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Amygdala as a potential biological mechanism in callous-uncaring traits: A critical review

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ABSTRACT

Externalizing behavior and psychopathy in early childhood are considered precursors to adolescent delinquency and criminal behavior. Psychopathic characteristics in adults consist of callousness, lack of empathy, shallowness, and impulsivity (Hare et al., 2000). A key trait associated with externalizing behaviors of children with a high callous-unemotional (CU) score is insensitivity to the sadness of others. CU characteristics are associated with a hypoactive amygdala, which has been found to modify the association between CU characteristics and externalizing tendencies (Saxbe et al., 2018). This paper analyses and synthesizes scholarly research articles and provides a critical review of the current state of this field of research.

Keywords: callous-unemotional (CU), Amydala

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Callous-unemotional (CU) characteristics are observed in childhood and adolescence as children exhibit relatively uniform conduct problems such as severe and persistent antisocial behaviors and violent activities; of concern is that such children are more susceptible to developing psychopathic features in adulthood (Cardinale et al., 2018). The Inventory of Callous Unemotional Traits (ICU) consists of three subfactors: callousness, indifference, and unemotionality, and it is most widely used to measure CU traits such as poor empathy, grief, and decreased emotional displays (Cardinale et al., 2018; Frick & Ray, 2015). A key CU trait associated with high CU-scoring children is insensitivity to the sadness of others. Even if the same stimuli are provided pre-attentively or when attention is shifted, youths with high CU exhibit persistent deficits in empathic accuracy, or the ability to identify fear and grief delivered by expression, voice, or body (Saxbe et al., 2018; White et al., 2012). Externalizing behavior and psychopathy in early childhood are considered precursors to adolescent delinquency and criminal behavior. Psychopathic characteristics in adults consist of callousness, lack of empathy, shallowness, and impulsivity (Hare et al., 2000). Research has expanded the concept of psychopathy to include adolescents by delineating some main characteristics, including CU traits (lack of empathy and shame, shallow and restricted emotions) and externalizing behaviors like violence, rule-breaking, and violations of social conventions infringing on others (Cardinale et al., 2018).

A significant correlation exists between externalizing behavior and CU characteristics (Saxbe et al., 2018), and increases in externalizing behavior are significantly associated with CU traits in youth. The presence of externalizing behaviors is particularly effective in predicting a subset of individuals with more severe and chronic antisocial behavior (White et al., 2009; Saxbe et al., 2018). The Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition (DSM-5) lists CU as a conduct disorder symptom specifier (American Psychiatric Association [APA], 2013). CU characteristics are associated with a hypoactive amygdala, which has been found to modify the association between CU characteristics and externalizing tendencies (Lozier et al., 2014; Marsh et al., 2011). The insensitivity towards others' fear is paralleled by a reduction in their own experiences, such as decreases in fear-induced startle reactions, galvanic skin response responses, Pavlovian fear training, and personal experience of dread. Neuroimaging studies have linked the amygdala's abnormal architecture, functioning, and connectivity to diminished fear sensitivity (Cohn et al., 2013; De Brito et al., 2011; Finger et al., 2012). The precursors to juvenile delinquency and criminal behavior in childhood are externalizing tendencies and psychopathic traits. In adults, psychopathic characteristics include callousness, a lack of empathy, shallowness, and impulsivity. The notion of psychopathy has been expanded to adolescents by defining the essential CU qualities: lack of empathy, guilt, and shallow and limited feeling. These findings reveal a physiological link between the lower perceived sensitivity to fear among CU kids and their reduced empathic sensitivity to the fear experienced by others.

