NEUROIMAGING IN PEOPLE WITH DEPRESSION: SEARCHING FOR PATTERNS AMONG ADOLESCENTS

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SEPTEMBER 10, 2024

Abstract

Neuroimaging visualizes the brain's activity and structure, focusing on functional magnetic resonance imaging (fMRI) and magnetic resonance imaging's (MRI) role in analyzing brain functions and deviations. Major Depressive Disorder (MDD) is a condition of the brain, known for continuous feelings of grief and loss of interest in life, accompanied by diverse physical issues in adolescence - the pivotal phase of growth - during which the brain undergoes notable transformations in both its structure and function. This makes it an important stage to investigate the onset of conditions, like depression as highlighted by research studies [15]. The current review focuses on using neuroimaging techniques, specifically fMRI with MRI, to explore abnormalities in adolescents with MDD. The findings reveal structural changes in specific brain regions: the amygdala, prefrontal cortex, and hippocampus, which are connected to both cognitive performance and emotional regulation. Consequently, during a time of significant brain development, understanding such neural mechanisms via neurofeedback could be key to developing more targeted treatments for adolescent depression [21].

1 Roadmap

This article will examine how brain activity of adolescents with MDD is studied via fMRI & MRI. Additionally, it will summarize the existing research analysis on the neural correlations of depression (particularly in the amygdala, hippocampus, and prefrontal cortex). It will also provide the advantages and disadvantages of the current methodology as well as future directions with limitations.

2 Introduction

Important features of neural development occur during adolescence, including the pruning of synapses and shaping connections between brain regions. These features of neural development are thought to reinforce emotional control and shape cognitive functions during the adolescent stage of life [15]. While emotional control and cognitive development are thought to be positives for the individual experiencing neural maturation, the phase of adolescent development can also increase mental and cognitive health risks. Specifically, the brain's high degree of plasticity during this developmental stage also makes it vulnerable to the impact of stress and other external influences. It is thought that the impact of stress and environment on the rapidly developing adolescent brain may be one of the central features that leads to conditions like depression [21]. Studies using neuroimaging have shown brain activity patterns in teenagers experiencing depression, particularly in the amygdala, hippocampus, and prefrontal cortex, which are linked to regulating emotions [15] [12].

According to a survey conducted by The World Health Organization (WHO) in 2020, 10-20% of young adults reported mental health issues with depression being prevalent among them. MDD can remarkably affect an individual's communication and academic performance. Additionally, the lost interest in life and increased burden of daily activities with trouble focusing results in a higher probability of suicide [3] [7] [19]. Therefore, it is important to understand the causes of adolescent depression to develop truly effective interventions and treatments [12][18].

Neuroimaging has provided insights into the development of depression in the brains of young adults via techniques like fMRI and MRI to identify key brain parts such as the prefrontal cortex, hippocampus, and amygdala that are strongly connected to symptoms of depression at a young age. Using such approaches, researchers can gain a better understanding of neural processes responsible for depression during adolescence [12] [18].

3 How We Study Brain Activity – fMRI and MRI

3.1 What is MRI & fMRI?

MRI (Magnetic Resonance Imaging) and fMRI (Functional Magnetic Resonance Imaging) are non-surgical techniques to investigate brain structure and function. Paul Lauterbur and Sir Peter Mansfield created MRI in the 1970s. The method uses magnetic fields and radio waves to monitor hydrogen atoms in organic tissues to create detailed brain architecture drawings. This approach has proven successful at recognizing brain volume deformations and structural deviations. Conversely, Seiji Ogawa and colleagues invented fMRI in the early 1990s to quantify brain activity by recording blood flow. This method implies cerebral blood flow and neuronal activity are linked. fMRI can map brain regions that grow

more active during cognitive tasks or at rest by measuring oxygen consumption. Both methods have greatly improved our knowledge of the neurological causes of various psychiatric disorders, including depression, in adolescents.

