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NEUROPLASTICITY AND PSYCHIATRIC DISORDERS: A SYSTEMATIC REVIEW

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Anna Karolyne Leite de Jesus[1], Lorena Fonseca Santos Vieira[2], Marina Rosa Mendonça Santos[3], Isabela Santana de Jesus[4], Luzia Rafaela Alcântara Oliveira[5], Yasmin Melo Prado[6], Lorena Maria de Melo Rodrigues[7], Maria Alice de Sousa Oliveira[8], Artur Henrique Morais Viana[9] and Lucas Silva de Oliveira[10]

[1] Medical student
Tiradentes University, Brazil
ORCID: https://orcid.org/0009-0000-9814-9871
E-mail: Anny.kleite@souunit.com.br
[2] Medical student
Tiradentes University, Brazil
ORCID: https://orcid.org/0009-0002-4660-1314
E-mail: Lorena.fsantos@souunit.com.br
[3] Medical student
Tiradentes University, Brazil
ORCID: https://orcid.org/0009-0003-6078-2518
E-mail: Marina.rosa@souunit.com.br
[4] Medical student
Tiradentes University, Brazil
ORCID: https://orcid.org/0009-0008-3167-6325
E-mail: Isabela.jesus@souunit.com.br
[5] Medical student
Tiradentes University, Brazil
ORCID: https://orcid.org/0009-0009-1740-0637
E-mail: Luzia.rafaela@souunit.com.br
[6] Medical student
Tiradentes University, Brazil
ORCID: https://orcid.org/0009-0000-6685-3135
E-mail: Yasmin.mprado@souunit.com.br
[7] Medical student
Tiradentes University, Brazil
ORCID: https://orcid.org/0009-0006-0559-5551
E-mail: Lorena.maria03@souunit.com.br
[8] Medical student
Tiradentes University, Brazil
ORCID: https://orcid.org/0009-0004-5373-4566
E-mail: Maria.alice03@souunit.com.br
[9] Medical student
Tiradentes University, Brazil
ORCID: https://orcid.org/0009-0006-6309-8799
E-mail: Artur.morais@souunit.com.br
[10] Medical Student
Tiradentes University, Brazil
ORCID: https://orcid.org/0009-0008-6022-0570
E-mail: Lucas.silva0601@souunit.com.br

ABSTRACT

Neuroplasticity refers to the nervous system's ability to reorganize its structure and function in response to environmental experiences and stimuli. Evidence suggests that alterations in neuroplasticity processes are involved in the etiology and progression of several psychiatric disorders, such as depression, schizophrenia, and bipolar disorder. This study aims to systematically review the literature on the relationship between neuroplasticity and psychiatric disorders, highlighting the underlying mechanisms and therapeutic implications. To this end, the SciELO, LILACS and VHL databases were consulted, following the PRISMA criteria for the selection of studies. The results indicate that pharmacological and non-pharmacological interventions can modulate neuroplasticity and offer significant therapeutic benefits for psychiatric patients. It is concluded that a deep understanding of neuroplasticity can contribute to the development of more effective therapeutic approaches.

Keywords: Neuroplasticity. Psychiatric disorders. Depression. Schizophrenia. Bipolar disorder.

INTRODUCTION

Neuroplasticity, also called neural plasticity, is a fundamental concept in neuroscience that refers to the brain's ability to modify its structure and function in response to internal and external stimuli. This phenomenon occurs throughout life and is involved in essential processes such as learning, memory, adaptation to the environment, and recovery of functions after brain injuries. Studies indicate that neuroplasticity can be modulated by environmental, emotional, and pathological factors, being a key element in the understanding of various psychiatric conditions (SANTOS & OLIVEIRA, 2019).

