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Medication and cognitive-behavioral therapy treatment effects on the brain in depression

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Abstract
Major depression is an affective disorder with a huge impact both on the quality of life at a personal level and on social or economic functioning. At a neurobiological level, depression may disturb brain activity, which emphasizes even more the need for implementing a highly efficient treatment in the case of major depressive disorder. The purpose of the present article is to present medication and cognitive-behavioral therapy (CBT) effects on the brain and to mention their implications in clinical practice. Research indicates that pharmacological treatment is associated mostly with a rapid remission of some symptoms, and psychotherapy may produce cognitive changes with long-term benefits.
Keywords: depression, brain, cognitive-behavioral therapy, medication, antidepressants.

Introduction

Major depression is one of the most frequent affective disorders and may strongly affect a person's functioning in the personal, professional or social area. Depression prevalence was estimated at 8% in the case of adults in Europe and the United States in 2018 (Brody et al., 2018).

The diagnosis of major depressive disorder involves the presence of significant modifications for at least two weeks, which are necessary to include a sad/ depressed mood or anhedonia. In addition, many symptoms may appear, such as significant and unintentional weight loss or gain, sleep problems, fatigue, inutility or guilt, psychomotor agitation or retardation, reduced thinking or concentration ability, and recurrent thoughts of death or suicide attempts (***, 2013).

Depression correlates negatively with multiple social functioning dimensions, such as interpersonal communication, group affiliation or expressing empathy (Kupferberg et al., 2016). In terms of its relation to physical health, research demonstrates that depression is commonly coupled with two or more somatic conditions (Stubbs et al., 2017).

Besides affecting the quality of life at an individual level, depression may have a significant economic impact through work performance impairments. It was shown that depression is associated with annual financial costs of more than $5500 per person in some countries (Evans-Lacko & Knapp, 2016).

Given the massive and global costs of depression, the collaboration between mental health professionals is important for the establishment of the most appropriate and efficient therapeutic scheme in its treatment.

Depression impact on the brain

At a cerebral level, depression is associated with particular changes related to the brain structure or functioning. For example, in the case of people who face depression, brain activity is reduced in the left part of the prefrontal cortex, a region which is correlated with reward seeking and positive emotions (Davidson, 2000). Thus, these people are less likely to look for pleasurable experiences. Generally, depression is correlated with a diminished activity in the prefrontal cortex, especially with medial prefrontal cortex deficits that are linked to high stress levels (Debener et al., 2000; Belleau et al., 2019). Moreover, it was shown that the hippocampus, an important area for both memory and emotion regulation, has a smaller volume in people who are diagnosed with

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depression (Sheline et al., 2019). Probably due to prolonged negative states, the amygdala is also more activated in those who display a cognitive vulnerability to depression (Drevets, 2001; Zhong et al., 2011).

The anterior cingulate cortex is a brain region that is more active in novel situations, especially in those requiring a fast decision and the adjustment of previously established action plans, activities that involve attention and executive functions (MacDonald et al., 2000). In the case of depression, the anterior cingulate cortex is less active, and these patients' reactions are slower (Pandya et al., 2012).

Nevertheless, depression effects on brain morphology and functioning may vary across individuals, which points to the necessity for adjusting different types of treatment to specific structures and traits (Müller et al., 2017).

Moreover, early negative experiences, which are common among patients who suffer from depression, may alter brain connectivity in many areas that are essential to emotion-regulation and cognitive functions (Yu et al., 2019).

The impact of pharmacologic and non-pharmacologic treatment on the brain in depression

In the case of major depression, research using neuroimaging techniques demonstrated that its treatment is associated with modifications related to the brain functioning or structure, but the effects of interventions are different (Linden, 2006). Medication is often accompanied by modifications at the level of subcortical regions such as the hippocampus or amygdala, which suggests a bottom-up effect, while CBT may influence brain activity especially at the level of the prefrontal cortex, exerting a top-down effect (Goldapple, 2004). A number of studies support this hypothesis. For example, a meta-analysis concluded that medication and CBT have different roles that complement each other in the treatment of depression (Boccacia et al., 2016). Specifically, medication treatment produces changes which are related mostly to subcortical areas of the brain, such as the amygdala or insula, which may provide a quick relief of some symptoms, particularly physical sensations and reward processing (Kalani et al., 2009). On the other hand, CBT mainly influences the prefrontal cortex, the temporal lobe and the middle cingulate cortex areas (Boccacia et al., 2016). These regions are responsible for cognitive processes involved in memory, retention and retrieval (de Zubicaray et al., 2001), but also for self-relevant information processing (Kelley et al., 2002). Hence, pharmacologic treatment generates an instant relief of some symptoms, especially physiological ones, while psychotherapy may profoundly influence the evolution of cognitive and emotional problems, bringing about stable and sustainable benefits for patients with depression (Boccacia et al., 2016). Li et al. (2018) also reported a different pattern of depressive symptom improvement after medication and psychotherapy, with medication preferentially reducing somatic manifestations such as diurnal variation in the first two weeks of treatment, and attribution retraining group therapy (a form of CBT) relieving anxiety, cognition disturbance, retardation and hopelessness in the sixth week of intervention (Li et al., 2018).

However, other investigations do not support the existence of a segregation of effects. The findings of another meta-analysis indicate decreases in the cingulate gyrus, inferior frontal gyrus and insula activation after patients with anxiety and depression received psychotherapy, suggesting that differentiation between treatment options may be more complex (Marwood et al., 2018).

Conclusions

1. Medication and cognitive-behavioral therapy interact in the treatment of major depressive disorder, accomplishing different functions that ensure the efficiency in reducing emotional difficulties on the long run. Research indicates that these treatment modalities have separated and interactive effects on brain functioning, thus targeting several clusters of symptoms.

2. The instant symptom remission due to medication, particularly related to somatic complaints, may represent the foundation for psychotherapeutic intervention, which is characterized by broader state improvements that persist after pharmacologic treatment has ended. Given their complementary effect, the implementation of a treatment scheme that combines the two intervention modalities is recommended, notably in the case of patients with severe depression.

Conflicts of interests

The authors declare that there is no conflict of interests.

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