



# Clinical Application of Computational Psychiatry in Non-Pharmacological Therapeutic Interventions for Individuals with Depressive Disorders: a Systematic Review

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## Keywords

Psychiatry; models, theoretical; depressive disorder

## Abstract

**Aim:** This systematic review aimed to explore whether knowledge gained through computational psychiatry can be applied in non-pharmacological therapeutic interventions for individuals with depressive disorders and to identify which non-pharmacological approaches utilize this knowledge. **Materials and Methods:** This systematic review was conducted according to the PRISMA guidelines. PubMed and Scopus databases were searched for articles published in the last ten years using the terms “computational psychiatry” and “depression.” The study protocol was registered on the Open Science Framework. **Results:** Out of 777 articles, 15 were included in the review. The studies were divided into two groups: those investigating various brain stimulation techniques (direct current stimulation, electroconvulsive therapy, deep brain stimulation, and transcranial magnetic stimulation) and those examining behavioral and neurofeedback techniques. Findings indicate that computational psychiatry can optimize existing therapeutic approaches, including specific methodological aspects. **Conclusion:** This review indicates the potential for applying compu-

tational psychiatry methods in the non-pharmacological treatment of depressive disorders. These approaches enable the optimization of therapeutic strategies and the personalization of treatment to individual patients, enhancing the effectiveness of existing therapies.

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## Introduction

Computational psychiatry is a relatively new field in psychiatry that uses mathematical and computational models of brain functioning [1,2]. This approach is important because it enables the connection of data obtained at different levels of neurobiology and psychiatry research data, from the level of genes to the proteins, cells, neural circuits, and laboratory findings. It also makes it possible to include imaging data, data collected through questionnaires, and data about environmental factors. Computational psychiatry enables the integration of data obtained in this way, which serves as a basis for developing models of individual brain regions, neural circuits, and even the entire brain, which are used to understand healthy behavior and functioning, as well as for research into the etiology of psychological symp-

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toms and psychiatric disorders [3,4]. In addition to research into the etiology of psychiatric disorders, computational psychiatry can also be used to predict the risk of developing specific psychiatric disorders based on biological characteristics [3,5].

Mujica and associates describe three broad approaches to such systems [6]. The first is “bottom-up”, which starts at the level of neurons and extends to groups of neurons and their dynamics, which can be measured by magneto/electroencephalography (M/EEG) oscillations [7,8]. Top-down approaches start from emergent phenomena, such as behavior and symptoms, and investigate the neurological mechanisms that may lead to them [9–12]. A third approach uses information-theoretic approaches that explore strategies the brain can use to optimize information dissemination [13–15].

Computational psychiatry enables the creation of complex models that can integrate biological and non-biological data and help tailor personalized treatment strategies.

Depressive disorders represent one of the significant health challenges in the world [16]. In the treatment of depressive disorders, in addition to pharmacological approaches, non-pharmacological approaches are also used, which include a wide range of therapeutic approaches. While computational psychiatry is used mainly in developing etiological models of psychiatric disorders, there is significant potential for integrating computational models into non-pharmacological treatment approaches for individuals with depressive disorders.

This systematic review aimed to explore whether the knowledge gained through computational psychiatry methods can be applied in non-pharmacological therapeutic interventions for individuals with depressive disorders and which non-pharmacological approaches implement the knowledge gained through computational psychiatry in the treatment of people with depressive disorders.

## Materials and Methods

We have systematically reviewed the literature according to the Preferred Reporting Items to Systematic Reviews and Meta-Analyses (PRISMA) guidelines. The study protocol was registered on Open Science Framework.

### Search strategy

We have explored PubMed and Scopus databases for articles published in the last ten years using search terms “computational psychiatry” AND “depression”.

The search terms were queried by PubMed as follows: (“comput psychiatr”[Journal] OR (“computational”[All

Fields] AND “psychiatry”[All Fields]) OR “computational psychiatry”[All Fields]) AND (“depressed”[All Fields] OR “depression”[MeSH Terms] OR “depression”[All Fields] OR “depressions”[All Fields] OR “depression s”[All Fields] OR “depressive disorder”[MeSH Terms] OR (“depressive”[All Fields] AND “disorder”[All Fields]) OR “depressive disorder”[All Fields] OR “depressivity”[All Fields] OR “depressive”[All Fields] OR “depressively”[All Fields] OR “depressiveness”[All Fields] OR “depressives”[All Fields])) AND ((y\_10[Filter]) AND (humans[Filter])).