Psychiatric disorders, such as depression, schizophrenia, and bipolar disorder, have complex and multifactorial neurobiological bases, involving changes in synaptic plasticity, neural connectivity, and the expression of neurotrophic factors. Depression, for example, has been linked to reduced hippocampal volume and decreased levels of brain-derived neurotrophic factor (BDNF), a protein essential for neuronal survival and regeneration. This reduction in plasticity can result in the brain's reduced ability to adapt to new challenges and respond appropriately to environmental stimuli. Treatment with antidepressants and repetitive transcranial magnetic stimulation (rTMS) has shown potential to reverse these changes, promoting neurogenesis and restoring synaptic function (COSTA & LIMA, 2017).

In schizophrenia, dysfunction of synaptic plasticity compromises the efficiency of communication between different brain regions. Deficiencies in glutamatergic neurotransmission and GABAergic inhibitory modulation are among the main factors contributing to cognitive deficits and the disorganization of thought characteristic of the disease. Research suggests that interventions such as transcranial direct current stimulation (tDCS) and the use of second-generation antipsychotics can modulate neural activity, favoring functional reorganization and improving patients' cognitive performance (MENDES & RODRIGUES, 2021).

Bipolar disorder also has a strong relationship with neuroplasticity. Studies suggest that recurrent episodes of mania and depression can induce structural changes in the brain, especially in the connectivity between the prefrontal cortex and limbic regions such as the amygdala and hippocampus. These modifications contribute to emotional instability and difficulty in mood regulation. Lithium, one of the most widely used mood stabilizers, has demonstrated neuroprotective effects by increasing BDNF expression and promoting neurogenesis, suggesting that part of its therapeutic effect is directly related to the modulation of neural plasticity (SILVA & PEREIRA, 2018).

In addition to these disorders, neuroplasticity is also implicated in other psychiatric conditions, such as anxiety disorders, obsessive-compulsive disorder (OCD), and autism

spectrum disorder (ASD). In anxiety disorders, amygdala hyperactivity and dysfunction of the prefrontal regulation of the stress response may be associated with difficulties in emotional adaptation. Therapeutic strategies that stimulate neural plasticity, such as cognitive-behavioral therapy (CBT) and meditation, have been shown to be effective in modulating connectivity between these regions, reducing anxious symptoms (BARBOSA & SILVA, 2022).

In this context, the investigation of the neurobiological mechanisms of neuroplasticity in psychiatric disorders has become an essential field of study for the development of new therapeutic strategies. Modulation of brain plasticity, whether through pharmacological interventions, neuromodulation, or psychotherapeutic approaches, represents a promising avenue for treating these conditions. However, there are still challenges, such as individual variability in response to therapies and the need for more standardized methodologies to assess neuroplastic changes over the course of treatment.

Thus, this systematic review aims to synthesize the available evidence on the relationship between neuroplasticity and psychiatric disorders, highlighting the mechanisms involved, the neurobiological alterations identified, and the potential clinical applications. From the analysis of the selected studies, it is intended to contribute to the advancement of knowledge about how neural plasticity can be modulated in psychiatric contexts and which strategies are most effective to improve patients' therapeutic outcomes.

METHODOLOGY

This systematic review was conducted based on the PRISMA guidelines to ensure a rigorous and transparent process in the selection and analysis of studies. The search was carried out in the SciELO, LILACS and VHL databases, considering publications from January 2015 to January 2025 that addressed the relationship between neuroplasticity and psychiatric disorders, using descriptors such as "neuroplasticity", "psychiatric disorders", "depression", "schizophrenia" and "bipolar disorder". Original articles, systematic reviews, and meta-analyses published in Portuguese, English, or Spanish were included, as long as they focused on neuroplasticity in humans, and studies without clear methodology, those based exclusively on animal models without clinical correlation, and duplicate publications were excluded. The selection began with the reading of titles and abstracts, followed by the complete analysis of the texts to confirm their eligibility, with the participation of two independent reviewers and, in case of divergences, a third reviewer. From the selected studies, essential information was extracted, such as bibliographic data, study design, sample characteristics, methods for assessing neuroplasticity, main findings and

therapeutic implications, which were organized and analyzed qualitatively. In addition, a critical evaluation of the methodological quality of the studies was carried out to ensure the inclusion of high-standard research, always respecting the ethical principles and copyright of the original researchers.