Brain structures involved in CU traits

Hyperactivity to incentives and/or hypoactivity to punishment are theorized to contribute to externalizing behavior. For example, reward hypersensitivity in externalizing teenagers might result in extended reward-seeking behavior (Ling et al., 2020). In addition, antisocial teenagers may prioritize satisfying their appetites over avoiding punishment (Aghajani et al., 2016). Insensitivity to punishment has also been linked to psychopathy and antisocial behavior. A lack of sensitivity to punishment effects may manifest in externalizing or antisocial conduct (Aghajani et al., 2016). Struggling to process punishment, also known as hypo-responsivity, might lead to lower anxiety levels and dread anticipation, which can nurture psychopathic and antisocial tendencies. According to one school of thought, psychopathy and behaviors that are externalizing and antisocial may result from problems in modulating reward and punishment systems (Ling et al., 2020). Studies using functional magnetic resonance imaging (fMRI) on adolescents and young adults with high CU characteristics lend credence to the supposition that the paralimbic dysfunction paradigm may apply to this patient population. Adolescents with increased CU characteristics consistently exhibit aberrant paralimbic hemodynamic activity throughout emotion regulation and decision-making tests (Finger et al., 2012; Lozier et al., 2014; Sebastian et al., 2012). Several structural magnetic resonance imaging (sMRI) studies have compared neurotypical controls and children with significant behavioral issues. Results have shown that gray matter volume (GMV) is reduced in the amygdala, anterior insula (aINS), orbitofrontal cortex (OFC), and anterior temporal lobe (aTL) of adolescents with significant behavioral problems (Dotterer et al., 2020; Fairchild et al., 2014). CU features and gray matter structure in the paralimbic regions of the brain have been the subject of multiple research findings showing favorable connections between the two (Dotterer et al., 2020). In contrast, a recent comparison revealed that children with conduct problems and increased CU traits have lower gray matter volume (GMV) in the left orbitofrontal cortex (OFC) and right anterior cingulate cortex (ACC) compared to young people with conduct problems, normative CU traits and neurotypical controls (Sebastian et al., 2016). Additionally, some studies have shown an inverse relationship between psychopathic traits and GMV in various paralimbic locations (Aghajani et al., 2016; Ermer et al., 2013; Yang et al., 2015).

Low emotional reactivity, poor emotion identification, and deficiencies in reversal learning are examples of neurocognitive impairments that can be found in young people with increased CU characteristics (Anderson & Kiehl, 2014). These cognition disorders are comparable to those that are observed in adult psychopaths. Using functional neuroimaging and electrophysiological research in clinical populations with particular brain lesions, several areas in the paralimbic cortex and limbic system that underlie these neurocognitive impairments in adult psychopaths have been identified. It is believed that these areas have a role in processing emotions and social signals, and the research findings have been included in neurobiological explanations of psychopathy (Anderson & Kiehl, 2014). As a component of what is known as the "paralimbic system," these areas share cytoarchitectural connections. The core components of the limbic system, as well as the regions of the brain to which they directly project, are included in the paralimbic system, which is a network of brain regions (Anderson & Kiehl, 2014). Some of the regions within the paralimbic system that are believed to play a central role in the affective processes include the amygdala, ventral striatum (vSTR), medial orbitofrontal cortex (mOFC), anterior insula (aINS), anterior and posterior cingulate (ACC and PCC), anterior temporal lobe (aTL), posterior superior temporal sulcus (pSTS), and parahippocampal gyrus (Anderson & Kiehl, 2014; Blair et al., 2006).

The paralimbic system is responsible for producing affective reactions to stimuli (e.g., pleasant or unpleasant, approach or avoid) and incorporating that information into higher-order emotional processing and decision-making systems (Anderson & Kiehl, 2014). In addition, these domains continue to be significant contributors to the field of structural study on adolescents and young adults with high levels of psychopathic tendencies. Because they show similar emotional and reinforcement learning deficiencies in young people with severe conduct issues and increased CU characteristics, brain regions that are part of the paralimbic system continue to be regions of interest in this research (Anderson & Kiehl, 2014).