For the Scopus database, the query was as follows: TITLE-ABS-KEY (computational AND psychiatry AND depression) AND PUBYEAR > 2013 AND PUBYEAR < 2025 AND (LIMIT-TO (EXACTKEYWORD , “Human”)).

We have reviewed studies from 2014 to 2024, with the last access date of August 10, 2024, for Pubmed and August 16, 2024, for the Scopus database. In Pubmed, we have included a filter to select only human studies. We have not applied restrictions to languages, and no filter was used to limit the language of the articles.

### Study selection and screening

Inclusion criteria were as follows: 1) Original research articles; 2) Research uses computational psychiatry methods; 3) The main topic of the research article is depressive disorder; 4) Research was done on the adult population; 5) The research is related to non-pharmacological therapeutic approaches for depressive disorders; 6. The study was published within the last ten years. Exclusion criteria were as follows: 1) Review articles, editorials, and commentary articles were not included; 2) Research that is related to other psychiatric disorders that are not depressive disorders were not included; 3) If the researched population is younger than 18 years the articles were not included.

The selection process consisted of two rounds. In the first round, the articles were selected based on their titles and abstracts. In the second round, the full texts of the studies that passed the first round were reviewed to determine their eligibility for inclusion. Both authors independently performed the selection process based on the predefined inclusion and exclusion criteria. Any discrepancies between the two screeners were discussed and resolved by consensus. No automation tools were used during the selection and deduplication process, and articles that required translation were translated using the Google Translate service.

### Data collection

The data collection process was carried out in the following stages: In the initial collection stage, key information from each included study was collected. The collected data included author(s), title, objective, therapeutic intervention or procedure, and main findings. After the initial collection of the data, a second pass was conducted to verify the accuracy of the collected data. This stage ensured the key information was correctly and

consistently extracted across all studies. In the final stage, the collected data was summarized and prepared for analysis.

Data was collected independently by both authors, who used a structured approach to collect data from papers, focusing on the aims, methods, and results of articles related to the application of computational psychiatry in non-pharmacological therapeutic interventions for depressive disorders. After both extractions were completed, the extracted data was compared to identify discrepancies, and differences were resolved through discussion and consensus. No automation tools were used for data collection.

Both authors independently assessed the risk of bias in the included studies, evaluating the key factors such as study design, sample size, data collection methods, and outcome reporting. The authors compared their results after completing their evaluations. Any differences in interpretation were resolved through consensus. No automation tools were used in the assessment of risk of bias.