RESULTS

The search in the databases identified 150 articles, of which 25 met the inclusion criteria. Among the selected studies, the findings related to depression demonstrated that patients have reduced hippocampal volume and decreased levels of BDNF, evidencing an impairment of neuroplasticity. Therapeutic interventions, such as the use of antidepressants and repetitive transcranial magnetic stimulation techniques, have been associated with reversing these changes and promoting the functional recovery of neural circuits (Costa & Lima, 2017; Moura, 2023). Studies on schizophrenia have shown deficits in neural connectivity, with alterations in glutamatergic transmission and GABA-mediated dysregulation of inhibitory systems, correlated with cognitive and negative symptoms (Mendes & Rodrigues, 2021). In bipolar disorder, it has been observed that recurrent episodes of mania and depression are associated with changes in connectivity between the prefrontal cortex and limbic regions, such as the amygdala and hippocampus, and that the use of mood stabilizers, such as lithium, can increase BDNF expression and stimulate neurogenesis, contributing to mood stabilization (Silva & Pereira, 2018).

Additionally, studies on anxiety disorders, obsessive-compulsive disorder (OCD) and autism spectrum disorder (ASD) have indicated that changes in neural plasticity significantly affect emotional regulation and behavioral adaptation. Amygdala hyperactivity, coupled with ineffective regulation by the prefrontal cortex, results in exacerbated stress responses, while interventions such as cognitive behavioral therapy and meditation practices have been shown to improve neural connectivity and reduce symptoms in these disorders (Barbosa & Silva, 2022). In summary, the results suggest that the modulation of neuroplasticity is fundamental for the understanding and treatment of psychiatric disorders, offering a promising therapeutic approach to improve clinical outcomes and quality of life of patients.

DISCUSSION

The findings of this systematic review highlight that neuroplasticity is a central mechanism in the pathogenesis of psychiatric disorders and offers an innovative therapeutic perspective for the management of these conditions. The analysis of the 25

selected studies showed marked changes in neurogenesis, expression of neurotrophic factors, and synaptic reorganization in different disorders, demonstrating that these changes can both contribute to the development of symptoms and represent therapeutic targets.

In depression, studies have consistently shown that there is a reduction in hippocampal volume and decreased levels of BDNF, which is critical for the maintenance and regeneration of neural circuits. These findings suggest that impaired neuroplasticity may limit the brain's ability to respond to environmental stimuli and adapt to new challenges, contributing to the persistence of depressive symptoms (Costa & Lima, 2017). In addition, investigations show that antidepressant treatments, such as selective serotonin reuptake inhibitors, and non-pharmacological approaches, such as repetitive transcranial magnetic stimulation, can reverse these changes, increasing BDNF expression and promoting neurogenesis. These results are encouraging, as they indicate that modulation of neural plasticity may be a crucial component for functional recovery in depressed patients (Moura, 2023).

In the case of schizophrenia, the studies included in this review point to a significant disorganization of neural circuits, evidenced by deficits in glutamatergic transmission and dysfunction of GABA-mediated inhibitory systems. This dysregulation compromises the integration of information between different areas of the brain, resulting in cognitive and negative symptoms, such as difficulties in memory, planning, and organizing thought (Mendes & Rodrigues, 2021). Some of the studies suggest that the application of neuromodulation techniques, such as transcranial direct current stimulation, can promote a functional reorganization of the affected circuits, improving cognitive performance and reducing negative symptoms. This approach represents a promising alternative to traditional treatment, which is often limited to symptom control without correcting underlying changes in neural connectivity.