Neurological models underlying CU traits

The present neuroimaging research has led to the establishment of two basic neurobiological models of psychopathy, both of which imply that components of the limbic system are the origin of the emotional and behavioral impairments that are associated with psychopaths. According to Blair's theoretical view, the development of psychopathy is connected to anomalies in the amygdala and the medial orbitofrontal cortex (Blair et al., 2014). To better understand the neurocognitive impairments typical of psychopaths, Kiehl's (2006) paralimbic dysfunction theory examines a more widely spread network of brain locations. In addition to the amygdala and the medial rbitofrontal cortex, Kiehl has drawn attention to several other cytoarchitecturally related regions that are especially relevant to psychopathy. These regions include the parahippocampal gyrus, the anterior temporal lobe, the anterior insula, and the cingulate (Kiehl, 2006). This theory explains that psychopaths have abnormal brain structure and function in brain areas that are not directly related to the fundamental limbic processes. Specifically, this theory explains why psychopaths have abnormal brain structure and function in the prefrontal cortex. Kiehl's theory, which he refers to as the "paralimbic hypothesis," is driven by the presumption that many parts of the brain have identical cytoarchitectonic qualities. These properties include the kind of neuron, the neuron's shape, and the neuron's density. Based on cytoarchitectonics findings, Kiehl (2006) has proposed that psychopaths have abnormalities in the amygdala, orbital frontal cortex, whole cingulate cortex, para-hippocampal region, and insula. This model's strength rests in swiftly accounting for failure signs that are not connected to these areas. This ability gives the model its name as the "all-regions model."

There are many parallels to be seen in both Blair's and Kiehl's models, yet, there are also several critical distinctions between the two models. Blair has focused chiefly on dysfunctions in the amygdala, a primary limbic region on both sides of the brain that can be found in the medial temporal lobe, immediately in front of the hippocampus. The amygdala is vital in linking environmental cues and emotional states and in activating core danger circuits. This amygdala dysfunction results in an inability to utilize affective signals to alter behavior because the amygdala is involved in activating core danger circuits and creating these links. This impairment has hierarchical repercussions for other functional circuits dependent on input from the amygdala, according to Blair (2006). A good illustration of this is the ventromedial prefrontal cortex, which maintains continuous behavior monitoring in contrast to previously established reward expectations. Because it can account for a greater variety of anomalies, the Kiehl model (2006) is also employed in neuroimaging investigations of psychopathy. These irregularities go beyond the amygdala's representation of fundamental emotional reactions and affect small areas of higher-order processing. The amygdala represents fundamental emotional reactions and reflects critical emotional responses. This is likely one example of compensating approach psychopaths adopt for social survival, as they cannot rely on essential emotional reactions. If these effects are hierarchical, it suggests that they emerge from fundamental abnormalities in a specific section of the brain like the amygdala, and the direct effect of hereditary variables and environmental factors on these functional brain areas. It is at least plausible to postulate that these underlying neural abnormalities will develop over time. Numerous failures to integrate these intrinsic emotional cues into adaptive responses guiding behavior aggregate and lead to an aberrant functional brain architecture over a lifetime, referred to as a "lifetime of many incorporation failures" (Blair et al., 2014; Anderson & Kiehl, 2014). It can be assumed that these functional brain abnormalities will evolve when considering the neuronal growth and plasticity in the brain.

Critical review

Limited studies exist on understanding the relationship between CU traits and externalizing behavior by studying the neural process. However, a study in 2018 by Cardinale et al. explored the significance of abnormal amygdala activity and functional connections during a socioemotional judgment test in children with conduct problems and CU characteristics. This work explored the relationship between these CU deficiencies and externalizing tendencies. This study used the active task of reading statements and providing responses to illuminate the neural processing which underpins the externalizing behavior of causing fear in others. During the task, individuals were presented with 20 neutral statements that evoked anger, disgust, fear, happiness, and sadness. They were asked to press a button if they disagreed or agreed with a statement. A 3 by 6 ANCOVA was used to analyze the data, in which intelligence quotient (IQ) and age were covariates. The results indicated that the left amygdala of adolescents with high CU was hypoactive when assessing the instillation of fear in others. The results show that CU characteristics modulated the link between externalizing behavior, amygdala activity, and functional connectivity patterns. Functional analysis demonstrated that teenagers with CU traits, and abnormal amygdala activity, influence their evaluations of the acceptability of inflicting emotional suffering on others. These abnormalities are risk factors for externalizing behaviors like rule-breaking and aggressiveness.