## Results

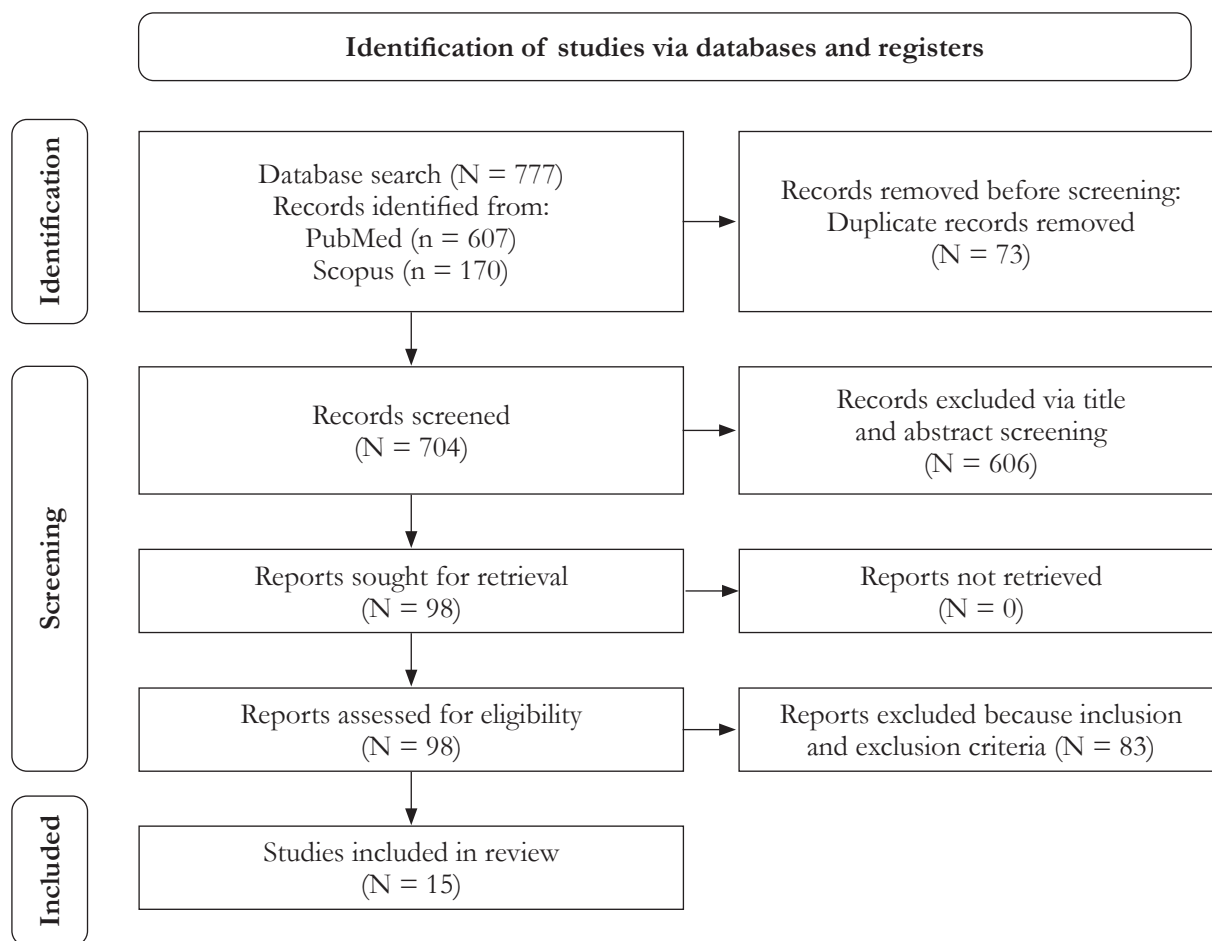
### Study selection

Searching the PubMed and Scopus databases according to the keywords resulted in a total of 777 papers. After removing duplicate papers and excluding articles in the primary selection, based on the title and abstract of the paper, 98 papers remained. A detailed review of 98 papers and the application of inclusion and exclusion criteria left the final 15 articles that were included in the systematic review.

The detailed process of selection of the studies is shown in PRISMA Flowchart in Figure 1.

Details of the studies are summarized in Table 1. The resulting studies can be divided into studies investigating the effects of various brain stimulation techniques (direct current stimulation, electroconvulsive therapy, deep

**Figure 1.** PRISMA Flowchart



**Table 1.** Studies on the clinical application of computational psychiatry in non-pharmacological therapeutic interventions for individuals with depressive disorders

