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Review article

Neuroimaging findings of adolescent depression: A review by the Research Domain Criteria (RDoC) framework

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ABSTRACT

This review examines neuroimaging studies on adolescent depression (AD) within the Research Domain Criteria (RDoC) framework, focusing on fMRI, DTI, and EEG findings. The research highlights disrupted connectivity in several neural networks—such as the affective, reward processing, cognitive control, and default mode networks—that underpin emotional and cognitive dysfunctions in AD. Notably, hypoconnectivity in the affective and cognitive control networks correlates with deficits in emotional processing and executive functioning, while hyperactivity in the default mode network relates to excessive self-referential thoughts. Additionally, blunted reward responses and frontal–striatal connectivity are discussed alongside the therapeutic potential of cognitive behavioral therapy (CBT) to modulate these dysfunctional circuits. Despite these insights, variability in findings due to small sample sizes and diverse methodologies suggests a need for further research to validate neuroimaging biomarkers for treatment efficacy and to explore less studied treatments like ECT and TMS in this population. This review underscores the importance of integrating neuroimaging findings to enhance understanding and treatment of AD.

Contents

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1. Introduction

Adolescent Depression (AD) has been significantly increasing its incidence and prevalence in the United States. A recent report by the National Survey on Drug Use and Health showed an increase in the prevalence of depression among adolescents from 8.1% in 2009 to 15.8% in 2019 (Daly, 2022). This number has further increased roughly by 62% during and after the COVID-19 pandemic (Hawes et al., 2022). In a comparable trend, the occurrence of a year-long bout of depression in adolescents aged 12–17 showed a consistent climb, going from 8.3% in 2011 to 12.9% in 2016 (Lu, 2019). Often, Adolescent Depression develops into life-long depression and causes significant societal and economic burdens. However, our understanding of the pathophysiology of depression in this population has still been very limited (Johnson et al., 2018; Lynch and Clarke, 2006). This has been a major obstacle against providing more effective, pathophysiology-targeted treatment for this challenging mental health issue in adolescents (Fava et al., 2014).

To address this, many neuroimaging modalities have been used to illustrate the neurobiology of adolescent depression, including structural and functional MRI (fMRI), electroencephalography (EEG), and Diffusion Tensor Imaging (DTI). In this regard, our goal of this article is to provide a comprehensive, up-to-date review of the neuroimaging findings of adolescent depression (Hermens et al., 2019; Kerestes et al., 2014; O'Callaghan and Stringaris, 2019; Sherbaf et al., 2018). Specifically, we applied a neurocircuitry/neural system approach to this review by adopting the Research Domain Criteria (RDoC) framework (Kerestes et al., 2014). The National Institute of Mental Health (NIMH) initiated the RDoC agenda to lay out fundamental biobehavioral dimensions that span multiple current heterogeneous disorder categories (Insel et al., 2010; Leibenluft and Stoddard, 2013). The RDoC framework contains six higher level domains: negative valence systems, positive valence systems, cognitive systems, social processes, arousal and regulatory systems, and sensorimotor systems (of Mental Health, 2023). Using this framework, we aim to illustrate common and specific pathways leading to the psychopathology of adolescent depression, focusing on the findings of neuroimaging modalities, thereby potentially illustrating underlying neurobiological mechanisms.

In addition, we provided our review of the neuroimaging findings related to specific issues critical to this population, such as familial risk and suicidality. These topics pertain to the multiple layers of neural systems, from the genetic level (family risk) to symptom manifestation (suicide) within the RDoC framework (Beauchaine and Hinshaw, 2020). Finally, we examined the neuroimaging evidence for the best-studied treatment modalities for this condition. We discussed the clinical implications of the recent neuroimaging research as well as future directions.

We anticipate that this study will deepen our understanding of the neurobiological underpinnings of adolescent depression. This enhanced understanding is expected to guide us towards development of more effective and personalized treatment methods, offering relief to many adolescents and their parents suffering from this condition. Furthermore, by bridging the gap between neuroscience and clinical practice, this research underscores the significance of a multidisciplinary approach to complex mental health issues.

2. Method

In this study, we conducted a comprehensive literature search using the PubMed database in April 2024, with the aim of reviewing neuroimaging studies of Adolescent Depression within the Research Domain Criteria (RDoC) framework. We selected PubMed as our primary database due to its extensive indexing of high-impact journals in the medical and psychological sciences, which ensures a robust representation of relevant studies. The search was performed using Python version 3.12.2 with the BeautifulSoup version 4.87.1 library to automate and streamline the extraction of relevant data. Keywords such as 'depression,' 'adolescent,' and specific imaging modalities (fMRI, resting state fMRI, EEG, DTI) were utilized to generate a broad spectrum of potential studies.

After removing duplicates, a total of 2013 articles were initially retrieved. By applying the computational techniques, we aimed to maximize the efficiency and coverage of our literature review, ensuring that we comprehensively included as many relevant studies as possible. This approach not only enhances the breadth of our review but also supports the depth of analysis necessary to understand the complex neurobiological underpinnings of Adolescent Depression.

Upon reviewing these articles, 1220 out of 2013 were excluded as they did not meet our inclusion criteria, which required: (1) utilization of neuroimaging techniques, (2) diagnosis of Major Depressive Disorder or Dysthymic Disorder according to DSM-IV, DSM-5, or ICD-10 criteria (Association et al., 2000; American Psychiatric Association et al., 2013; Organization, 1992) or reliable measurements of depression such as the Beck Depression Inventory-II (Wu, 2017), and (3) study populations comprising adolescents aged 12–19 at the onset of the study. Consequently, a total of 793 studies remained eligible for our review. The trends of these selected studies by publication year can be seen in Fig. 1.

The results of these processes were systematically recorded and are presented in Table 1. This table categorizes the studies into different neuroimaging modalities as well as highlights major findings in specific neuro-circuitries implicated in each system of RDoC. We gave particular attention to findings involving neural areas implicated in the negative valence system functions such as emotional responding and emotion regulation (e.g., the amygdala, ventromedial prefrontal cortex (vmPFC), and anterior cingulate cortex (ACC)) as well as the reward processing system (e.g., ventral striatum (VST), anterior insula cortex (AIC), and posterior cingulate cortex (PCC)) since they are known to play critical roles in the neurobiology of Adolescent Depression (Clithero and Rangel, 2014; Critchley et al., 2000; Ernst and Paulus, 2005; Keren et al., 2018; McClure et al., 2004; Pessoa, 2009).

In addition to the RDoC approach, we provided a separate summary review of the DMN, a large-scale neural network that monitors self-referential brain activity and comprises the mPFC, PCC, and parietal regions (Horn et al., 2014). The DMN has been implicated in the development of Adolescent Depression due to dysfunctions that span multiple RDoC domains, including cognitive and social processing (Forbes et al., 2021). This system warrants a separate due to its significant role in AD (Coutinho et al., 2016; Schreiner et al., 2019).

To further refine our selection of articles, we employed a transformer-based bart-large model trained on the MultiNLI (MNLI) dataset to conduct zero-shot classification (Yin et al., 2019). Zero-shot classification is a machine-learning approach where a model is trained to recognize and categorize new, unseen categories without having been explicitly trained on those specific categories. This method leverages general knowledge and context to make accurate predictions, making it particularly useful in identifying relevant studies without requiring extensive labeled data. This process involved classifying each study according to its relevance to specific RDoC keywords based on classification scores. Studies with high similarity scores were prioritized in our review, allowing for a more focused and efficient analysis of the literature. This innovative method enhanced our review's efficiency by systematically identifying the most relevant studies based on their alignment with the targeted RDoC domains.

We then analyzed the frequency with which specific brain regions are mentioned in the abstracts of these selected papers. The frequency analysis highlights the principal brain areas that each RDoC domain focuses on, allowing for an effective overview of the neurobiological aspects extensively studied in these domains. This computational approach has efficiently pinpointed the principal brain areas, enhancing our understanding of the neural mechanisms involved in each domain

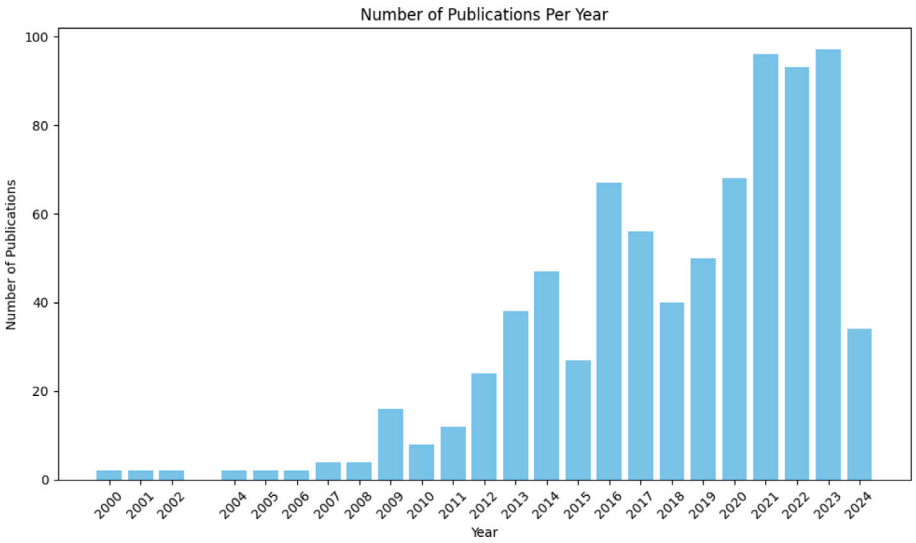

Fig. 1. Number of publications per year.

by systematically categorizing and analyzing the focal points of current research.

To identify the key papers matching specific keywords, we employed Eq. (1). This equation helped us to pinpoint the papers with the highest relevance to the keywords by finding the point of maximum change in relevance scores.

$$C = \arg\max(\Delta X) + 1 \text{ where } \Delta X = \{x_i - x_{i+1} | i = 1, \ldots, n-1\} \quad (1)$$

By applying this systematic approach, we provide a thorough overview of the current state of neuroimaging research in Adolescent Depression, emphasizing significant findings and suggesting directions for future research.

3. Results

3.1. Rdoc systems

3.1.1. Negative valence systems

Among the studies selected through specific search methods and inclusion criteria, a significant body of research was found to be within the negative valence system (NVS) of the RDoC framework. NVS is primarily implicated in responses to aversive situations or contexts such as fear, anxiety, and loss. These systems encompass subdomains like acute threat, potential threat, sustained threat, loss, and frustrative non-reward processes (of Mental Health, 2023).

Our zero-shot classification revealed that there were 115 studies highly relevant to NVS. The frequency with which specific brain regions are mentioned in the abstracts of these selected papers can be shown in Fig. 2.