This was one of the few studies that focused on understanding this relationship by employing an active reading task while using fMRI to measure neural responses. The researchers used fMRI to understand the relationship between CU and externalizing behaviors while referencing a systematic review from 2008 to support the use of the selected measures. Of note, using an updated measure may have provided varied scores. This real-time active investigation of adolescent behavior, alongside reports from parents and teachers regarding externalizing behaviors, provided a holistic picture of the teenagers' behaviors. However, limitations in this work should be considered. Comparing groups with real-time tasks versus reported measures could have helped to explore the influence of the task on the results. Regarding the diversity of the sample, the data was collected primarily from English-speaking people and females, and Asians were underrepresented in the sample, creating difficulty in generalizing the findings. A replication study with a more heterogeneous sample could extend the utility of the research findings.

A study by Aghajani et al. (2016) examined the intrinsic functional connectivity of the amygdala sub-regional network (basolateral amygdala; BLA and ventromedial amygdala; CMA) and the volume and shape of the amygdaloid complex. The study investigated teenagers aged 15 to 19 years old in three matched groups: conduct-disordered (CD) juveniles with CU traits (CD/CU+; N = 25); CD juveniles without CU traits (CD; N = 25) and healthy controls (HC; N = 24). Results showed that when compared to CD and HC groups, CD/CU+ teens retained an exceptionally enlarged BLA link with a cluster encompassing both dorsal and ventral sections of the anterior cingulate, medial prefrontal cortices, and the posterior cingulate, sensory associative, and striatal regions. CD/CU+ adolescents also demonstrated a lower CMA link to the ventromedial/orbitofrontal region than CD and HC adolescents. These connection changes in CD/CU+ patients were significantly associated with local hypotrophy of BLA and CMA subregions and more severe CU symptoms.

The study was one of the first that explored the connectivity profiles of the amygdala sub-regional network; however, with the specific population type of juvenile males and small sample size, the results may be difficult to generalize. The study also failed to provide the sample's ethnicity or describe age's influence on brain structure, which could have helped delineate effects on the amygdala and related regions. Additionally, the study was cross-sectional; hence causal effects could not be determined. The authors used self-report measures, which may have biased the results; including a clinician-rated scale with the self-report measures could have increased the reliability of the reported measure scores. Comparative analyses of groups based on the type of crime committed could have added another good factor for results analysis.

A 2019 study by Cardinale et al. explored the aberrant structure of the amygdala in association with CU total scores, three CU subfactor scores (callous, uncaring, and nemotional traits), and externalizing behaviors in a sample of 93 children aged 9-18 years old. The Strengths and Difficulties Questionnaire (SDQ; Goodman, 1997) and the Child Behavior Checklist (CBCL; Achenbach & Rescorla, 2000) collected information from the children's parents regarding behavioral issues. The Inventory of Callous and nemotional Traits (ICU; Kimonis et al., 2008) was utilized to evaluate CU characteristics, and the relationship between reduced amygdala volume and externalizing behavior severity mediated by CU traits was also measured. Results indicated that decreased bilateral amygdala volume and increased externalizing behavior were associated with the CU measure's callous and uncaring sub-factor scores. The scores of the callous and uncaring subfactors were independently linked with greater levels of externalizing, but this relationship was not demonstrated between scores of externalizing and the nemotional subfactor. Regarding amygdala volume, it was found that the decreased left and right amygdala volume was associated with the total ICU scores and callous and uncaring subfactor scores. Study results demonstrated that the CU traits mediated reduced amygdala volume and externalizing severity. The study's unique feature included exploring the subfactors of the CU traits and the moderating effect of age and gender on amygdala volume. The study also included a mixed-gender sample representing various ethnicities, strengthening its generalizability. However, the data collected was from a particular geographic location, and the underrepresentation of some ethnicities reduces the potential to generalize the findings; using a nationally representative sample would improve generalizability. The sample included youth with attentional deficits but provided no information regarding ADHD diagnosis, which is cause for concern. The limbic system is implied in the etiology of ADHD and may contribute to the change in the amygdala volume, thereby impacting the current study results. Lastly, having a teacher version and self-report for CBCL could provide a complete picture of the externalizing symptoms rather than relying solely on the parent rating version, which could contribute to biased data.