Author(s)	Title	Number of participants	Objective	Therapeutic intervention or procedure	Main findings
Ho, et al. 2015 (17)	Clinical pilot study and computational modeling of bitemporal transcranial direct current stimulation, and safety of repeated courses of treatment, in major depression	N = 4	The aim of the study was to examine a bitemporal transcranial direct current stimulation (tDCS) electrode placement for the treatment of depression through a clinical pilot study and computational modeling.	Participants with depression who had previously undergone multiple tDCS treatments received a 4-week course of bitemporal tDCS, with mood and neuropsychological assessments, and results were compared to their previous treatments using different electrode placements, while computational modeling analyzed the electric field map produced by different placements.	Three participants showed clinical improvement with bitemporal transcranial direct current stimulation, with no adverse effects; computational modeling showed that the bitemporal placement activates the anterior cingulate cortices and brainstem; modeling suggested that fronto-extracerebral placement stimulated these areas more effectively.
Bai, et al. 2019 (19)	Computational comparison of conventional and novel electroconvulsive therapy electrode placements for the treatment of depression	N = 3	The aim of the study was to use computational modelling to perform examination into regional differences in brain excitation by the electroconvulsive (ECT) stimulus for different electrode placements, aiming to identify placements that may optimize clinical outcomes.	High resolution models were generated from MRI scans and the models were used to compare regional differences in average electric field magnitude among a total of thirteen bipolar ECT electrode placements, which included conventional placements as well as lesser known and novel placements.	The study found that some novel placements, effectively stimulated brain regions considered important for efficacy, while reducing stimulation of regions linked to side effects. The findings also highlighted the importance of individual differences, such as head size, in determining stimulation outcomes.
Howell, et al. 2019 (24)	Quantifying the axonal pathways directly stimulated in therapeutic subcallosal cingulate deep brain stimulation	N = 6	The aim of the study was to identify the axonal pathways that were directly stimulated by subcallosal cingulate (SCC) deep brain stimulation (DBS) in patients with depression using advanced DBS models.	The study involved SCC DBS therapy in patients with chronic depression, with computational models used to analyse the activation of specific axonal pathways. The modeling was conducted using field-cable pathway-activation models based on patient-specific imaging data.	The study quantified the activation of four major pathways in the SCC region and suggested the most likely therapeutic targets for SCC DBS. It also found that excessive activation of specific brain pathways may extend the time to achieve a stable therapeutic response, suggesting the importance of careful targeting to optimize treatment outcomes.
Hilland, et al. 2020 (29)	Attentional bias modification is associated with fMRI response toward negative stimuli in individuals with residual depression: a randomized controlled trial	N = 134	The aim of the study was to explore the neural effects of Attentional Bias Modification (ABM) in individuals previously treated for depression and with various degrees of residual symptoms, using functional MRI (fMRI) to assess changes in brain activity in response to emotional stimuli.	Participants were randomized to 14 days of active ABM or a closely matched placebo training, and the effects of ABM were then assessed using fMRI during an emotion regulation task.	The study found that the ABM group showed reduced activation in the amygdala and the anterior cingulate cortex when passively viewing negative images, compared with the placebo group. No group differences were observed in brain regions associated with emotion regulation strategies. The response in the temporal cortices was associated with the extent of change in attentional bias and the degree of depressive symptoms in the ABM group compared to the placebo group.

**Table 1.** (Continued)

Author(s)	Title	Number of participants	Objective	Therapeutic intervention or procedure	Main findings
Steward et al. 2020 (20)	The left anterior right temporal (LART) placement for electroconvulsive therapy: A computational modelling study	N = 3	The aim of the study was to explore how stimulation effects from left anterior right temporal (LART) electrode placement in electroconvulsive therapy (ECT) and two novel variants compared to the more common bilateral placements of bitemporal and bifrontal ECT, using computational modelling.	High-resolution head models were generated from MRI scans, and differences in regional stimulation were examined.	The original LART resulted in greater stimulation of the left cingulate gyrus, which is hypothesized to be associated with treatment efficacy, and relatively reduced stimulation of the bilateral hippocampi, which are potentially associated with cognitive side effects. No additional clinical benefit was suggested with the novel LART placements.
Brown, et al. 2021 (30)	Reinforcement learning disruptions in individuals with depression and sensitivity to symptom change following cognitive behavioral therapy	N = 101	The aim of the study was to determine associations among computational model-derived reinforcement learning parameters, depression symptoms, and symptom changes after cognitive behavioral therapy (CBT).	Participants with and without a depression diagnosis completed a probabilistic learning task during functional magnetic resonance imaging (fMRI) at baseline and follow-up. A subset of participants with depression received cognitive behavioral therapy between the baseline and follow-up assessments. Computational modeling was used to analyze participants' choices and fMRI data to investigate the associations between reinforcement learning parameters and symptom changes after CBT.	The study identified associations between reinforcement learning parameters and symptoms of major depression, namely linking anhedonia with reward learning and negative affect with loss learning. Symptom improvement following Cognitive Behavioral Therapy was associated with normalization of disrupted learning parameters.
Suen, et al. 2021 (18)	Association between tDCS computational modeling and clinical outcomes in depression: data from the ELECT-TDCS trial	N = 16	The aim of the study was to investigate whether the strength of the electric field (EF) induced by transcranial direct current stimulation (tDCS) in specific brain regions was associated with changes in behavioral outcomes in depressed patients using computational modeling.	The included participants who were diagnosed with major depressive disorder and who received active tDCS applied over 22 sessions during a ten-week period.	The main findings included correlations between simulated EF strength in specific brain regions and changes in depression scores, negative affect, and the potential role of EF strength in influencing behavioral changes in depressed patients undergoing tDCS treatment.
Taylor, et al. 2022 (31)	Depressive symptoms reduce when dorsolateral prefrontal cortex-precuneus connectivity normalizes after functional connectivity neurofeedback	N = 19	The aim of the study was to evaluate whether fMRI functional connectivity neurofeedback (FCNef) targeting the dorsolateral prefrontal cortex (DLPFC) and precuneus/posterior cingulate cortex (PCC) could lead to a reduction in depressive symptoms, particularly those related to rumination, in individuals with subclinical depression.	Participants underwent FCNef training, where they were rewarded when the connectivity between the DLPFC and PCC became more anticorrelated, aiming to normalize this connectivity pattern.	The study found that normalization of this connectivity contributed to reductions in depressive symptoms and brooding.