- Functional MRI Findings
  The use of functional MRI has become integral in studies examining negative valence systems in adolescent depression. This imaging technique has been valued for its high spatial and temporal resolution. The main findings of fMRI studies on adolescent depression have revealed that the amygdala—a central region in negative valence systems—repeatedly exhibits heightened activation towards negative emotional stimuli or alterations in connectivity in this population. Research using resting state fMRI (rs-fMRI) has particularly revealed diminished functional connectivity between the amygdala and both the dorsolateral and ventromedial prefrontal cortex, as well as the pregenual anterior cingulate cortex, hippocampus, and precuneus in adolescents who are at high risk for depression (Connolly et al., 2017; Rzepa and McCabe, 2016). Interestingly, some studies show no differences in connectivity between the amygdala and the dorsolateral prefrontal cortex in affected adolescents, suggesting

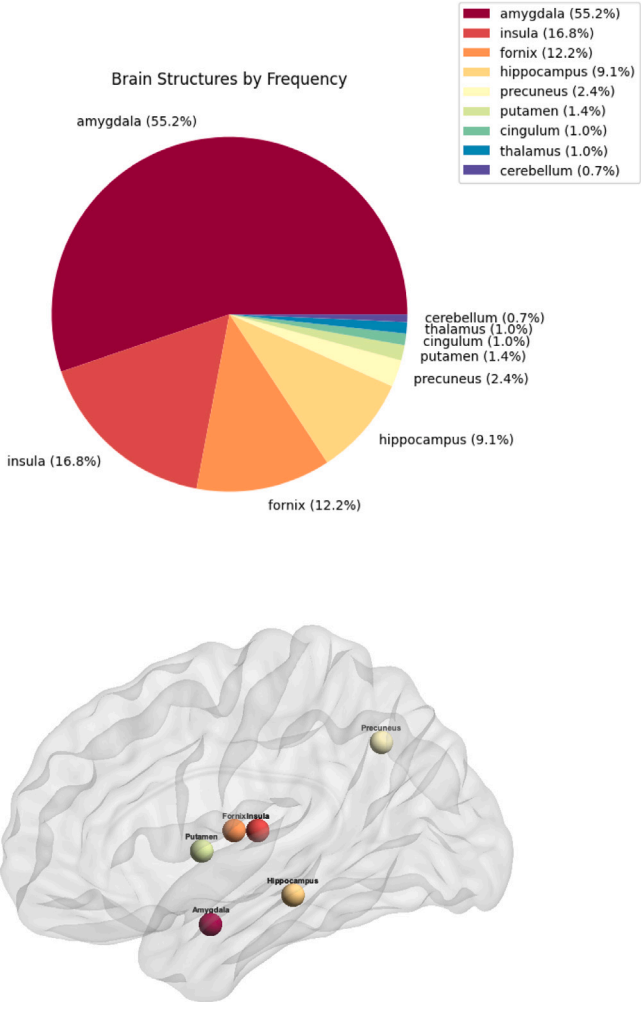

Fig. 2. Brain Structures in NVS-related articles.

Table 1
Methodology summary: Search strategy and inclusion criteria.

Summary of Search Strategy		
Database	PubMed	
Period	Latest search: April 2024	
Search Term Combination	((Resting state fMRI) AND (depression [Title])) AND (adolescent [Title])	28
	(“Depression” AND ((“Child” OR “Children”) OR (“Adolescent” OR “Adolescents”))) AND (“fMRI” OR “functional magnetic resonance imaging” OR “resting fMRI” OR “resting functional magnetic resonance imaging”)	1032
	(“adolescent” AND “depression” AND “fMRI”) (((Resting state fMRI) AND depression [Title]) AND adolescent [Title])	15
	((depression AND adolescent) AND (“fMRI” OR “functional magnetic resonance imaging”))	935
	(depression AND adolescent) AND (“resting state fMRI” OR “resting state functional magnetic resonance imaging”)	251
	(depression AND adolescent) AND (“Diffusion Tensor Imaging” OR DTI)	197
	((depression AND adolescent) AND electroencephalogram)	1113
	((brain structure) AND depression [Title]) AND adolescent [Title]	229
	Total of Non-Duplicate Entries =	2013
Summary of Inclusion Criteria		
Neuroimaging Modalities Used	Functional MRI	1152
	Resting State Functional MRI	187
	EEG	47
	DTI	37
Diagnostic Criteria	Major Depressive Disorder and Dysthymic Disorder by DSM-IV, DSM-5, or ICD-10	48
	Major Depressive Disorder and Dysthymic Disorder by ICD-10	6
	Reliable measurement of AD, such as Beck Depression Inventory-II	74
Study Population Age Range	Adolescents aged 12–19 at the inception of the study	905
RDoC Systems and Neural Areas	Negative Valence Systems: Amygdala	451
	Ventromedial Prefrontal Cortex (vmPFC)	72
	Anterior Cingulate Cortex (ACC)	446
	Reward Processing: Ventral Striatum (VST)	226
	Anterior Insula Cortex (AIC)	103
	Posterior Cingulate Cortex (PCC)	266
Focus of Assessment	Emotional Regulation	36
	Emotional Response	29
	Reward Processing	341
	Searched Article (2013) - Excluded by criteria (1220) = Total	793

that the relationship between amygdala connectivity and depression is complex and may vary depending on the specific target population (LeWinn et al., 2018).

Further functional MRI research has consistently found reduced connectivity in key brain regions involved in emotional regulation, such as the anterior cingulate cortex, hippocampus, insula, and the prefrontal cortex, among depressed adolescents, implicating dysfunctional/decreased connectivity of these areas as one of the key neurobiological mechanisms of adolescent depression (Plener et al., 2012).

Moreover, the role of familial risk on the negative valence system of adolescent depression has also been explored through functional MRI studies. One notable study involving typically developing adolescents demonstrated that those with a familial risk for depression showed heightened amygdala activation in response to negative stimuli compared to peers without such a background (Pilhatsch et al., 2014). Conducted during a perceptual discrimination task that systematically varied emotional valence, this study underscores the potential of amygdala reactivity as an early indicator of depression risk in genetically predisposed youths.

These findings affirm the importance of integrating both environmental and genetic perspectives when investigating the neural underpinnings of depression, providing a more comprehensive understanding of its complex etiology.

- EEG Findings Electroencephalography (EEG) has served as another critical tool in understanding the neurobiology of adolescent depression (AD), offering a less invasive and more cost-effective alternative to other neuroimaging methods. EEG studies have shown increased activity in the right medial frontal regions, which can predict the development of depression in adolescent males 12 months later, even after accounting for baseline depressive symptoms (Mitchell and Pössel, 2012). This demonstrates how EEG can be used to explore neural markers related to the negative valence system, making it a useful modality in understanding AD.

EEG studies related to the NVM have also revealed specific patterns in theta and alpha current density in the frontal region, differentiating depressed females from healthy controls. For example, females with AD exhibit greater alpha and theta current densities in the left dorsolateral prefrontal cortex (dlPFC), specifically in Brodmann Areas 9 and 46, compared to their healthy peers as they process negative emotional stimuli (Auerbach et al., 2015b,a). Adolescents with depression are more likely to recognize sad facial expressions and less likely to recognize low-intensity happy facial expressions, reflecting heightened sensitivity to negative emotional stimuli (Auerbach et al., 2015b). Female adolescents show reduced inferior frontal gyrus activity in response to negative words, suggesting biased self-referential processing (Auerbach et al., 2015a). Collectively, these findings underscore the role of the NVM in the emotional and cognitive biases observed in AD.

Additional findings highlight differences in brain activity when comparing adolescents with major depressive disorder (MDD) and comorbid anxiety to those with only MDD. Those with both conditions exhibit greater alpha power in the left frontal regions relative to the right, while no such interhemispheric differences are noted in adolescents only with MDD (Feldmann et al., 2018). This suggests that comorbid anxiety can impact neural activity patterns, emphasizing the importance of considering comorbid

conditions in studies of depression. Similarly, adolescents with AD show less alpha power in the left frontal regions compared to the right, indicating variations in neural activity patterns depending on the specific cohort and conditions studied (Grünewald et al., 2018). This asymmetry in frontal brain activity suggests that neural mechanisms related to negative valence systems, such as responses to psychosocial stressors and depression, are altered in depressed adolescents. Moreover, a higher average delta power has been noted in depressed adolescents compared to healthy controls, along with lower average coherence in the theta band within frontal regions (McVoy et al., 2019).

Overall, these EEG findings underscore the potential of neural activity in the frontal regions to serve as an indicator for the development of depressive symptoms in adolescents.

- DTI and White Matter Integrity

Diffusion tensor imaging (DTI) provides valuable insights into the impact of white matter microstructure alterations on the development of adolescent depression (AD). Notably, DTI has been instrumental in identifying specific neural pathways where changes may be linked to the onset and severity of AD, particularly those associated with the negative valence system (NVM). For instance, one study discovered reductions in fractional anisotropy (FA) across 19 different tracts in individuals with AD, including the internal capsule, thalamic radiations, and cerebellar tracts, illustrating the broad impact of AD on brain connectivity (Bessette et al., 2014). These findings are particularly relevant to the NVS, as regions such as the internal capsule and thalamus play crucial roles in emotional processing and regulation. The alterations in white matter integrity in these regions suggest that disruptions in neural pathways associated with the NVS may contribute to the emotional and behavioral symptoms observed in adolescents with depression.

Expanding on these findings, another investigation assessed the amygdala–prefrontal circuit, a key component of the NVM, in adolescents with major depressive disorder (MDD) using both resting-state functional magnetic resonance imaging (rs-fMRI) and DTI. This study revealed reduced functional connectivity between the left amygdala and left ventral prefrontal cortex, accompanied by lower FA values in the left uncinate fasciculus of the MDD group (Wu et al., 2020). These results emphasize the crucial role of both functional and structural connectivity impairments in the amygdala–prefrontal circuit in the neuropathophysiology of early-onset MDD.

Further investigations have shown that alterations in axial diffusivity (AD) and radial diffusivity (RD) in the dorsal cingulum bundle, which is involved in emotional regulation, were correlated with a history of major depression and increased overall severity of depression in adolescents. Similarly, reductions in FA, lower AD, and higher RD in the ventral cingulum, another NVM-related pathway, have been associated with greater depression severity (Barch et al., 2022). In contrast, some studies have found no significant differences in FA between youths with and without AD (Cullen et al., 2020), indicating the complexity and variability in how depression manifests in the brain's structural connectivity. These DTI findings highlight the multifaceted nature of neural changes in adolescent depression, particularly within the NVM.

3.1.2. *Positive Valence Systems*

Positive Valence Systems (PVS) play a crucial role in how individuals respond to positive stimuli and situations, influencing behaviors such as consummatory actions, responses to rewards, and overall engagement and interest (of Mental Health, 2023). These systems incorporate neural areas such as the frontostriatal pathways, the ventral tegmental area, and the nucleus accumbens, which are pivotal in the development of anhedonia—a lack of pleasure or interest in previously rewarding activities—in adolescents with depression (AD) (Medeiros et al., 2020; Henderson et al., 2013).