3.2 Empirical Research Validating Specific Perspectives or Discoveries

The research performed by Yang et al. (2010) [19] revealed that teenagers suffering from significant depression showed increased activation of the amygdala in comparison to healthy people when engaged in emotional processing activities. Moreover, the study conducted by Hulvershorn et al. (2011)[7] revealed consistent evidence of impaired connectivity in pediatric major depressive illness, including in the brain response to emotional stimuli. Cullen et al. (2014)[3] stipulated evidence that adolescents suffering from depression exhibited atypical functional connectivity in the amygdala during resting states. This finding implies that these disturbances may be the underlying cause of mood regulation difficulties related to depression. The congruity of results across several research studies underscores the important role of the amygdala in impairments in emotional processing during depression. However, although these results offer convincing proof supporting the importance of the amygdala, they additionally highlight the complicated nature of depression, suggesting that abnormal neural activity and connections in this region are part of a broader network of dysfunctions. The consistent results from various studies support the conclusion that the heightened activity and disturbed connection of the amygdala represent important features of adolescent depression, suggesting that it could be an exciting field of study for therapies. Despite a number of convincing studies supporting the role of the amygdala in adolescent depression symptoms, several studies are inconsistent with that view. For instance, Ho et al. (2014)[6] noted that though the amygdala is often associated with MDD in adolescents, not all research provides consistent information about its functional connection with other areas of the brain. The discrepancies may be ascribed to differences in the design of the investigations, the size of the samples, and the methodology used for analysis. Besides, Zhang et al. (2018)[20] did a systematic review which found that although neuroimaging studies offer useful insights, their predictive capacity into the emergence and development of depression remains restricted. This highlights the importance of carrying out longitudinal studies to demonstrate a causal relationship [20].

4 Brain activity and depression

4.1 Where is depression in the brain & what does it look like in the brain?

Young people with age-associated MDD can experience health issues, reduced immune systems, and suicide [1]. MRI and fMRI studies have greatly improved

our understanding of depression-related brain activity. Neuroimaging has identified MDD areas of the brain with structural and functional abnormalities. The prefrontal cortex, hippocampus, and amygdala have links to depression. Depression impairs these brain regions, which control emotions, make decisions, and retain memories.[13] [10]

4.2 Regions indicating activity during MDD

Many neuroimaging studies consistently emphasize the important role of the prefrontal cortex (PFC) in the onset of clinical depression. The primary function of this area is to enable complicated mental processes such as critical thinking, strategic planning, impulse management, and emotional control. Executive functions, such as attention maintenance, working memory, and the integration of cognitive and emotional information, are mainly controlled by the dorsolateral subregion of the prefrontal cortex [12]. The ventral frontal cortex, located in the medial area of the prefrontal cortex, plays a vital role in regulating feelings and identifying potential conflicts between emotional stimuli and cognitive control [5] [16]

In the context of depression, hyperactivity in the ventral anterior cingulate cortex (ACC), which is also located in the medial wall of the frontal lobe, refers to the increased activation of this structure in response to emotional stimuli, particularly those that are negative or stressful. It has been suggested that this excessive activity plays a role in the emotional processing impairments seen in depression, notably heightened sensitivity to negative feelings and challenges in controlling feelings of anger [5]. The increased activity in the ventral anterior cingulate cortex (ACC) during periods of depression indicates that this neuronal area may be excessively involved in the processing of emotional information, resulting in the widespread sensations of sadness as well as despair that are typical of depression. Hare et al. (2020)[5] conducted a meta-analysis that highlights the essential function of hyperactivity in the ventral anterior cingulate cortex (ACC) in MDD, connecting it to the emotional dysregulation that characterizes the condition. The hippocampus is an essential cortical area that is involved in the formation, retrieval, and spatial orientation of recollections and is frequently impacted by MDD. In studies unrelated to depression, the hippocampus plays an essential part in the consolidation of short-term memories into long-term memories and is crucial for providing context to emotional experiences [9]. In addition, its linkages with the hypothalamus and the limbic system lead to its involvement in the processing and regulation of responses to stress[20]. Structural MRI examinations in people with MDD systematically demonstrate a decrease in hippocampus volume, a factor often linked with poor memory and cognitive performance. The decrease in volume is believed to be caused by the neurotoxic consequences of persistent stress, which can precipitate the depletion of hippocampus neurons and a decline in neurogenesis [12]. The decreasing size and activity of the hippocampus in depression may be a contributing factor to the cognitive manifestations of the condition, including challenges in concentration, memory retrieval, and a general slowdown of cognitive functions [21].

