higher relapse rate [68].

From a clinical perspective, studies comparing the effectiveness of combined treatment versus monotherapy seem particularly important. A network meta-analysis by Cuijpers *et al.* [70] found combined treatment to be more effective than monotherapy in achieving response at the end of treatment; in addition, no significant difference was found between psychotherapy and pharmacotherapy alone. Similar results were found for the remission phase. Combined treatment and psychotherapy alone were more acceptable than pharmacotherapy alone. Similar results were obtained for chronic and treatment-resistant depression. It is worth emphasising that combined therapy proved to be the most effective form of treatment for moderate depression.

A meta-analysis of Furukawa *et al.* [71] led to similar conclusions, i.e., that combined treatment and psychotherapy alone have more enduring effects than pharmacotherapy. In the acute phase, combined treatment resulted in a more sustained response than medications, both when these treatments were continued into the maintenance phase and when they were followed by discretionary treatment. Psychotherapy also turned out to be more effective than medications in the maintenance phase and discretionary treatment.

Considering the use of particular psychotherapeutic approaches in combined treatments, it should be emphasised that in the short and long term, pharmacotherapy plus CBT is more effective than medications alone, yet not more effective than CBT alone [47]. Also combined treatment of antidepressants and short-term psychodynamic therapy was found to be significantly more effective than antidepressants, with or without brief supportive psychotherapy [73].

The latest meta-analyses generally indicate that combination therapies offer superior effectiveness to monotherapies. This does not mean, however, that combining pharmacotherapy with psychotherapy is always the most effective strategy, although it certainly generates a relatively high cost. To optimise the cost-effectiveness of treatment, precise indicators for the inclusion of specific combined treatment strategies should be determined. A study comparing the cost-effectiveness of monotherapy and combined treatment indicates the advantage of cognitive-behavioural therapy alone over other forms of treatment [74]. It has also been found out that combination treatment is cost-effective only in the case of moderate to severe depression [75].

The key issue when deciding whether to combine pharmacotherapy and psychotherapy is the issue of moderators, i.e., characteristics enabling the actual identification of patients who will benefit most from combined treatment, as well as the issue of diversified strategies for combined treatment. A review by Dunlop [36] suggests that the appropriacy of employing combined therapy in a particular case is best determined based on the following

factors: chronicity, severity, patient preference, socioeconomic deprivation, personality characteristics, and childhood trauma. It is therefore advisable to further develop research in this direction, which would enable the implementation of personalised treatment for depression, instead of applying treatment based on general standards.

CONCLUSIONS

Depression is a common mental disorder and represents a growing problem. Currently, treatment is based primarily on pharmacotherapy using antidepressants and psychotherapy. While a wide range of psychotherapeutic approaches can be used to treat depression, research indicates that all leading approaches are effective. Pharmacotherapy and psychotherapy offer comparable effectiveness in reducing depressive symptoms and demonstrate similar effects on neuronal activity, and combined treatment may offer optimal effectiveness in mild to severe depression. Meta-analyses indicate that, especially in the case of moderate and severe depression, it is advisable to implement combined treatment.

Nevertheless, there is a need for further research on the effectiveness of different depression treatment strategies to identify moderating factors which will enable the development of effective personalised treatment.

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