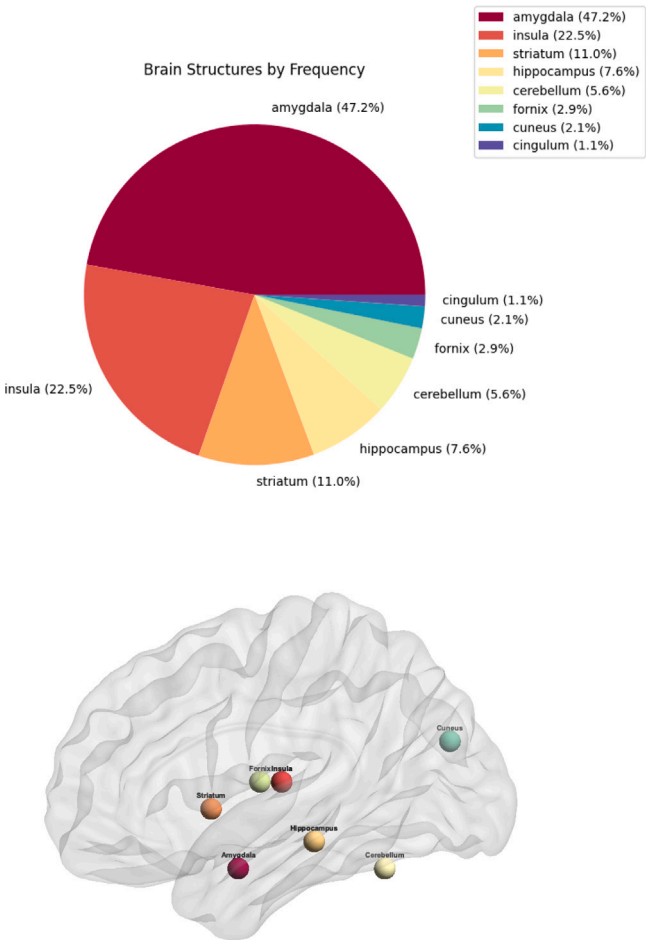

Fig. 3. Brain Structures in PVS-related articles.

By employing computational techniques, we identified 74 papers with high relevance to PVS. The frequency of mentioned brain regions within the abstracts is presented in Fig. 3. This figure highlights the primary brain areas that are the focus of PVS-related research, providing a visual summary of the key neural structures involved in the positive valence systems.

- Functional MRI Findings

There is compelling evidence to suggest impairments in the Positive Valence Systems in AD, particularly in the processing of rewards (Medeiros et al., 2020). Adolescents are particularly sensitive to rewards and more inclined to take risks compared to adults. This heightened reward sensitivity is due to increased activation in brain regions associated with reward processing during anticipatory phases of reward assessment (Luciana and Collins, 2012).

A central framework used to understand motivated behaviors in adolescents is the Triadic Model, which describes how three neural systems—the approach, avoidance, and control modules—interact to shape responses to reward stimuli (Richards et al., 2013). The approach module primarily involves the striatum and medial prefrontal cortices and is activated by rewarding stimuli, directly relating to PVS. The avoidance module, involving the amygdala, hippocampus, and insula, responds to aversive stimuli and is generally subdued in adolescents, who show lower aversive responses when potential rewards are at stake.

The control module, comprising prefrontal cortical structures, is crucial for attention and executive control. During adolescence, the balance of these modules shifts to favor the approach system, leading to increased seeking of rewards over aversive and control considerations (Richards et al., 2013).

In the context of AD, several studies have shown alterations of balance in the Triadic Model, highlighting disruptions in PVS. For example, adolescents with depression often exhibit reduced activation in the striatum and medial prefrontal cortex in response to rewarding stimuli, indicating a disruption in the approach system and thus in PVS (Kujawa et al., 2020). The avoidance system also shows altered activation patterns, with depressed adolescents exhibiting heightened amygdala responses to negative stimuli even in the presence of potential rewards, contrary to the typical adolescent response (Young et al., 2019). Furthermore, the control module's activity is often diminished, reflecting deficits in executive function and attention regulation in AD (Vilgis et al., 2015). These impairments collectively contribute to the altered reward processing observed in depressed adolescents, underscoring the significance of PVS disruptions in AD.

- DTI Studies on White Matter Integrity
  Diffusion tensor imaging (DTI) studies have illuminated the association between decreased white matter integrity and reward processing deficits in major depressive disorder (MDD) during adolescence. Specifically, one study identified reduced white matter integrity in critical areas such as the anterior corona radiata, anterior cingulum, and the genu of the corpus callosum, all correlating with depression severity (Henderson et al., 2013). Anhedonia, a hallmark symptom of MDD characterized by a diminished ability to experience pleasure, has been linked to decreased white matter integrity in the anterior limb of the internal capsule and projection fibers leading to the orbitofrontal cortex (OFC), which are vital in reward processing and the emotional valence of rewards (Henderson et al., 2013). Despite these findings, it is important to note that they did not withstand correction for multiple comparisons, indicating a need for cautious interpretation.
- EEG and Reward Sensitivity
  EEG studies provide additional insight into reward processing abnormalities in adolescent depression. Reward-related positivity (RewP), a neural marker of reward processing, is often blunted in adolescents with a history of depression or those predicted to develop depressive symptoms. RewP observed as a positive component during frontocentral EEG tasks involving monetary rewards, has been shown to be diminished in amplitude during positive outcomes in depressed adolescents (Proudfit, 2015; Bress et al., 2013). Moreover, increased delta activity related to monetary gains and theta activity related to losses has been implicated in the neural response to rewards, with altered delta activity predicting the development of depression later in life (Nelson et al., 2018). These findings emphasize the role of impaired reward processing mechanisms in the onset and progression of adolescent depression.

  In summary, youths with AD have demonstrated dysfunctional activation as well as connectivity in neural areas implicated in reward processing, especially social reward processing. However, this requires further future studies, potentially focusing on the differential phases of reward processing (anticipation phase versus appraisal of outcome phase) and the distinction between social versus non-social rewards (Richards et al., 2013).

3.1.3. Cognitive systems

Cognitive systems in the Research Domain Criteria (RDoC) framework, are essential for higher-level cognitive functions such as attention, working memory, planning, and decision-making (LeWinn et al., 2018). These systems play a crucial role in cognitive control processes, and their dysfunction can lead to altered top-down regulation of emotions. Specifically, abnormalities in cognitive control regions, such as the frontal cortices, are significant in adolescent depression (AD). Impairments in these areas may hinder the development of effective cognitive reappraisal strategies, which are vital for selecting goal-appropriate responses (Villalobos et al., 2021).

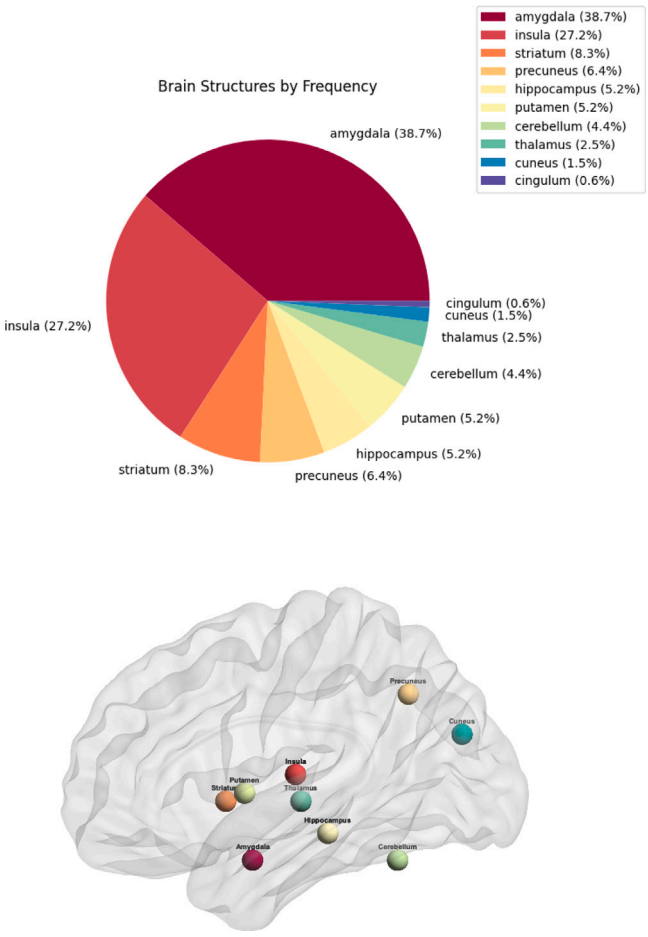

Fig. 4. Brain Structures in Cognitive-related articles.

To further our understanding of the Cognitive Systems as defined by the RDoC, we applied the same advanced computational methods previously described to select research papers that focus on these systems within the context of adolescent depression. A total of 288 papers were identified and analyzed, shedding light on how dysfunctions in cognitive control regions contribute to the complexities of AD. The specifics of the brain regions discussed in these studies and their frequency of mention are illustrated in Fig. 4.

- Functional MRI Findings
  The dorsolateral prefrontal cortex (dlPFC) and dorsomedial prefrontal cortex (dmPFC) are integral to cognitive control. The dlPFC is involved in attributing attention to salient stimuli, while the dmPFC plays a critical role in cognitive reappraisal (LeWinn et al., 2018). Studies using fMRI show that in healthy controls, increased activation in both the dmPFC and dlPFC correlates with reduced negative affect during cognitive reappraisal tasks. However, increased activation of these neural areas are often not shown in adolescents with depression, indicating a potential deficiency in cognitive control over negative affect, a pattern also observed in adult depression (LeWinn et al., 2018).

Interestingly, the connectivity between the dmPFC and regions like the anterior insula and inferior frontal gyri also appears diminished in AD, highlighting a possible disruption in cognitive appraisal mechanisms. Adolescents with depression often exhibit difficulties with cognitive control, particularly in areas related to impulse control and goal-directed behavior, which are closely associated with depressive symptoms, including suicide attempts and difficulties of concentration/diminished ability to think or concentrate (Defayette et al., 2021).

Conversely, some studies report preserved or even enhanced prefrontal cortex activity in depressed adolescents, suggesting variability in response patterns. One hypothesis is that increased activation in the prefrontal region in adolescents with major depressive disorder (MDD) may serve to suppress overactivity in the amygdala and insula in response to negative stimuli (Poon et al., 2022). This variability in findings might be attributable to differences in the emotional potency of the stimuli used in different studies as well as the variety of the symptom presentations/severity. Similarly, there were studies found no difference between depressed adolescents and healthy controls in their ability to activate the frontal cortex during instructed cognitive appraisal tasks, suggesting that while depressed adolescents can employ cognitive appraisal strategies, they may not do so spontaneously (Capitão et al., 2023).

The inconsistencies across studies regarding dmPFC and dlPFC activation and their connectivity with other brain regions reflect the complexity of depressive symptoms and their management in adolescents. These differences underscore the potential of tailored cognitive behavioral therapy, focusing on enhancing cognitive appraisal abilities as a viable treatment strategy (LeWinn et al., 2018).

The hippocampus is crucial for memory encoding, emotional regulation, and cognitive processing. Research has consistently shown that adolescents with first-episode depression often exhibit reduced hippocampal volume, suggesting a strong link between hippocampal abnormality and the onset of depressive symptoms (Zheng et al., 2023). Additionally, imaging studies highlight alterations in white matter structure within hippocampal circuitry. For instance, a study found that adolescents with depression showed disrupted structural and functional connectivity in the prefrontal-hippocampus circuit, with decreased fractional anisotropy (FA) in the fornix and reduced functional connectivity from the parahippocampus to areas of the prefrontal cortex compared to healthy controls (Geng et al., 2016). Furthermore, the correlation typically seen between FA in the fornix and the hippocampus-PFC tract in healthy individuals was absent in the depressed group, indicating a significant deviation in neural connectivity associated with depression (Geng et al., 2016).