**Table 1.** (Continued)

Author(s)	Title	Number of participants	Objective	Therapeutic intervention or procedure	Main findings
Fu, et al. 2023 (21)	Cerebro-cerebellar functional neuroplasticity mediates the effect of electric field on electroconvulsive therapy outcomes	N = 62	The aim of the study was to investigate cerebro-cerebellar functional connectivity neuroplasticity and its relationships with electric field (E-field) strength during electroconvulsive therapy (ECT), antidepressant outcomes and cognitive side effects.	The study utilized data from a clinical trial in which participants with major depressive disorder received ECT with different electrode placements and varying pulse amplitudes. The therapeutic procedure involved a series of ECT sessions, while resting-state fMRI and computational modeling were employed to measure E-field strength and analyze changes in cerebro-cerebellar functional network connectivity (FNC) in relation to clinical outcomes.	The study found that increased E-field strength was associated with changes in specific cerebro-cerebellar functional network connectivity (FNC) patterns, which in turn mediated the effects of ECT on both antidepressant outcomes and cognitive impairment. Higher E-field strength enhanced antidepressant effects but also increased cognitive side effects, particularly verbal fluency impairment. The findings suggest that balancing E-field strength is important to optimizing both antidepressant and cognitive outcomes.
Kaboodvand, et al. 2023 (27)	Macroscopic resting state model predicts theta burst stimulation response: A randomized trial	N = 42	The aim of the study was to evaluate the predictive value of whole-brain computational modeling in determining the therapeutic response to accelerated intermittent theta burst stimulation (iTBS) targeting the dorsomedial prefrontal cortex (dmPFC) in patients with treatment-resistant depression.	The study involved a randomized controlled trial where participants received either active or placebo iTBS treatment over the dmPFC. Whole-brain computational modeling was used to analyze baseline resting-state fMRI data to identify depression subtypes based on brain dynamics and predict responses to iTBS.	The study identified two depression subtypes based on pre-treatment resting-state functional connectivity patterns. Subtype characterized by reduced frequency dynamics in intrinsic brain activity at baseline, showed greater improvements in mood, initiative, suicidality and motivation for work and school following active iTBS treatment compared to the other subtype. The findings highlight the potential of whole-brain modeling in identifying clinically relevant subtypes within depression and predicting their response to rTMS treatment.
Lai, et al. 2023 (25)	Structural and functional correlates of the response to deep brain stimulation at ventral capsule/ventral striatum region for treatment-resistant depression	N = 10	The aim of the study was to explore functional and structural connectivities that are associated with the clinical response to deep brain stimulation (DBS) targeting the ventral capsule/ventral striatum (VC/VS) region in patients with treatment-resistant depression.	The study involved DBS therapy with bilateral electrode implantation in the VC/VS region. The effectiveness of the stimulation was evaluated using clinical scales, and computational modeling was used to estimate the electric fields and connectivity profiles from preoperative and postoperative imaging data.	The study found that specific frontothalamic pathways and cortical projections were associated with improved clinical outcomes following DBS. The optimal structural and functional connectivity patterns that mainly converged on the prefrontal and orbitofrontal cortices were predictive of antidepressant responses. Findings suggest that connectivity profiles can guide pre- and postoperative planning for DBS in patients with treatment-resistant depression.