The amygdala, a small almond-shaped structure deep within the brain, plays an important part in the cognitive processing of emotions, namely those related to fear, identification of threats, and acquisition of rewards [11]. Moreover, it plays a role in the control of social conduct and the process of making judgments affected by emotional signals [9]. Yet, the most important role of the amygdala is to evaluate the emotional significance of inputs and to assist significantly in the formation of emotional memories. Under the overall picture of depression, the amygdala frequently displays heightened activity in response to negative stimuli, as evidenced by task-based fMRI investigations of depressed adolescents. The observed hyperactivity in the amygdala is symptomatic of an increased emotional reactivity, wherein those suffering from depression might experience greater levels of persistent negative emotions when confronted with common stressors [11]. The comprehensive review performed by Kerestes et al. (2014) [9] revealed that adolescents with depression have a specific substantial rise in their amygdala response. This suggests that the excessive activity of the amygdala might have a role in the emotional dysregulation and negative affective bias that occur in this illness. MDD involves broken connectivity across numerous brain regions, creating a network of malfunction that complicates significant signs of depression. The prefrontal cortex, anterior cingulate cortex (ACC), hippocampus, and amygdala affect mood, emotions, and cognition[20]. Empirical evidence shows that depression often results in disrupted communication across these regions, characterized by both excessive and insufficient activity in multiple domains depending on the particular circumstances. As a case study, the amygdala may have greater activity when exposed to negative stimuli, but the prefrontal cortex may display reduced activity, indicating a reduced capacity for controlling emotional reactions from a higher level of the brain [5]. An inequality in activation might cause a failure in the synchronization between mental control (prefrontal cortex) and emotional processing (amygdala and ACC), resulting in the extensive emotional and cognitive disruptions observed in depression. The meta-analysis conducted by Zhang et al. (2018)[20] offers evidence that depression is defined by a lack of efficient communication between various brain regions, which could be the underlying cause of the chronic and recurrent nature of the illness.

In addition, studies have shown that the degree of connectivity between prefrontal cortex, hippocampus, and amygdala can change based on the developmental stage of depression (e.g., acute vs remission) and individual differences in the severity of symptoms [12]. The observed variation in association patterns suggests that the brain circuits involved in depression have adaptability and the capacity to experience modifications over time, therefore influencing the development and therapeutic choices for the disorder.

5 Neurofeedback for Adolescent Depression

5.1 What is Neurofeedback?

Neurofeedback is a form of treatment that uses real-time mapping of brain activity to instruct individuals in self-regulating their brain function. Based on the premise that individuals have the ability to modify their brainwaves through deliberate practice and constructive critique, this approach has the potential to result in the amelioration of symptoms associated with mental health conditions like depression. Neurofeedback usually entails the use of an electroencephalogram (EEG) to observe brainwaves and provide feedback to the individual, thus allowing them to acquire the ability to control their brain activity [8].

5.2 Positive Aspects & Limitations of Neurofeedback

Studies have demonstrated that neurofeedback is an effective, non-invasive, and free drug therapy for depression [16]. Several studies have demonstrated that it can result in improved mood, cognitive function, and overall health among individuals suffering from depression [4]. Neuro management is particularly beneficial for teenagers since it builds a sense of subjectivity and empowerment, enabling them to actively engage in therapy [8]. Although neurofeedback has the potential to provide beneficial results, it also has certain constraints. Ongoing discussion surrounds the effectiveness of neuromanagement in treating depression since some research has reported ambiguous or conflicting findings [17]. In addition, Neurofeedback necessitates particular supplies and skilled professionals, rendering it less cost-effective when compared to alternative therapy modalities. Further broad research is required to establish consistent processes and determine the most efficient learning paradigms for different people and forms of depression [14]. Cohen Kadosh et al. (2013)[8] showed that regulating the prefrontal cortex neurobiologically can profoundly alleviate symptoms of depression in teenagers. It is established that the prefrontal cortex, or PFC, is crucial in cognitive processes including decision-making, emotional regulation, and executive control, which can frequently be impaired in people who suffer from depression. By employing neurobiocontrol to regulate activity in this specific area of the brain, participants achieved better regulation of their emotional responses and experienced an overall improvement in their mental well-being. The results indicate that neurofeedback psychotherapy can successfully enhance the operation of the prefrontal cortex, resulting in a decrease in depressive symptoms. The significance of this study lies in the emphasis it places on the therapeutic potential of neurofeedback as a non-invasive and personalized treatment for adolescents, a population that is especially vulnerable to depression and frequently unresponsive to conventional pharmacological therapies. The capacity to selectively target particular brain regions and deliver immediate feedback is a distinct benefit, rendering neurobiological management a viable field for further study and use in clinical settings [8]. In their randomized controlled playaround, Fernández-Alvarez et al. (2022) [4] showed

the efficacy of neurobiological therapy in mitigating depressive symptoms and enhancing emotional regulation among adolescents diagnosed with depression. The evaluation demonstrated that a mix of neurobiological treatment with cognitive behavioral therapy (CBT) yielded even more significant outcomes. Signs point to a synergistic impact whereby neurobiological management improves the cognitive techniques investigated in CBT by directly addressing brain areas implicated in emotional regulation, such as the prefrontal cortex and amygdala. The integrated tactics, which combine neurological treatment with cognitive-behavioral therapy, enable a more thorough treatment that tackles both cognitive and neurobiological components of depression. Specifically, the findings of this study indicate that combining neurobiology management with established psychotherapy methods might improve treatment results for teenagers who may benefit from an integrated approach to addressing depression. This study emphasizes the need to consider combined therapies to optimize the effectiveness of treatment. It proposes that neurobiological management could be a useful additional component in the therapy of depression in adolescents [4]