- DTI and Causal Awareness

  DTI findings provides insights into deficits in causal awareness, which involves understanding the consequences of one's actions—a cognitive ability often impaired in adolescent depression. Studies have shown that adolescents with depression have reduced volume in the right pallidum, which correlates with decreased causal awareness and contributes to social and occupational dysfunction (Griffiths et al., 2015). Additionally, DTI has revealed disrupted white matter tracts from the right pallidum to key brain areas such as the striatum, dorsal thalamus, and hippocampus, suggesting aberrations in the cortico–striato–pallidal–thalamic circuits. These neural circuit disruptions may serve as biomarkers for identifying youths at risk for depression who could benefit from targeted cognitive-based interventions (Griffiths et al., 2015).

  In further studies, higher self-compassion in depressed adolescents was found to correlate with reduced activity in regions like the posterior cingulate cortex (PCC) and precuneus during negative self-appraisals and in the superior temporal gyrus, operculum, postcentral gyrus, and insula during positive self-appraisals. Interestingly, in healthy youths, higher self-compassion was associated with increased activity in these areas, highlighting the complex role that self-compassion plays in modulating brain activity and its potential influence on mental health outcomes (Liu et al., 2023). These findings suggest that self-compassion can be considered within the cognitive functions domain as it involves cognitive processes such as self-evaluation and emotional regulation, and also indicate these are crucial in understanding the pathophysiology of adolescent depression (Pullmer et al., 2019).

In summary, these findings emphasize the complex interplay between structural and functional brain abnormalities in adolescent depression and underscore the importance of employing advanced imaging techniques to elucidate the neural underpinnings of this disorder. While this section primarily discusses the role of the prefrontal cortex (PFC) within the cognitive systems domain, it is worth noting that the amygdala appears more frequently in the word frequency analysis (Fig. 4). This prominence is expected, given the amygdala's extensive interactions with various brain regions, especially top-down attention control areas such as the PFC, and its critical role in emotion regulation. These interactions suggest that cognitive systems are not only related to the PFC but are also influenced by the amygdala's connectivity and regulatory functions (Banks et al., 2007). This highlights the need to consider both PFC activity and amygdala interactions to fully understand the cognitive and emotional dysregulation observed in adolescent depression.

3.1.4. Arousal and regulatory systems

The domain of Arousal and Regulatory Systems (ARS), particularly the sleep–wakefulness construct, is pivotal in understanding adolescent depression (AD) (of Mental Health, 2023). Sleep patterns, as studied through EEG, have emerged as potential biomarkers for AD, highlighting distinct differences in sleep architecture between adolescents with AD and healthy controls.

In an effort to thoroughly explore the impact of sleep–wake patterns on AD, a comprehensive review of the literature was conducted, resulting in the selection of 212 research papers. These studies emphasized the critical role that sleep disturbances play in the onset and progression of AD and further validates the importance of sleep regulation in the clinical assessment and treatment planning for adolescents with depression. The selected studies enrich our understanding of how disruptions in sleep patterns can affect the broader spectrum of arousal and regulatory systems, providing valuable insights into potential therapeutic targets and intervention strategies.

The specifics of these findings and the relationships between key variables are visually represented in Fig. 5.

- Sleep EEG

  Studies utilizing sleep EEG have consistently demonstrated unique sleep characteristics in adolescents with AD compared to their healthy peers. Notably, these studies have found that adolescents with AD exhibit lower beta-delta wave intrahemispheric and interhemispheric coherence during sleep compared to healthy controls (Armitage et al., 2006). This suggests a disruption in normal sleep architecture, which may reflect underlying neural dysregulation.

  Gender differences in sleep patterns have also been observed, with AD males showing poorer sleep quality than both AD females and healthy controls. Specifically, AD males have less delta activity during the first non-rapid eye movement (NREM) sleep period and more irregular dissipation of delta activity throughout the night compared to healthy male controls. These gender-specific differences were not observed between AD females and their healthy counterparts (Lopez et al., 2012).

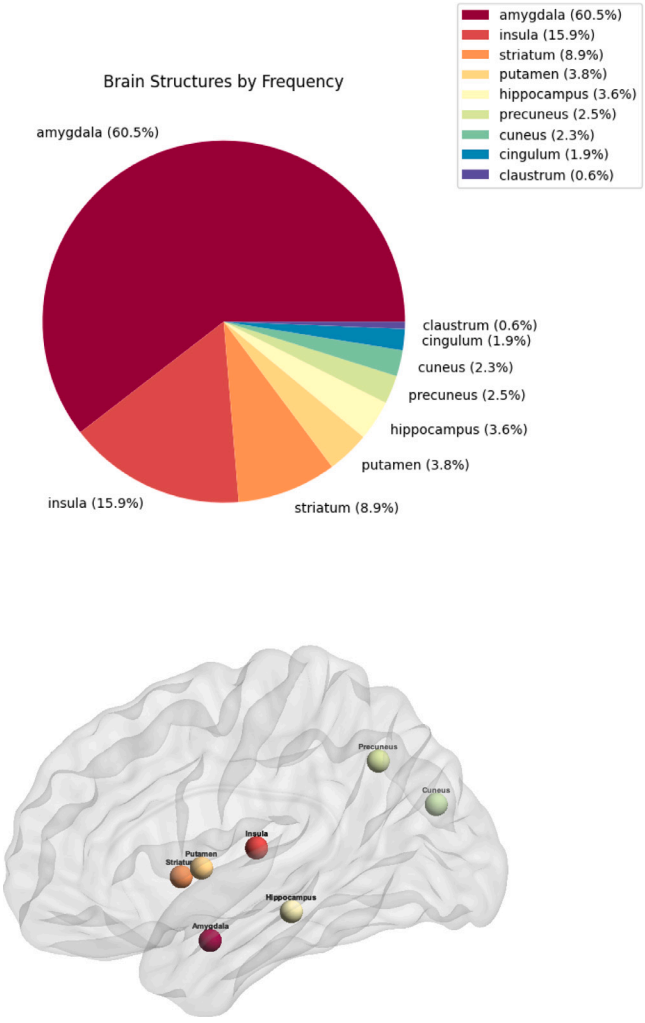

Fig. 5. Brain Structures in ARS-related articles.

Additionally, measures of rapid eye movement (REM) sleep have been shown to differentiate not only between adolescents with and without AD but also between those with unipolar and bipolar depression. Adolescents who later developed unipolar depression exhibited reduced REM latency, higher REM density, and longer REM sleep duration at baseline compared to those who later developed bipolar disorder (Rao et al., 2002, 1996). This finding suggests differing mechanisms may underlie sleep dysregulation in bipolar disorder versus unipolar depression.

These insights into the sleep disturbances associated with AD underscore the importance of including sleep assessments in the diagnostic and therapeutic processes for adolescent depression. Understanding the specific sleep anomalies associated with different forms of depression can aid in more accurate diagnosis and tailored treatment strategies, potentially improving outcomes for affected adolescents.

- Sleep Patterns on Neural Functioning

  The relationship between sleep patterns and neural functioning in adolescents, particularly in the context of reward processing and emotional regulation, underscores the critical influence of sleep on these domains. Research has demonstrated various ways in which altered sleep patterns impact the developing brain and contribute to psychopathologies such as depression and substance abuse.

  Studies have shown that shifts in adolescent sleep timing, particularly on weekends versus weekdays, often conflict with early school start times, leading to circadian misalignment. This misalignment is associated with decreased neural reactivity in key reward processing regions, such as the medial prefrontal cortex (mPFC) and striatum (Hasler et al., 2012). The resulting irregular sleep patterns can impair regulatory responses and reduce reward sensitivity, potentially increasing the risk of depression and substance abuse among adolescents.

  In a diverse sample of children and adolescents, shorter sleep durations and later sleep midpoints were found to significantly affect resting-state functional connectivity (RS-FC) within corticolimbic circuits (Hehr et al., 2019). These changes were notably prominent in brain regions involved in emotion regulation, sensory processing, and motor control. The data indicate widespread interactive effects of sleep duration and timing, highlighting the complex interactions between homeostatic and circadian processes in the brain.

  The collective findings from these studies emphasize the significant impact that sleep patterns have on various aspects of neural functioning in adolescents. The observed changes in reward processing, emotional regulation, and brain connectivity due to altered sleep patterns stress the importance of adequate sleep management in this vulnerable age group. Effective sleep strategies are crucial to mitigate potential behavioral and emotional health problems. The complex interactions between sleep-related changes in corticolimbic circuitry underline the necessity for both homeostatic and circadian processes to be considered in maintaining emotional and cognitive health during adolescence. This integrated approach to understanding sleep's role in adolescent mental health is essential for developing targeted interventions and support systems.

3.1.5. Default Mode Network (DMN)

The Default Mode Network (DMN) plays a crucial role in the pathophysiology of adolescent depression (AD), and integrates multiple domains of the Research Domain Criteria (RDoC) framework, including the negative valence system, positive valence system, social processes, and cognitive processes (Coutinho et al., 2016). Since it encompasses many systems of the RDoC, it merits its own discussion on its role in the pathophysiology of AD. This network, essential for inwardly focused cognitive tasks, includes the medial prefrontal cortex, posterior cingulate cortex, precuneus, inferior parietal lobule, lateral temporal cortex, and hippocampal formation (Koshino et al., 2014).

Although the DMN findings cannot be explicitly explained within the RDoC framework since majority of findings of DMN are from the resting-state fMRI (i.e., no active brain activity is required), the areas implicated in the pathophysiology of adolescent depression within DMN are well aligned within the RDoC framework, such as self-referential thinking (the cognitive system), emotion regulation (the negative and positive valence system), and internal mental processes (the cognitive system) (Gong and He, 2015). The inclusion of the DMN in this study allows for a comprehensive exploration of adolescent depression's neurobiological mechanisms, as the DMN's dysfunction is closely associated with depressive symptomatology and its interactions with multiple RDoC domains.

Upon completing a detailed review of the literature, a total of 134 studies were identified that focused on the involvement of DMN in adolescent depression. These studies provide comprehensive insights into how the DMN's dysfunction correlates with various clinical symptoms and cognitive processes in AD. The findings from these studies underscore the importance of DMN in maintaining cognitive and emotional balance and how its disruption can lead to depressive states. The relationships and patterns identified in these selected studies are detailed in Fig. 6.

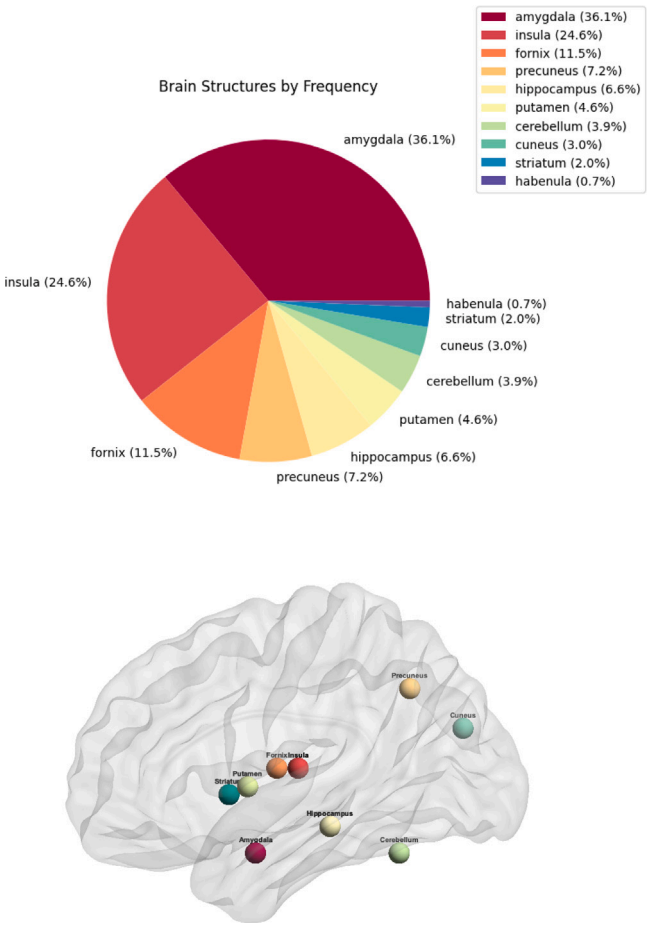

Fig. 6. Brain Structures in DMN-related articles.