**Table 1.** (Continued)

Author(s)	Title	Number of participants	Objective	Therapeutic intervention or procedure	Main findings
Miller, et al. 2023 (22)	Electric Field, Ictal Theta Power, and Clinical Outcomes in Electroconvulsive Therapy	N = 27	The aim of the study was to determine the relationships between electroconvulsive therapy (ECT) dosing, ictal theta power, and mood and cognitive outcomes in patients receiving ECT for treatment-resistant depression. It also explored ictal theta power as a potential biomarker for cognitive and therapeutic responses.	The study involved participants diagnosed with major depressive disorder or bipolar II disorder with a current depressive episode who received right unilateral (RUL) ECT. Clinical and cognitive outcomes were assessed pre-, mid-, and post-ECT. The relationship between the electric field in the brain, ictal theta power, clinical outcome, and cognitive outcomes was assessed with linear models.	The study found that higher ictal theta power was associated with electric fields and was linked to cognitive outcomes, particularly phonemic and semantic fluency, but electric field strength did not correlate with antidepressant outcomes. The study suggests that ictal theta power could serve as a potential cognitive biomarker early on during the ECT course, aiding in adjustments to treatment parameters.
Smith, et al. 2023 (23)	Clinical EEG slowing induced by electroconvulsive therapy is better described by increased frontal aperiodic activity	N = 9	The aim of the study was to investigate how electroconvulsive therapy (ECT) influences EEG activity, with an emphasis on aperiodic activity in the frontal cortex and its relationship with clinical improvements in patients with depression.	The study involved participants with major depressive disorder undergoing a 12-session ECT treatment. Resting-state EEG data were collected before and after selected ECT sessions to analyze changes in aperiodic and periodic activity in the brain.	The study found that ECT was associated with an increase in aperiodic activity, particularly in the frontal cortex, which was more strongly related to clinical improvement than changes in traditional delta band power. The findings suggest that ECT may alleviate depressive symptoms by restoring normal levels of inhibition in the frontal cortices.
Bi, et al. 2024 (28)	Brain stimulation over the left DLPFC enhances motivation for effortful rewards in patients with major depressive disorder	N = 50	The aim of the study was to investigate whether transcranial magnetic stimulation (TMS) over the left dorsolateral prefrontal cortex (DLPFC) enhances motivation for effortful rewards in patients with major depressive disorder (MDD), focusing on behavioral, computational, and neural measures.	The study involved patients with major depressive disorder who underwent both active and placebo TMS sessions targeting the left DLPFC. After each session, participants completed the Effort-Expenditure for Rewards Task to measure effortful decision-making.	The study found that active TMS over the left DLPFC increased patients' willingness to exert effort for rewards compared to placebo, along with a trend of increased brain activity related to attention toward chosen options, greater activity during effort preparation, and heightened activity when anticipating a high reward. The findings suggest that stimulating the DLPFC enhances motivation for effortful rewards and could serve as a potential treatment for improving motivation in MDD.

**Table 1.** (Continued)

Author(s)	Title	Number of participants	Objective	Therapeutic intervention or procedure	Main findings
Cha, et al. 2024 (26)	Whole brain network effects of subcallosal cingulate deep brain stimulation for treatment-resistant depression	N = 22	The aim of the study was to examine the longitudinal brain changes associated with deep brain stimulation (DBS) in the subcallosal cingulate (SCC) region for patients with treatment-resistant depression. The researchers sought to understand the time course of brain network changes and their relationship to clinical improvement with DBS therapy by analyzing longitudinal changes in regional cerebral blood flow (rCBF) and glucose metabolism over a 6-month period.	The study involved SCC DBS treatment in two cohorts of patients with treatment resistant depression. Bilateral SCC DBS was administered, and participants underwent PET scans at baseline, 1-month post-surgery, and at 1 and 6 months of chronic DBS therapy. The scans measured changes in rCBF and glucose metabolism to evaluate the effects of DBS on intrinsic connectivity networks.	The study found that SCC DBS induced time-specific changes in the salience network and default mode network. The findings suggest that SCC DBS has both acute and chronic effects on brain networks, and that default mode network activity could serve as a biomarker for tracking clinical progress in patients with treatment resistant depression.

brain stimulation, and transcranial magnetic stimulation) and studies investigating behavioral and neurofeedback techniques.

### Brain stimulation techniques

Most of the studies in this systematic review can be categorized into one of the categories related to brain stimulation techniques. These methods encompass a variety of approaches aimed at modulating brain activity.