In bipolar disorder, the reviewed data indicate that recurrent episodes of mania and depression are associated with structural and functional changes, especially in connectivity between the prefrontal cortex and limbic regions, such as the amygdala and hippocampus. This dysfunction in neural communication can be interpreted as a marker of the emotional instability that characterizes the disease. Studies have shown that mood stabilizers, particularly lithium, can exert a neuroprotective effect by increasing BDNF expression and stimulating neurogenesis, which contributes to mood stabilization and relapse prevention (Silva & Pereira, 2018). These findings reinforce the hypothesis that neuroplasticity modulation is a central mechanism in the efficacy of treatments for bipolar disorder,

suggesting that strategies aimed at restoring neural circuits may be essential for controlling acute episodes and maintaining long-term emotional stability.

In addition to the disorders mentioned, the reviewed studies also addressed aspects related to anxiety disorders, obsessive-compulsive disorder (OCD) and autism spectrum disorder (ASD). In individuals with anxiety disorders, amygdala hyperactivity and impaired prefrontal regulation result in an exacerbated stress response, which impairs the ability to adapt emotionally. Interventions that stimulate the reorganization of neural circuits, such as cognitive-behavioral therapy and meditation practices, have shown positive results in normalizing these neural patterns, contributing to the reduction of anxiety symptoms (Barbosa & Silva, 2022). In OCD, the rigidity of neural circuits, which prevents the extinction of compulsive behaviors, can be attenuated by novel neuromodulation approaches, suggesting that the reestablishment of synaptic plasticity may facilitate behavioral flexibility. In patients with ASD, the early promotion of neuroplasticity has been shown to be fundamental for the development of social and adaptive skills, reinforcing the importance of interventions that stimulate synaptic reorganization in early stages of development (Barbosa & Silva, 2022).

Additionally, other important findings point to the influence of environmental and behavioral factors on the modulation of neuroplasticity. For example, regular exercise and participation in cognitively stimulating activities were associated with improvements in neural plasticity, suggesting that non-pharmacological interventions may complement conventional treatments and offer long-term benefits. These data reinforce the idea that the promotion of neuroplasticity is multifaceted, involving everything from pharmacological treatments to lifestyle changes and psychosocial interventions.

In summary, the discussion of the results of this systematic review shows that the modulation of neuroplasticity is an integrated and promising therapeutic strategy for the treatment of psychiatric disorders. Although methods and individual responses vary considerably between studies, the convergence of current findings suggests that interventions that promote the reorganization of neural circuits can significantly improve clinical outcomes. However, the heterogeneity of the evaluation methods and the variability of the samples highlight the need for future research with standardized methodologies, which can better clarify the underlying mechanisms and guide the development of more personalized therapies. Thus, an in-depth understanding of neuroplasticity not only expands knowledge about the pathophysiology of psychiatric disorders, but also opens new perspectives for therapeutic interventions aimed at restoring and strengthening neural circuits, promoting an overall improvement in the quality of life of patients.

CONCLUSION

Therefore, this study shows that changes in neuroplasticity are strongly linked to the pathogenesis of psychiatric disorders, such as depression, schizophrenia, and bipolar disorder. The reduction in hippocampal volume, low levels of BDNF and the disorganization of neural circuits compromise the adaptive capacity of the brain, contributing to the emergence and maintenance of symptoms. At the same time, interventions that stimulate the modulation of plasticity, whether through antidepressants, mood stabilizers, or neuromodulation techniques, have shown potential to reverse these changes, promoting improvements in clinical outcomes and quality of life of patients.

However, the heterogeneity of the methods and the variability of the samples used in the studies reinforce the need for future research with standardized methodologies and larger samples, in order to deepen the understanding of neuroplastic mechanisms. Thus, the modulation of neuroplasticity is configured as a promising and integrated therapeutic strategy for the treatment of psychiatric disorders, paving the way for more personalized and effective interventions in the field of clinical neurosciences.

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