- Task-based fMRI Findings
  Depressed adolescents often exhibit more negative self-perceptions compared to healthy controls, especially during self-judgment tasks involving positive and negative trait words. Functional MRI studies have shown that these adolescents display greater activation in the posterior cingulate cortex/precuneus, areas involved in affective processing when engaging with positive traits (Bradley et al., 2016). This might indicate that depressed adolescents perceive positive traits more negatively. Additionally, task-based fMRI studies have revealed that the DMN shows abnormal functional connectivity in depressed adolescents, with reduced connectivity between the dorsomedial prefrontal cortex and other prefrontal areas, such as the anterior cingulate cortex and orbitofrontal cortex, particularly during self-referential processing (Bradley et al., 2016). Other studies have noted that reduced deactivation of the medial prefrontal cortex and posterior cingulate cortex during resting states in AD correlates with more severe depression symptoms and earlier onset (Ho et al., 2015).

3.2. Specific topics

3.2.1. Familial risk of AD

Familial risk is a significant factor in the development of adolescent depression (AD). Studies have shown that children with a familial history of affective disorders are at a considerably higher risk of developing major depressive disorder (MDD) compared to those with low familial risk (Williamson et al., 2004). Neuroimaging has played a crucial role in identifying structural and functional abnormalities in the brains of individuals at risk before the clinical onset of depression.

- fMRI Findings
  Increased activation of the emotion responding areas especially towards negative valence of emotional stimuli has been identified in youths with a familial history of depression, highlighting their potential vulnerability to emotional dysregulation. For instance, functional MRI (fMRI) studies have revealed that at-risk youths exhibit increased activation in several emotion processing and cognitive control areas such as the amygdala, superior temporal gyrus, posterior cingulate cortex, and medial prefrontal cortex when exposed to fearful facial expressions, and conversely decreased activation to happy expressions (Colich et al., 2017; Pilhatsch et al., 2014). These findings indicate that there are pre-existing functional abnormalities that may be associated with familial risk of AD (Chai et al., 2015).

- Dysfunctional Connectivity
  Resting-state fMRI (rs-fMRI) has shown that high-risk youth demonstrate altered connectivity within and between various neural networks. For example, increased connectivity has been observed between the default mode network (DMN) and subgenual anterior cingulate cortex (sgACC)/orbitofrontal cortex, while connectivity within the cognitive control network and between the left dorsolateral prefrontal cortex and sgACC is decreased (Chai et al., 2016). These connectivity patterns suggest that the predisposition to depressive rumination and cognitive deficits in at-risk youths may contribute to the development of AD.

- DTI and Familial Risk
  Diffusion tensor imaging (DTI) has provided insights into the microstructural integrity of white matter pathways in youths with familial risk for depression. Studies have reported lower fractional anisotropy in regions such as the left cingulum and corpus callosum in high-risk youths compared to their low-risk counterparts (Huang et al., 2011). These findings suggest potential biomarkers that could be targeted in early intervention strategies.

- Potential Biomarkers and Early Intervention
  The observed abnormalities in brain structure and function among at-risk youths underscore the importance of early detection and intervention. Neuroimaging findings, such as those from rs-fMRI and DTI, offer valuable biomarkers for identifying youths at high risk for developing AD. For instance, alterations in the connectivity of the DMN and cognitive control networks, as well as changes in white matter integrity, could serve as early indicators of AD, facilitating preventative measures before the onset of clinical symptoms (Bellgowan et al., 2015; Clasen et al., 2014; Hirshfeld-Becker et al., 2019).

In summary, the integration of familial risk factors with neuroimaging findings provides a comprehensive approach to understanding and potentially mitigating the onset of adolescent depression. The identification of neurobiological markers linked to familial risk offers promising avenues for the development of targeted interventions aimed at preventing the progression of depressive disorders in high-risk populations.

3.2.2. Suicidality in AD

Suicidality represents one of the most serious clinical concerns in adolescent depression, with suicide ranking as the second leading cause of death among Americans aged 10 to 24 (Rihmer, 2007; Miller et al., 2018). Understanding the underlying neurological processes that contribute to suicidality ideation is crucial for developing effective interventions.

- fMRI Findings
  Neuroimaging studies have identified key brain areas involved in emotional regulation that differ in activity between suicidal and non-suicidal youths. For instance, youths with a history of suicidal ideation (SI) show decreased activation in the dorsolateral prefrontal cortex (dlPFC), temporoparietal junction, and cerebellum when viewing negative stimuli. However, these individuals can activate the dlPFC when instructed to regulate their emotions, suggesting a potential for therapeutic interventions such as dialectical behavior therapy to enhance emotional regulation capabilities (Miller et al., 2018).

- Functional and Structural Brain Abnormalities
  Further studies have demonstrated that adolescents at risk for suicide exhibit distinct patterns of brain activity and structural changes. For example, increased functional connectivity in the default mode network (DMN) and abnormal connectivity patterns within cognitive control networks have been observed. These findings are consistent across various studies, indicating dysfunctional connectivity and potential heritability of these brain abnormalities, predisposing individuals to depression and suicidal behaviors (Schreiner et al., 2019; Ordaz et al., 2018; Zhang, 2017; Ho et al., 2021).

- Frontal Lobe Implications in Suicidality
  The frontal lobe, particularly the prefrontal cortex, shows significant differences in gray matter volume and white matter integrity between suicidal and non-suicidal adolescents. Reduced activity and structural changes in the prefrontal cortex are linked to impulsivity, poor decision-making, and ultimately, increased risk of suicidal actions (Cao et al., 2016; Fan et al., 2019; Lippard et al., 2019).

- Insula in Affective and Cognitive Processing
  The insula, crucial for affective and cognitive processing, also exhibits abnormalities in adolescents with AD, particularly in those who show suicidality. Alterations in insular activation may lead to maladaptive emotional regulation and cognitive deficits, heightening the risk for poor decision-making such as suicide attempt (Zheng et al., 2023; Liu et al., 2023).

- Potential Biomarkers for Early Intervention
  Advances in neuroimaging have led to the identification of potential biomarkers that could help predict which adolescents are at increased risk of suicide. These include changes in the connectivity of the DMN, cognitive control networks, and structural integrity in the frontal lobe (Schreiner et al., 2019; Bellgowan et al., 2015; van Dijk et al., 2024). Such biomarkers could be pivotal for early screening and intervention, potentially mitigating the risk before the development of severe outcomes.

Overall, the integration of neuroimaging findings with clinical assessments offers promising avenues for understanding the complex interplay between brain function, familial risk, and suicidality in adolescent depression. These insights are critical for developing targeted interventions aimed at preventing the tragic outcomes associated with AD.

3.2.3. Treatment response in AD

It is critical to fully understand the clinical and neurobiological responses to therapy and pharmacological treatment for AD is crucial. SSRIs and cognitive behavioral therapy (CBT) are the primary pharmacological and therapeutic treatments studied for AD.

- Pharmacological Treatment Responses
  SSRIs are the first line of pharmacological treatment for AD, but their effects on neural circuitry are not fully understood. Research has shown that antidepressant treatments can normalize the resting-state functional connectivity (RSFC) of the frontal-limbic network. Specifically, one study found that after 12 weeks of antidepressant treatment, there was a reduction in the functional connectivity between the anterior cingulate cortex (ACC) and the left pre-central gyrus, indicating a potential decrease in negatively biased cognitive processes and poor impulse control (Chi et al., 2021; Cullen et al., 2016). Furthermore, improvements in depressive symptoms were associated with changes in brain activity and connectivity, including decreased activity in the rostral and subgenual ACC and increased connectivity between the amygdala and right frontal cortex, suggesting normalization of over-activated DMN in AD (Cullen et al., 2016).
  A study exploring the effects of fluoxetine demonstrated that fluoxetine treatment increased activation in the fusiform gyrus, which is involved in attentional processing, possibly helping patients focus on aversive stimuli as part of cognitive reappraisal strategies rather than avoiding them (Capitão et al., 2023).

- Predictors of Treatment Response
  Despite the effectiveness of SSRIs, 30%–50% of adolescents do not respond to these treatments. It would be critical to identify neurobiological predictors of treatment response. For example, pre-treatment fMRI scans showing specific patterns of connectivity involving the amygdala and various cortical areas were predictive of better treatment responses to SSRIs (Klimes-Dougan et al., 2018). These predictors may potentially help clinicians tailored treatments more effectively in the future.

- Cognitive Behavioral Therapy (CBT) Effects
  Cognitive Behavioral Therapy (CBT), a well-established treatment for AD, focuses on altering dysfunctional cognitive and behavior patterns. Neuroimaging studies of post-CBT have shown normalization in the activation of the orbitofrontal cortex and changes in connectivity between critical areas like the ACC and insula, correlating with reductions in depressive symptoms (Chuang et al., 2016; Chattopadhyay et al., 2017). Group CBT has also shown promising results, showing changes in limbic regions such as the sgACC and amygdala, which are crucial for processing negative stimuli and mediating affective responses (Straub et al., 2015).
  Furthermore, CBT has been shown to affect connectivity between the affective network (including the amygdala and sgACC) and cognitive networks, potentially increasing the control of cognitive processes over affective responses, which is vital for managing rumination—a known factor in the persistence of depression (Straub et al., 2015; Roberts et al., 2021).

- Rumination-Focused Cognitive Behavioral Therapy (RFCBT) and Connectivity Changes
  Rumination-Focused Cognitive Behavioral Therapy (RFCBT) has been shown to reduce connectivity between the left posterior cingulate cortex and areas involved in emotional regulation, which may help decrease rumination and improve emotional processing in adolescents with a history of major depressive disorder (Jacobs et al., 2016).

Overall, these findings underscore the importance of integrating neuroimaging insights into treatment planning and evaluation for adolescent depression, aiming to enhance the efficacy of existing interventions and provide targeted therapeutic options based on individual neurobiological profiles.