### Studies investigating transcranial direct current stimulation

Two of the included studies investigate the effects of transcranial direct current stimulation (tDCS) in patients with depressive disorder. Ho and associates explored tDCS electrode placement for the treatment of depression [17]. Their findings suggested that the bitemporal placement of the electrodes had a positive impact on clinical outcomes, with no adverse effects, and suggested that placement on some specific regions stimulated these areas more effectively. Suen and associates examined the association between the strength of the electric field induced by transcranial direct current stimulation in specific brain regions with changes in behavioral outcomes in depressed patients, using computational modeling [18]. The findings of their study showed the correlation

between electric field strength and depressive symptoms, as well as the potential role of electric field strength on behavioral changes in depressive patients.

### Studies investigating electroconvulsive therapy

Five studies investigated the possibilities of applying computational psychiatry methods in combination with electroconvulsive therapy.

Bai and associates used computational modeling to evaluate electrode placement with the aim of identifying placements that may optimize clinical outcomes and found that some novel placements effectively stimulated brain regions considered important for efficacy while reducing stimulation of regions linked to side effects [19]. The authors also emphasized the importance of individual differences in determining stimulation outcomes. Adding to the field, Steward and associates used computational modeling to explore how stimulation effects from left anterior right temporal electrode placement in ECT and two novel variants compared to the more common placements [20]. Their results suggested that the original placement resulted in greater stimulation of the area associated with treatment efficacy and relatively reduced stimulation of the areas that are potentially associated with cognitive side effects, while the novel variants of placements did not

show additional benefits. Fu and associates investigated the relationship between cerebro-cerebellar functional connectivity neuroplasticity, electric field strength, and clinical outcomes of electroconvulsive therapy, and the findings suggest that balancing electric field strength is important to optimizing both antidepressant and cognitive outcomes [21].

Miller and associates investigated the relationships between electroconvulsive therapy dosing, ictal theta power, and mood and cognitive outcomes and found that increased ictal theta power was associated with electric fields and was linked to cognitive outcomes, but electric field strength did not correlate with antidepressant outcomes [22]. The study also suggested that ictal theta power could serve as a potential cognitive biomarker early on during the ECT course.

The study of the Smith and associates found that ECT was associated with an increase in aperiodic activity, particularly in the frontal cortex, which was more strongly related to clinical improvement than changes in traditional delta band power, suggesting that ECT may alleviate depressive symptoms by restoring normal levels of inhibition in the frontal cortices [23].

#### Studies investigating deep brain stimulation

Three studies focused on using deep brain stimulation (DBS) in combination with computational psychiatry to explore the neuronal pathways stimulated by DBS.

The study by Howell and associates, which focused on identifying the axonal pathways that were directly stimulated by subcallosal cingulate (SCC) deep brain stimulation using advanced DBS models, identified four major pathways in the SCC region, and suggested the most likely therapeutic targets for SCC DBS [24].

Lai and associates explored functional and structural connectivities associated with the clinical response to deep brain stimulation DBS targeting the ventral capsule/ventral striatum region and found that specific frontothalamic pathways and cortical projections were associated with improved clinical outcomes following DBS, suggesting that connectivity profiles can guide pre- and postoperative planning for DBS [25].

Cha and associates investigated the longitudinal brain changes associated with deep brain stimulation in the subcallosal cingulate (SCC) region and attempted to discern the time course of brain network changes and their relationship to clinical improvement with DBS therapy [26]. The study found that SCC DBS induced time-specific changes in the salience network and default mode network. Authors suggested that SCC DBS has both acute and chronic effects on brain networks and that default mode network activity could serve as a biomarker for tracking clinical progress in patients.

#### Studies investigating transcranial magnetic stimulation

Two studies explored the use of transcranial magnetic stimulation (TMS) in combination with computational psychiatry.

In the study by the Kaboodvand and associates The authors aim was to evaluate the predictive value of whole-brain computational modeling in determining the therapeutic response to accelerated intermittent theta burst stimulation [27]. The study identified two depression subtypes based on pre-treatment resting-state functional connectivity patterns and highlighted the potential of whole-brain modeling in identifying clinically relevant subtypes within depression and predicting their response to treatment.

Bi and associates explored the enhancement of motivation for effortful rewards through TMS [28]. The results suggest that stimulating the dorsolateral prefrontal cortex enhances motivation for effortful rewards and could serve as a potential treatment for improving motivation in major depressive disorder.

#### Studies investigating behavioral and neurofeedback techniques

Three studies were found that explored the effects of specific behavioral interventions.