The study by Ling et al., 2020 examined the relationship between CU traits and the amygdala and the hemispheric differences between amygdala structure and CU traits. The Antisocial Process Screening Device (APSD) was used to collect CU characteristics data (APSD; Frick & Hare, 2001). A composite measure of each item was created by combining child self- reports and parent report scales, with the highest rating of each symptom serving as the basis for the calculation. The sample included 454 children aged 11-13 years, with equal representation of males and females. Results indicated no association was found between CU characteristics and overall amygdala volume. Results also demonstrated that females with high CU characteristics and males with low CU displayed an enhanced rightward amygdala volume asymmetry compared to males with high CU and females with low CU traits. This study explored the age- related effects in the sample; this was a unique study feature as none of the studies discussed explored the effects of age on the structure of the amygdala. However, the studies contained an overrepresentation of

African American participants, creating challenges in generalizing the results to other ethnicities. The study used APSD as a measure for CU traits which is different from the measures used by other studies. The ASPD scale has poor internal consistency indices for the Callous-Unemotional (CU) traits across studies; the study authors also failed to justify the use of the scale, providing additional scrutiny regarding the selection of this measure for use in investigating CU traits. Additionally, the authors did not use any adolescent-provided self-report measures, which may prevent the generation of a holistic picture of present CU traits. Finally, immature brains continue to develop between 11-13 years of age, which age range comprises this study sample; this makes the applicability of study results less clear.

Another study by Saxbe et al., 2018 investigated whether amygdala volume is predicted by externalizing behavior if the resting state connection of the amygdala is predicted by familial aggressiveness and the mediation effects of externalizing behavior. The authors longitudinally assessed 21 individuals for family aggression (via mother, father, and youth report) in early adolescence, externalizing behavior in mid-adolescence, and magnetic resonance imaging (MRI) data in late adolescence. According to the findings, family anger and subsequent externalizing behavior were associated with greater right amygdala sizes, higher amygdala-fronto-limbic, salience network connections, and decreased amygdala-posterior cingulate connectivity. During late adolescence, externalizing behavior impacted early adolescent familial hostility and resting state connectivity between the amygdala and the subgenual anterior cingulate cortex, medial prefrontal cortex, orbitofrontal cortex, and posterior cingulate cortex.

This longitudinal study improves understanding of the causal relationship between CU, externalizing behavior, and amygdala volume, a unique feature of this study. One limitation is that individuals were assessed at different stages of life, but the MRI was performed in late adolescence. Thus, brain changes may have been caused by other forces like stress, trauma, other significant events, or normal brain development. These potential factors are not mentioned in the study, but they could severely impact the results. Additionally, age-related differences were not examined in the study, which may cause differences in understanding casual relationships. Including an MRI at each measurement stage in the study could have provided a clearer picture of contributing factors, but doing so may not have been cost-effective.

A 2020 study by Dotterer et al. explored the relationships between antisocial behavior (AB), CU, amygdala reactivity, and functional connectivity during socio-emotional processing. The adolescent sample (N = 165) was engaged in event-related emotional faces tasks during fMRI in which the participants recognized emotional faces. Results indicated that AB was linked with higher amygdala activation in response to all emotions, but CU characteristics were associated only with enhanced amygdala responsiveness to emotion at low levels. AB and CU features were related to different amygdala connection patterns. This study explored the reactions of the sample to both happy and sad emotions, which were missing from other studies exploring reactions to emotions related to fear or sadness. The sample was a mixed gender sample with equal representation of females and males. However, 73% of the sample were African American and belonged to lower socioeconomic status, making the generalization of the results difficult. Additional limitations include the concert that no gender differences, age-related differences, or socioeconomic factors affecting brain development were explored.

Conclusion

Although the specific link between the anatomy of the brain and its functions is not entirely known, recognizing the structural functioning regarding CU characteristics will lead to considerable advances in etiological explanations of CU trait development. Having this understanding can assist in formulating effective psychological interventions, identifying accurate biomarkers and prospective treatment targets when studying psychological disorders and other disturbances impacted by CU traits. Additionally, research is required to define CU characteristics as a personality construct. Notably, there have been considerable limitations in its measurement, partly due to its historical status as a subset of psychopathy rather than a prominent dimension in its own right. Consequently, numerous existing measures have limited coverage of CU characteristics and a variety of psychometric shortcomings. Consequently, the creation of exhaustive assessments of these characteristics is an important topic of future research.

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