4. Discussion

In this review, we explored up-to-date neuroimaging findings for adolescent depression using the RDoC framework, focusing on modalities such as fMRI, DTI, and EEG. Despite extensive research, the

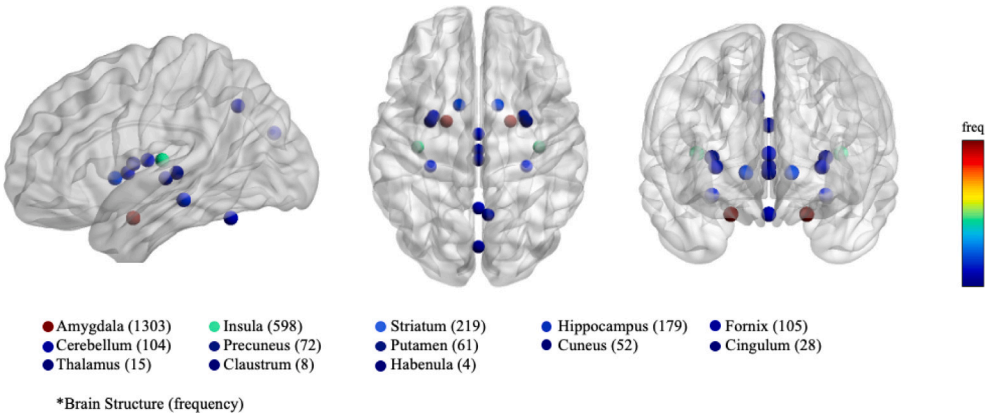

Fig. 7. Frequency of brain structure mentions in adolescent depression studies.

neurobiology of adolescent depression has often yielded conflicting results due to factors such as specific target populations, choice of methodology, treatment status, and presence/absence of comorbidities. However, by very comprehensive review and machine-learning algorithm, we were also able to identify repeated patterns and neural areas implicated in the pathophysiology of adolescent depression. More specifically, the methods we have applied allowed us to identify major areas within the RDoC domains and their relative roles in the pathophysiology of adolescent depression.

To efficiently review a large number of studies and select relevant ones, this study employed a natural language processing machine learning technique called zero-shot classification. As a result, we were able to review 793 studies out of 2013 identified through our search strategy. However, by very comprehensive review and machine-learning algorithm, we were also able to identify repeated patterns and neural areas implicated in the pathophysiology of adolescent depression. More specifically, the methods we have applied allowed us to identify major areas within the RDoC domains and their relative roles in the pathophysiology of adolescent depression. Among these, the cognitive systems domain had the most studies within the RDoC frame, with a total of 288 papers, while the positive valence systems domain had the fewest, with 74 papers. There were 115 studies related to the negative valence system.

In terms of the brain regions mentioned in relation to the RDoC domains in adolescent depression, the negative valence system (NVS) frequently mentioned regions such as the amygdala, insula, fornix, and hippocampus. For the positive valence systems (PVS), the regions most commonly noted were the amygdala, insula, striatum, and hippocampus. In the cognitive systems domain, the amygdala and insula were mentioned with similar frequency, followed by the striatum and precuneus. For the arousal and regulatory systems domain, the amygdala was predominantly cited, followed by the insula, striatum, and putamen. The default mode network (DMN) was the focus of 134 studies, with frequent mentions of the amygdala and insula, followed by the fornix and precuneus.

The overlap of many neural areas across different RDoC domains indicates the multifaceted role of these regions in various emotional and cognitive processes. For example, the amygdala's frequent mention across all domains underscores its central role in processing both positive and negative emotions (Hamann and Mao, 2002), as well as its involvement in cognitive and regulatory functions (LeDoux, 2007). The insula's consistent mention highlights its importance in interoceptive awareness and emotional experience (Simmons et al., 2013).

The striatum and hippocampus also play crucial roles across multiple domains. The striatum is key for reward processing and motivation, which aligns with its mention in both the positive valence systems and cognitive systems domains. The hippocampus is involved in memory and contextual processing, relevant to both the negative valence systems and cognitive systems domains.

Put together, these findings help us towards better understanding on the roles of specific brain regions associated with each RDoC domain in adolescent depression. Again, it is noteworthy that the amygdala was the most frequently mentioned brain region across all studies, with a total of 1303 mentions. This was followed by the insula (598 mentions), striatum (219 mentions), hippocampus (179 mentions), fornix (105 mentions), and cerebellum (104 mentions). A visualization of these brain regions, as mentioned in the studies, is provided in Fig. 7 (Xia et al., 2013).

Resting-state fMRI functional connectivity studies have helped elucidating neural networks implicated in adolescent depression, including abnormalities in the affective network, reward processing network, cognitive control network, and default mode network (Chai et al., 2016; Richards et al., 2013). These networks interact with various RDoC domains, affecting how adolescents respond to negative and positive stimuli.

The frequent presence of conflicting findings depending on specific target populations, choice of methodology, treatment status, and presence/absence of comorbidities emphasizes the current limitation in understanding the core neurobiology of adolescent depression (Palazidou, 2012). This also may affect the generalizability of specific findings (Ruggiero et al., 1999). Methodological differences, such as variations in imaging techniques, analysis pipelines, and statistical methods, can lead to inconsistent findings as well (Bair et al., 2003). These limitations highlight the need for standardized protocols and a larger sample size in future studies to reduce variability and improve comparability across studies.

Our review revealed that there is an interconnected nature of neural networks in adolescent depression, suggesting that interventions targeting these neural circuits could be effective. For instance, CBT has shown promise in modulating connectivity within the DMN and cognitive control networks, indicating its potential to improve emotional regulation and reduce depressive symptoms. However, the mixed results of impacting amygdala connectivity emphasize the need for more nuanced research to understand the variability in neural responses across different individuals and contexts.

The studies we reviewed have also demonstrated limitations such as small sample sizes and a lack of longitudinal design, which are crucial for understanding the development and progression of depression over time. Future research should focus on larger, more diverse populations and consider longitudinal designs to track changes in neural connectivity and their relation to treatment outcomes.

Further studies are also needed to investigate the neural mechanisms underlying specific treatment modalities like electroconvulsive therapy (ECT) and transcranial magnetic stimulation (TMS), which have shown potential in adult populations but are understudied in adolescents. Understanding how these treatments affect neural connectivity

could lead to more targeted and effective interventions for adolescent depression.

Overall, neuroimaging studies have led us toward a better understanding of the neurobiological processes underpinning adolescent depression, especially as being considered within the RDoC framework. These insights could potentially help identify the target mechanism for currently existing treatment modalities as well as the development of new therapeutic tools for this challenging condition in adolescents in the future.

CRediT authorship contribution statement

Harim Jeong: Writing – original draft, Visualization, Methodology, Formal analysis, Conceptualization. **Tianqi Luo:** Writing – original draft, Methodology, Formal analysis, Conceptualization. **Minjoo Kang:** Resources. **William Frederick Garvey:** Writing – original draft, Conceptualization. **George Blankenau:** Conceptualization. **Ji-Woo Suk:** Conceptualization. **Mohadese Tarzaben:** Writing – original draft. **Soonjo Hwang:** Writing – review & editing, Supervision, Project administration, Investigation, Conceptualization.

Declaration of competing interest

All authors declare that they have no conflicts of interest to report regarding this study.

References

American Psychiatric Association, D., Association, A.P., et al., 2013. Diagnostic and Statistical Manual of Mental Disorders: DSM-5, vol. 5. American psychiatric association Washington, DC.

Armitage, R., Hoffmann, R., Emslie, G., Rintelmann, J., Robert, J., 2006. Sleep microarchitecture in childhood and adolescent depression: temporal coherence. Clin. EEG Neurosci. 37 (1), 1–9.

Association, A.P., et al., 2000. Diagnostic and statistical manual of mental disorders. Text Rev..

Auerbach, R.P., Stanton, C.H., Proudfit, G.H., Pizzagalli, D.A., 2015a. Self-referential processing in depressed adolescents: A high-density event-related potential study.. J. Abnormal Psychol. 124 (2), 233.

Auerbach, R.P., Stewart, J.G., Stanton, C.H., Mueller, E.M., Pizzagalli, D.A., 2015b. Emotion-processing biases and resting EEG activity in depressed adolescents. Depress. Anxiety 32 (9), 693–701.

Bair, M.J., Robinson, R.L., Katon, W., Kroenke, K., 2003. Depression and pain comorbidity: a literature review. Arch. Internal Med. 163 (20), 2433–2445.

Banks, S.J., Eddy, K.T., Angstadt, M., Nathan, P.J., Phan, K.L., 2007. Amygdala–frontal connectivity during emotion regulation. Soc. Cognit. Affect. Neurosci. 2 (4), 303–312.

Barch, D.M., Hua, X., Kandala, S., Harms, M.P., Sanders, A., Brady, R., Tillman, R., Luby, J.L., 2022. White matter alterations associated with lifetime and current depression in adolescents: Evidence for cingulum disruptions. Depress. Anxiety 39 (12), 881–890.

Beauchaine, T.P., Hinshaw, S.P., 2020. RDoC and psychopathology among youth: Misplaced assumptions and an agenda for future research. J. Clin. Child Adolesc. Psychol. 49 (3), 322–340.

Bellgowan, J.F., Molfese, P., Marx, M., Thomason, M., Glen, D., Santiago, J., Gotlib, I.H., Drevets, W.C., Hamilton, J.P., 2015. A neural substrate for behavioral inhibition in the risk for major depressive disorder. J. Am. Acad. Child Adolesc. Psychiatry 54 (10), 841–848.

Bessette, K.L., Nave, A.M., Caprihan, A., Stevens, M.C., 2014. White matter abnormalities in adolescents with major depressive disorder. Brain Imaging Behav. 8, 531–541.

Bradley, K.A., Colcombe, S., Henderson, S.E., Alonso, C.M., Milham, M.P., Gabbay, V., 2016. Neural correlates of self-perceptions in adolescents with major depressive disorder. Dev. Cognit. Neurosci. 19, 87–97.

Bress, J.N., Foti, D., Kotov, R., Klein, D.N., Hajcak, G., 2013. Blunted neural response to rewards prospectively predicts depression in adolescent girls. Psychophysiology 50 (1), 74–81.

Cao, J., Chen, X., Chen, J., Ai, M., Gan, Y., Wang, W., Lv, Z., Zhang, S., Zhang, S., Wang, S., et al., 2016. Resting-state functional MRI of abnormal baseline brain activity in young depressed patients with and without suicidal behavior. J. Affect. Disorders 205, 252–263.

Capitão, L.P., Chapman, R., Filippini, N., Wright, L., Murphy, S.E., James, A., Cowen, P.J., Harmer, C.J., 2023. Acute neural effects of fluoxetine on emotional regulation in depressed adolescents. Psychol. Med. 53 (10), 4799–4810.

Chai, X.J., Hirshfeld-Becker, D., Biederman, J., Uchida, M., Doehrmann, O., Leonard, J.A., Salvatore, J., Kenworthy, T., Brown, A., Kagan, E., et al., 2015. Functional and structural brain correlates of risk for major depression in children with familial depression. NeuroImage: Clinical 8, 398–407.

Chai, X.J., Hirshfeld-Becker, D., Biederman, J., Uchida, M., Doehrmann, O., Leonard, J.A., Salvatore, J., Kenworthy, T., Brown, A., Kagan, E., et al., 2016. Altered intrinsic functional brain architecture in children at familial risk of major depression. Biol. Psychiatry 80 (11), 849–858.

Chattopadhyay, S., Tait, R., Simas, T., van Nieuwenhuizen, A., Hagan, C.C., Holt, R.J., Graham, J., Sahakian, B.J., Wilkinson, P.O., Goodyer, I.M., et al., 2017. Cognitive behavioral therapy lowers elevated functional connectivity in depressed adolescents. EBioMedicine 17, 216–222.

Chi, S., Song, M., Lee, J.-h., Ko, M., Suh, S.-i., Lee, M.-S., 2021. Prospective study on resting state functional connectivity in adolescents with major depressive disorder after antidepressant treatment. J. Psychiatric Res. 142, 369–375.