The study by Hilland and associates was conducted on 134 participants and explored the neural effects of Attentional Bias Modification (ABM) using functional MRI to assess changes in brain activity in response to emotional stimuli [29]. The study found that the ABM group showed reduced activation in the amygdala and the anterior cingulate cortex when passively viewing negative images and that the response in the temporal cortices was associated with the extent of change in attentional bias and the degree of depressive symptoms in the ABM group.

Brown and associates carried out the study on 101 participants investigating associations among computational model-derived reinforcement learning parameters, depression symptoms, and symptom changes after cognitive behavioral therapy [30]. The authors identified associations between reinforcement learning parameters and symptoms of major depression and found that symptom improvement following cognitive behavioral therapy was associated with the normalization of disrupted learning parameters.

Taylor and associates evaluated whether functional connectivity neurofeedback targeting the dorsolateral prefrontal cortex and precuneus/posterior cingulate cortex could lead to a reduction in depressive symptoms, and authors found that normalization of this connectivity contributed to reductions in depressive symptoms and brooding [31].

## Discussion

With this systematic review, we wanted to investigate whether the knowledge gained through the use of computational psychiatry methods can be applied in non-pharmacological therapeutic interventions for people with depressive disorders and which non-pharmacological approaches implement the knowledge gained through the use of computational psychiatry.

Reviewing the databases PubMed and Scopus using keywords related to computational psychiatry and depression found a significant number of articles, which mainly focus on creating models that aim to identify individuals with increased risk of developing a depressive disorder based on biological variables. This is understandable, considering that computational methods require structured databases on which models are formed.

The results of our research indicate that computational psychiatry methods in the non-pharmacological treatment of depressive disorders are, in most cases, used in the field of brain stimulation techniques, including direct current stimulation, electroconvulsive therapy, deep brain stimulation, and transcranial magnetic stimulation. This is logical as these therapeutic approaches generate large amounts of data that are favorable for use in computer models.

The research indicates that the knowledge gathered using computational psychiatry can be utilized in optimizing existing therapeutic approaches, both in terms of optimizing the therapeutic approach itself and in some specific aspects, such as electrode placement. The articles indicate that with current technology, the use of brain stimulation techniques, neuroimaging methods, and computational psychiatry, it is possible to monitor the activation of specific brain regions. Connecting this data with the patient's symptomatology enables the optimization of therapeutic techniques to achieve positive effects of therapy and reduce potential side effects [17,19,20].

Some studies, such as the research of Miller and associates indicate that certain parameters can also serve as biomarkers in the early stages of ECT treatment [22].

Studies that used deep brain stimulation in combination with computational psychiatry focused on researching specific neuronal connections and brain regions that are shown to be potential therapeutic targets [24-26]. Cha and associates suggest that certain brain activity patterns have the potential to be used as a biomarker to monitor clinical progress in patients [26].

The approach of Kaboodvand and associates indicates both the possibility of whole-brain computational

modeling in recognizing subtypes of depression and assessing therapeutic response [27].

Surprisingly, there is only a small number of identified studies that are grouped into the category that investigated behavioral and neurofeedback techniques. However, these studies also indicate that the approaches using the mentioned techniques can benefit from the computational psychiatry approach in the optimization of therapeutic protocols and techniques [29-31].

Limitations of using computational psychiatry include limited accessibility to necessary computational resources, the expertise required to utilize specific models, and the high costs associated with equipment and training for these methods.

The limitations of the current research include the possibility that additional papers could have been identified using alternative keywords. The findings of the study may have limited generalizability, influenced in part by the small sample sizes of some studies. Nonetheless, they highlight emerging trends in the use of computational psychiatry methods in the non-pharmacological treatment of patients with depressive disorders.

Computational psychiatry has a lot of potential for application in therapeutic procedures in psychiatry. Given that it enables the integration of data from different domains, it has significant potential in the prevention and risk prediction of psychiatric disorders based on biological and non-biological data, as well as in treatment through optimization and individualization of therapeutic procedures.

In conclusion, this systematic review indicates the possibility of using computational psychiatry methods in the non-pharmacological treatment of patients with depressive disorders. These approaches enable the optimization of therapeutic strategies as a whole and adaptation to individual patients, increasing the effectiveness of already existing therapeutic approaches.

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## Conflict of Interest

None to declare.

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