6 Summary

Several similar themes were identified in neuroimaging research for the treatment of adolescent depression, including the possibility of neurobiocontrol that might improve mood and cognitive performance by regulating specific brainwave patterns. Nevertheless, the inherent diversity in the methodology of research, training procedures, and measurement methods poses challenges in establishing conclusive findings regarding their effectiveness. In the realm of depression treatment, neurobiocontrol presents a non-invasive and individualized modality, which may hold particular appeal for adolescents. This intervention can enhance standard treatments by modifying specific brainwave patterns linked to depressive symptoms [8] [4] Nevertheless, there is no strong and clear evidence supporting the efficacy of neurobiological therapy in treating depression. The dearth of uniform procedures and the lack of consistency in research design pose challenges in formulating definitive conclusions. Furthermore, neurofeedback requires specialized equipment and knowledge, thus potentially restricting its accessibility [17] [14].

6.1 Future Directions

1. **The use of neuroimaging as a means to identify trends in brain growth in adolescents:** Neuroimaging offers significant potential as an approach for identifying anomalies and trends in brain development among teenagers. By applying strategies like fMRI and magnetic resonance imaging (MRI), scientists are able to track alterations in brain structure and function over time, therefore potentially identifying the first indications of mental health conditions such as depression. Putting early intervention first and utilizing more focused therapies can enhance outcomes for

adolescents who are susceptible to depression [12] [21].

2. **Impact on treatment modalities:** Enhanced understanding of the brain activity patterns linked to depression enables medical professionals to devise more efficacious therapies. One application of neuroimaging data is the recognition of specific brain regions that ought to be focused on in therapeutic interventions like neurobiocontrol. Using this personalized treatment strategy has the potential to enhance the effectiveness of treatment and decrease the possibility of relapse [18] [15].

3. **Contribution to the understanding of neural mechanisms:** A closer examination of the brain processes that underlie adolescent depression might improve our comprehension of the development and progress of the condition. The discovery of the precise brain regions and circuitry involved in depression allows researchers to acquire an understanding of the biological foundation of this condition, which helps with the development of novel treatment and prevention strategies [2] [3]

6.2 Limitations

1. **Cost and availability of fMRI and MRI:** An intrinsic constraint of neuroimaging research is the exorbitant expense and resource requirements related to fMRI and MRI. These methodologies necessitate costly technology and specialized facilities, so restricting their accessibility and capacity for growth. In addition, the exorbitant costs related to neuroimaging studies can restrict the scale and variety of study groups, consequently leading to partially biased findings [12] [15].

2. **Participant pool bias:** The volunteer pool in neuroimaging research may exhibit bias due to the limited accessibility of these techniques. For instance, research is more inclined to include individuals from higher socioeconomic situations who have the means to avail themselves of medical institutions that offer neuroimaging services. Such limitations may restrict the generality of findings and fail to consider substantial differences in brain anatomy and function among various categories [6] [20].

3. **Inaccuracies in data interpretation:** Analysis of neuroimaging data is an intricate procedure that entails making inferences about the correlation between brain activity and behavior. However, other variables could influence brain activity, therefore confounding the identification of the precise origin of the observed pattern. For example, specific parts of the brain may exhibit activity during fMRI scans for reasons that are not directly related to the task under investigation, which can result in potential mistakes in the interpretation of the information that is given [2] [21].

7 Conclusion

Functional magnetic resonance imaging (fMRI) and fMRI have greatly enhanced our comprehension of depression in adolescents by uncovering distinct patterns of brain activity linked to this condition. The discoveries have yielded an invaluable understanding of the neural mechanisms that underlie depression, particularly in the amygdala or prefrontal cortex. However, there are still substantial research gaps that need to be solved, such as the requirement for longitudinal investigations, consistent neurobiocontrol techniques, and more diverse study groups. Despite these difficulties, the ongoing investigation of neuroimaging in research on adolescent depression shows enormous promise for enhancing therapy and acquiring a broader understanding of the neurological substrate of depression [3] [15].

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