Chuang, J.-Y., Whitaker, K.J., Murray, G.K., Elliott, R., Hagan, C.C., Graham, J.M., Ooi, C., Tait, R., Holt, R.J., van Nieuwenhuizen, A.O., et al., 2016. Aberrant brain responses to emotionally valent words is normalised after cognitive behavioural therapy in female depressed adolescents. J. Affect. Disorders 189, 54–61.

Clasen, P.C., Beevers, C.G., Mumford, J.A., Schnyer, D.M., 2014. Cognitive control network connectivity in adolescent women with and without a parental history of depression. Dev. Cognit. Neurosci. 7, 13–22.

Clithero, J.A., Rangel, A., 2014. Informatic parcellation of the network involved in the computation of subjective value. Soc. Cognit. Affect. Neurosci. 9 (9), 1289–1302.

Colich, N.L., Ho, T.C., Foland-Ross, L.C., Eggleston, C., Ordaz, S.J., Singh, M.K., Gotlib, I.H., 2017. Hyperactivation in cognitive control and visual attention brain regions during emotional interference in adolescent depression. Biol. Psychiatry: Cognit. Neurosci. Neuroimaging 2 (5), 388–395.

Connolly, C.G., Ho, T.C., Blom, E.H., LeWinn, K.Z., Sacchet, M.D., Tymofiyeva, O., Simmons, A.N., Yang, T.T., 2017. Resting-state functional connectivity of the amygdala and longitudinal changes in depression severity in adolescent depression. J. Affect. Disorders 207, 86–94.

Coutinho, J.F., Fernandesl, S.V., Soares, J.M., Maia, L., Gonçalves, Ó.F., Sampaio, A., 2016. Default mode network dissociation in depressive and anxiety states. Brain Imaging Behav. 10, 147–157.

Critchley, H., Daly, E., Phillips, M., Brammer, M., Bullmore, E., Williams, S., Van Amelsvoort, T., Robertson, D., David, A., Murphy, D., 2000. Explicit and implicit neural mechanisms for processing of social information from facial expressions: a functional magnetic resonance imaging study. Hum. Brain Mapp. 9 (2), 93–105.

Cullen, K.R., Brown, R., Schreiner, M.W., Eberly, L.E., Klimes-Dougan, B., Reigstad, K., Hill, D., Lim, K.O., Mueller, B.A., 2020. White matter microstructure relates to lassitude but not diagnosis in adolescents with depression. Brain Imaging Behav. 14, 1507–1520.

Cullen, K.R., Klimes-Dougan, B., Vu, D.P., Westlund Schreiner, M., Mueller, B.A., Eberly, L.E., Camchong, J., Westervelt, A., Lim, K.O., 2016. Neural correlates of antidepressant treatment response in adolescents with major depressive disorder. J. Child Adolesc. Psychopharmacol. 26 (8), 705–712.

Daly, M., 2022. Prevalence of depression among adolescents in the US from 2009 to 2019: analysis of trends by sex, race/ethnicity, and income. J. Adolesc. Health 70 (3), 496–499.

Defayette, A.B., Whitmyre, E.D., López Jr., R., Brown, B., Wolff, J.C., Spirito, A., Esposito-Smythers, C., 2021. Adolescent depressed mood and difficulties with emotion regulation: Concurrent trajectories of change. J. Adolesc. 91, 1–14.

van Dijk, M.T., Talati, A., Kashyap, P., Desai, K., Kelsall, N.C., Gameroff, M.J., Aw, N., Abraham, E., Cullen, B., Cha, J., et al., 2024. Dentate gyrus microstructure is associated with resilience after exposure to maternal stress across two human cohorts. Biol. Psychiatry 95 (1), 27–36.

Ernst, M., Paulus, M.P., 2005. Neurobiology of decision making: a selective review from a neurocognitive and clinical perspective. Biol. Psychiatry 58 (8), 597–604.

Fan, S., Lippard, E.T., Sankar, A., Wallace, A., Johnston, J.A., Wang, F., Pittman, B., Spencer, L., Oquendo, M.A., Blumberg, H.P., 2019. Gray and white matter differences in adolescents and young adults with prior suicide attempts across bipolar and major depressive disorders. J. Affect. Disorders 245, 1089–1097.

Fava, G.A., Tossani, E., Bech, P., Berrocal, C., Chouinard, G., Csillag, C., Wittchen, H.-U., Rief, W., 2014. Emerging clinical trends and perspectives on comorbid patterns of mental disorders in research. Int. J. Methods Psychiatric Res. 23 (S1), 92–101.

Feldmann, L., Piechaczek, C.E., Grünewald, B.D., Pehl, V., Bartling, J., Frey, M., Schulte-Körne, G., Greimel, E., 2018. Resting frontal EEG asymmetry in adolescents with major depression: Impact of disease state and comorbid anxiety disorder. Clin. Neurophysiol. 129 (12), 2577–2585.

Forbes, E.E., Eckstrand, K.L., Rofey, D.L., Silk, J.S., 2021. A social affective neuroscience model of risk and resilience in adolescent depression: Preliminary evidence and application to sexual and gender minority adolescents. Biol. Psychiatry: Cognit. Neurosci. Neuroimaging 6 (2), 188–199.

Geng, H., Wu, F., Kong, L., Tang, Y., Zhou, Q., Chang, M., Zhou, Y., Jiang, X., Li, S., Wang, F., 2016. Disrupted structural and functional connectivity in prefrontal-hippocampus circuitry in first-episode medication-naive adolescent depression. PLoS One 11 (2), e0148345.

Gong, Q., He, Y., 2015. Depression, neuroimaging and connectomics: a selective overview. Biol. Psychiatry 77 (3), 223–235.
Griffiths, K., Lagopoulos, J., Hermens, D.F., Hickie, I., Balleine, B., 2015. Right external globus pallidus changes are associated with altered causal awareness in youth with depression. Transl. Psychiatry 5 (10), e653.
Grünewald, B.D., Greimel, E., Trinkl, M., Bartling, J., Groß heinrich, N., Schulte-Körne, G., 2018. Resting frontal EEG asymmetry patterns in adolescents with and without major depression. Biol. Psychol. 132, 212–216.
Hamann, S., Mao, H., 2002. Positive and negative emotional verbal stimuli elicit activity in the left amygdala. Neuroreport 13 (1), 15–19.
Hasler, B.P., Dahl, R.E., Holm, S.M., Jakubcak, J.L., Ryan, N.D., Silk, J.S., Phillips, M.L., Forbes, E.E., 2012. Weekend–weekday advances in sleep timing are associated with altered reward-related brain function in healthy adolescents. Biol. Psychol. 91 (3), 334–341.
Hawes, M.T., Szenczy, A.K., Klein, D.N., Hajcak, G., Nelson, B.D., 2022. Increases in depression and anxiety symptoms in adolescents and young adults during the COVID-19 pandemic. Psychol. Med. 52 (14), 3222–3230.
Hehr, A., Marusak, H.A., Huntley, E.D., Rabinak, C.A., 2019. Effects of duration and midpoint of sleep on corticolimbic circuitry in youth. Chronic Stress 3, 2470547019856332.
Henderson, S.E., Johnson, A.R., Vallejo, A.I., Katz, L., Wong, E., Gabbay, V., 2013. A preliminary study of white matter in adolescent depression: relationships with illness severity, anhedonia, and irritability. Front. Psychiatry 4, 152.
Hermens, D.F., Hatton, S.N., White, D., Lee, R.S., Guastella, A.J., Scott, E.M., Naismith, S.L., Hickie, I.B., Lagopoulos, J., 2019. A data-driven transdiagnostic analysis of white matter integrity in young adults with major psychiatric disorders. Prog. Neuropsychopharmacol. Biol. Psychiatry 89, 73–83.
Hirshfeld-Becker, D.R., Gabrieli, J.D., Shapero, B.G., Biederman, J., Whitfield-Gabrieli, S., Chai, X.J., 2019. Intrinsic functional brain connectivity predicts onset of major depression disorder in adolescence: a pilot study. Brain Connect. 9 (5), 388–398.
Ho, T.C., Connolly, C.G., Blom, E.H., LeWinn, K.Z., Strigo, I.A., Paulus, M.P., Frank, G., Max, J.E., Wu, J., Chan, M., et al., 2015. Emotion-dependent functional connectivity of the default mode network in adolescent depression. Biol. Psychiatry 78 (9), 635–646.
Ho, T.C., Walker, J.C., Teresi, G.I., Kulla, A., Kirshenbaum, J.S., Gifuni, A.J., Singh, M.K., Gotlib, I.H., 2021. Default mode and salience network alterations in suicidal and non-suicidal self-injurious thoughts and behaviors in adolescents with depression. Transl. Psychiatry 11 (1), 38.
Horn, A., Ostwald, D., Reisert, M., Blankenburg, F., 2014. The structural–functional connectome and the default mode network of the human brain. Neuroimage 102, 142–151.
Huang, H., Fan, X., Williamson, D.E., Rao, U., 2011. White matter changes in healthy adolescents at familial risk for unipolar depression: a diffusion tensor imaging study. Neuropsychopharmacology 36 (3), 684–691.
Insel, T., Cuthbert, B., Garvey, M., Heinssen, R., Pine, D.S., Quinn, K., Sanislow, C., Wang, P., 2010. Research domain criteria (RDoC): toward a new classification framework for research on mental disorders. Am. J. Psychiatry 167 (7), 748–751.
Jacobs, R.H., Watkins, E.R., Peters, A.T., Feldhaus, C.G., Barba, A., Carbray, J., Langenecker, S.A., 2016. Targeting ruminative thinking in adolescents at risk for depressive relapse: rumination-focused cognitive behavior therapy in a pilot randomized controlled trial with resting state fMRI. PLoS One 11 (11), e0163952.
Johnson, D., Dupuis, G., Piche, J., Clayborne, Z., Colman, I., 2018. Adult mental health outcomes of adolescent depression: A systematic review. Depress. Anxiety 35 (8), 700–716.
Keren, H., O'Callaghan, G., Vidal-Ribas, P., Buzzell, G.A., Brotman, M.A., Leibenluft, E., Pan, P.M., Meffert, L., Kaiser, A., Wolke, S., et al., 2018. Reward processing in depression: a conceptual and meta-analytic review across fMRI and EEG studies. Am. J. Psychiatry 175 (11), 1111–1120.
Kerestes, R., Davey, C.G., Stephanou, K., Whittle, S., Harrison, B.J., 2014. Functional brain imaging studies of youth depression: a systematic review. NeuroImage: Clinical 4, 209–231.
Klimes-Dougan, B., Schreiner, M.W., Thai, M., Gunlicks-Stoessel, M., Reigstad, K., Cullen, K.R., 2018. Neural and neuroendocrine predictors of pharmacological treatment response in adolescents with depression: A preliminary study. Prog. Neuro-Psychopharmacol. Biol. Psychiatry 81, 194–202.
Koshino, H., Minamoto, T., Yaoi, K., Osaka, M., Osaka, N., 2014. Coactivation of the default mode network regions and working memory network regions during task preparation. Sci. Rep. 4 (1), 5954.
Kujawa, A., Klein, D.N., Pegg, S., Weinberg, A., 2020. Developmental trajectories to reduced activation of positive valence systems: A review of biological and environmental contributions. Dev. Cognit. Neurosci. 43, 100791.
LeDoux, J., 2007. The amygdala. Curr. Biol. 17 (20), R868–R874.
Leibenluft, E., Stoddard, J., 2013. The developmental psychopathology of irritability. Development Psychopathol. 25 (4pt2), 1473–1487.
LeWinn, K.Z., Strigo, I.A., Connolly, C.G., Ho, T.C., Tymofiyeva, O., Sacchet, M.D., Weng, H.Y., Blom, E.H., Simmons, A.N., Yang, T.T., 2018. An exploratory examination of reappraisal success in depressed adolescents: Preliminary evidence of functional differences in cognitive control brain regions. J. Affect. Disord. 240, 155–164.
Lippard, E.T.C., Johnston, J.A., Spencer, L., Quatrano, S., Fan, S., Sankar, A., Weathers, J., Pittman, B., Oquendo, M.A., Blumberg, H.P., 2019. Preliminary examination of gray and white matter structure and longitudinal structural changes in frontal systems associated with future suicide attempts in adolescents and young adults with mood disorders. J. Affect. Disorders 245, 1139–1148.
Liu, G., Santana-Gonzalez, C., Zeffiro, T.A., Zhang, N., Engstrom, M., Quevedo, K., 2023. Self-compassion and neural activity during self-appraisals in depressed and healthy adolescents. J. Affect. Disorders 339, 717–724.
Lopez, J., Hoffmann, R., Emslie, G., Armitage, R., 2012. Sex differences in slow-wave electroencephalographic activity (SWA) in adolescent depression. Mental Illness 4 (1), 15–20.
Lu, W., 2019. Adolescent depression: national trends, risk factors, and healthcare disparities. Am. J. Health Behav. 43 (1), 181–194.
Luciana, M., Collins, P.F., 2012. Incentive motivation, cognitive control, and the adolescent brain: Is it time for a paradigm shift? Child Dev. Perspect. 6 (4), 392–399.
Lynch, F.L., Clarke, G.N., 2006. Estimating the economic burden of depression in children and adolescents. Am. J. Preventive Med. 31 (6), 143–151.
McClure, S.M., York, M.K., Montague, P.R., 2004. The neural substrates of reward processing in humans: the modern role of FMRI. The Neuroscientist 10 (3), 260–268.
McVoy, M., Aebi, M.E., Loparo, K., Lytle, S., Morris, A., Woods, N., Deyling, E., Tatsuoka, C., Kaffashi, F., Lhatoo, S., et al., 2019. Resting-state quantitative electroencephalography demonstrates differential connectivity in adolescents with major depressive disorder. J. Child Adolesc. Psychopharmacol. 29 (5), 370–377.
Medeiros, G.C., Rush, A.J., Jha, M., Carmody, T., Furman, J.L., Czysz, A.H., Trombello, J.M., Cooper, C.M., Trivedi, M.H., 2020. Positive and negative valence systems in major depression have distinct clinical features, response to antidepressants, and relationships with immunomarkers. Depress. Anxiety 37 (8), 771–783.
of Mental Health, N.I., 2023. Definitions of the RDoC domains and constructs. https://www.nimh.nih.gov/research/research-funded-by-nimh/rdoc/definitions-of-the-rdoc-domains-and-constructs.shtml (Accessed 15 May 2023).
Miller, A.B., McLaughlin, K.A., Busso, D.S., Brueck, S., Peverill, M., Sheridan, M.A., 2018. Neural correlates of emotion regulation and adolescent suicidal ideation. Biol. Psychiatry: Cognit. Neurosci. Neuroimaging 3 (2), 125–132.
Mitchell, A.M., Pössel, P., 2012. Frontal brain activity pattern predicts depression in adolescent boys. Biol. Psychol. 89 (2), 525–527.
Nelson, B.D., Infantolino, Z.P., Klein, D.N., Perlman, G., Kotov, R., Hajcak, G., 2018. Time-frequency reward-related delta prospectively predicts the development of adolescent-onset depression. Biol. Psychiatry: Cognit. Neurosci. Neuroimaging 3 (1), 41–49.
O'Callaghan, G., Stringaris, A., 2019. Reward processing in adolescent depression across neuroimaging modalities. Zeitschrift für Kinder-und Jugendpsychiatrie und Psychotherapie.
Ordaz, S.J., Goyer, M.S., Ho, T.C., Singh, M.K., Gotlib, I.H., 2018. Network basis of suicidal ideation in depressed adolescents. J. Affect. Disorders 226, 92–99.
Organization, W.H., 1992. The ICD-10 Classification of Mental and Behavioural Disorders: Clinical Descriptions and Diagnostic Guidelines, vol. 1. World Health Organization.
Palazidou, E., 2012. The neurobiology of depression. Br. Med. Bull. 101 (1), 127–145.
Pessoa, L., 2009. How do emotion and motivation direct executive control? Trends Cognit. Sci. 13 (4), 160–166.
Pilhatsch, M., Vetter, N.C., Hübner, T., Ripke, S., Müller, K.U., Marxen, M., Rodehacke, S., Mennigen, E., Schmidt, D., Kroemer, N.B., et al., 2014. Amygdala-function perturbations in healthy mid-adolescents with familial liability for depression. J. Am. Acad. Child Adolesc. Psychiatry 53 (5), 559–568.
Plener, P.L., Bubalo, N., Fladung, A.K., Ludolph, A.G., Lulé, D., 2012. Prone to excitement: Adolescent females with non-suicidal self-injury (NSSI) show altered cortical pattern to emotional and NSS-related material. Psychiatry Res.: Neuroimaging 203 (2–3), 146–152.
Poon, J.A., Thompson, J.C., Chaplin, T.M., 2022. Task-based functional connectivity patterns: links to adolescent emotion regulation and psychopathology. J. Affect. Disorders 302, 33–40.
Proudfit, G.H., 2015. The reward positivity: From basic research on reward to a biomarker for depression. Psychophysiology 52 (4), 449–459.
Pullmer, R., Chung, J., Samson, L., Balanji, S., Zaitsoff, S., 2019. A systematic review of the relation between self-compassion and depressive symptoms in adolescents. J. Adolesc. 74, 210–220.
Rao, U., Dahl, R.E., Ryan, N.D., Birmaher, B., Williamson, D.E., Giles, D.E., Rao, R., Kaufman, J., Nelson, B., 1996. The relationship between longitudinal clinical course and sleep and cortisol changes in adolescent depression. Biol. Psychiatry 40 (6), 474–484.
Rao, U., Dahl, R.E., Ryan, N.D., Birmaher, B., Williamson, D.E., Rao, R., Kaufman, J., 2002. Heterogeneity in EEG sleep findings in adolescent depression: unipolar versus bipolar clinical course. J. Affect. Disorders 70 (3), 273–280.
Richards, J.M., Plate, R.C., Ernst, M., 2013. A systematic review of fMRI reward paradigms used in studies of adolescents vs. adults: the impact of task design and implications for understanding neurodevelopment. Neurosci. Biobehav. Rev. 37 (5), 976–991.

Rihmer, Z., 2007. Suicide risk in mood disorders. Curr. Opin. Psychiatry 20 (1), 17–22.
Roberts, H., Jacobs, R.H., Bessette, K.L., Crowell, S.E., Westlund-Schreiner, M., Thomas, L., Easter, R.E., Pocius, S.L., Dillahunt, A., Frandsen, S., et al., 2021. Mechanisms of rumination change in adolescent depression (RuMeChange): study protocol for a randomised controlled trial of rumination-focused cognitive behavioural therapy to reduce ruminative habit and risk of depressive relapse in high-ruminating adolescents. BMC Psychiatry 21 (1), 206.
Ruggiero, K.J., Morris, T.L., Beidel, D.C., Scotti, J.R., McLeer, S.V., 1999. Discriminant validity of self-reported anxiety and depression in children: Generalizability to clinic referred and ethnically diverse populations. Assessment 6 (3), 259–267.
Rzepa, E., McCabe, C., 2016. Decreased anticipated pleasure correlates with increased salience network resting state functional connectivity in adolescents with depressive symptomatology. J. Psychiatric Res. 82, 40–47.
Schreiner, M.W., Klimes-Dougan, B., Cullen, K.R., 2019. Neural correlates of suicidality in adolescents with major depression: resting-state functional connectivity of the precuneus and posterior cingulate cortex. Suicide Life-Threatening Behav. 49 (3), 899–913.
Sherbaf, F.G., Same, K., Ashraf-Ganjouei, A., Aarabi, M.H., 2018. Altered white matter microstructure associated with mild and moderate depressive symptoms in young adults, a diffusion tensor imaging study. Neuroreport 29 (8), 685–689.
Simmons, W.K., Avery, J.A., Barcalow, J.C., Bodurka, J., Drevets, W.C., Bellgowan, P., 2013. Keeping the body in mind: insula functional organization and functional connectivity integrate interoceptive, exteroceptive, and emotional awareness. Hum. Brain Mapp. 34 (11), 2944–2958.
Straub, J., Plener, P., Sproeber, N., Sprenger, L., Koelch, M., Groen, G., Abler, B., 2015. Neural correlates of successful psychotherapy of depression in adolescents. J. Affect. Disorders 183, 239–246.
Vilgis, V., Silk, T.J., Vance, A., 2015. Executive function and attention in children and adolescents with depressive disorders: a systematic review. Eur. Child Adolesc. Psychiatry 24, 365–384.
Villalobos, D., Pacios, J., Vázquez, C., 2021. Cognitive control, cognitive biases and emotion regulation in depression: A new proposal for an integrative interplay model. Front. Psychol. 12, 628416.
Williamson, D.E., Birmaher, B., Axelson, D.A., Ryan, N.D., Dahl, R.E., 2004. First episode of depression in children at low and high familial risk for depression. J. Am. Acad. Child Adolesc. Psychiatry 43 (3), 291–297.
Wu, P.-C., 2017. Longitudinal measurement invariance of beck depression inventory–II in early adolescents. Assessment 24 (3), 337–345.
Wu, F., Tu, Z., Sun, J., Geng, H., Zhou, Y., Jiang, X., Li, H., Kong, L., 2020. Abnormal functional and structural connectivity of amygdala-prefrontal circuit in first-episode adolescent depression: a combined fMRI and DTI study. Front. Psychiatry 10, 983.
Xia, M., Wang, J., Viewer, Y.H.B., 2013. A network visualization tool for human brain connectomics. http://dx.doi.org/10.1371/journal.pone.68910, 8, e68910.
Yin, W., Hay, J., Roth, D., 2019. Benchmarking zero-shot text classification: Datasets, evaluation and entailment approach. arXiv preprint arXiv:1909.00161.
Young, K.S., Sandman, C.F., Craske, M.G., 2019. Positive and negative emotion regulation in adolescence: links to anxiety and depression. Brain Sci. 9 (4), 76.
Zhang, F., 2017. Resting-state functional connectivity abnormalities in adolescent depression. EBioMedicine 17, 20–21.
Zheng, R., Chen, Y., Jiang, Y., Zhou, B., Han, S., Wei, Y., Wang, C., Cheng, J., 2023. Abnormal voxel-wise whole-brain functional connectivity in first-episode, drug-naive adolescents with major depression disorder. Eur. Child Adolesc. Psychiatry 32 (7), 1317–1327.