Title

The Effect of 5-HTTLPR Polymorphism on Callous-Unemotional Traits in Adolescent Psychopaths



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# The Effect of 5-HTTLPR Polymorphism on Callous-Unemotional Traits in Adolescent Psychopaths

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**Abstract**

This paper reviews the outcome of serotonin production in callous-unemotional (CU) traits, varied by the SLC6A4 gene's 5-HTTLPR repeat polymorphisms, which includes the short-allele by 44bp deletion and long-allele by 44bp insertion. Specifically, this research looked into the long-allele possibly causing decreased serotonin production, resulting in CU-traits. Previous studies found psychopathic key characteristics to be environmentally and genetically influenced in unique ways, with CU-traits being genetically affected by 5-HTTLPR polymorphisms. This research was conducted by searching for articles with keywords on the Google Scholar search engine, such as "*psychopathic risk factors*" and "*psychopathy in adolescents.*" A focus of 5-HTTLPR polymorphisms was established by its observed repetitive mentions, followed by filtering out unrelated sources already collected, then synthesizing the remaining information deemed relevant to the respectively formed research question. The data search surrounded adolescents between 12-19 year-olds, but was supported by data of other age groups, also due to severely limited research on CU-adolescents. Results within these studies were typically derived from neuroimaging, PCR, twin studies, and checklists. Treatments for psychopathic adolescents are based on positive encouragement, a preventative technique stemming from the biological foundations of CU-specific psychopathy. It was concluded that serotonin production is not depleted, but has fast reuptake from the synaptic cleft by increased 5-HT transporter mRNA. This lowers serotonin usage availability, which has been tightly associated with CU traits from previous research. Further studies should focus more on trying to understand the mechanisms of the long-allele directly impacting increased 5-HT transporter mRNA concentrations.

## Introduction

### I. Psychopathy in Adolescents

Psychopathy is a category of antisocial behavior (AB) that can be seen across criminal contexts expressed at an early age and has a prevalence between 10-30% among the general population's incarcerated criminals (Larsson, 2006; Tiihonen et al., 2019). From quite recent studies, its defining characteristics seem to be well understood (Larsson, 2006; Tiihonen et al., 2019), with research on sixteen-year-olds establishing a relationship between psychopathic personality disorder (PPD) characteristics and conduct problems (Tiihonen et al., 2019). Psychopathy can be broken down into traits, with one study listing irregular expression of emotional behavioral features, fear absence, and callous attitude (Sadeh et al., 2010).

Although the multitude of factors across genetic to environmental contexts that may significantly impact development of PPD, studies found that sex does not impact heritability nor environmental susceptibility of PPD across its trait dimensions (Tiihonen et al., 2019). However, in comparison to boys, girls begin displaying AB at lower expression levels and at later stages, usually during adolescence (Brammer et al., 2016). Psychopathic features such as callous-unemotional (CU) traits may be used to predict the development of psychopathy at an early age, appearing as early as three years (Brammer et al., 2016; Palma-Gudiel & Fañanás, 2017).

#### A. Callous-Unemotional (CU) Traits

The CU-trait is an often-discussed dimension of psychopathy, with characteristics primarily being a lack of empathy, guilt, and experiencing limited emotions (Viding et al., 2005). Among youth with conduct problems, those with CU-trait patterns have been found through screening to express intensified aggression compared to the rest of conduct-problem youth

(Larsson et al., 2006). This behavioral difference, also associated with low neurotic traits, has been suggested to root from genetic factors due to the CU dimension's decreased negative emotional reactions including anxiety, depression, and anger (Widiger & Oltmanns, 2017). The integration of various genes involved in general psychopathy have been suggested to be of concern in emotional callousness, as presented by a study's psychopathic violent offender group (Tiihonen et al., 2019).

### B. Study Significance

The purpose of this article is to understand the roots of psychopathy's callous-unemotional trait by discussion beyond behavioral-based analysis to strengthen diagnosis and prediction accuracy, thus allowing for earlier and more adequate treatment. Although psychopathy is an individual diagnosis, it is closely associated with violent criminal behaviors that create societal-level impacts (Gacono, 2000). This article aims to fill the gap of knowledge of CU development during adolescence, including this period's key features and developmental trajectory, since most studies thus far have been done on children.

Understanding the subcategories is an important aspect of psychopathy, as one study found that different combinations and individual traits in psychopathy have varying corresponding rates of AB. In 1941, Karpman was the first to establish primary and secondary subtypes of psychopathy, allowing for a clearer image of psychopathic traits and influences of particular behavioral sets, and corresponding appropriate interventions for each (Lee et al., 2009). Children with specifically combined symptoms of conduct disorder (CD) and attention deficit hyperactivity disorder (ADHD) most frequently executed antisocial and criminal behaviors (Gacono, 2000). In addition, specifically psychopathic adolescent criminal offenders

tend to commit more violent crimes, more serious offenses, and increased violence during incarceration compared to the general antisocial youth population (Larsson et al., 2006).

Psychopathic individuals often refuse treatment during adulthood, so it is best to intervene in early life stages while the brain is still in development, therefore more flexible (Gacono, 2000). As PDD in adolescents and adults correspond with higher rates of violence and recidivism, allowing PDD behaviors to prevail without the adequate interventions and timing may put the surrounding public in danger (Lee et al., 2009). Thus, understanding specific psychopathic traits at earlier stages of life can help entrench protective measures along its progression.

### C. Data Collection Methods

From the various sources considered, the most evidence-prominent and discussed data collection methods include the Psychopathy Checklist-Revised: Youth Version (PCL:YV), Antisocial Process Screening Device (APSD), Developmental Trends Study, Pittsburgh Youth Study, Psychopathy Checklist-Revised (PCL-R), Hare Psychopathy Checklist, and Youth Psychopathic Traits Inventory (YPI). The Developmental Trends Study and Pittsburgh Youth Study are used to understand long-term development (McMurran, 2010). The Hare Psychopathy Checklist is mostly used in clinical practice to detect psychopathy, and the YPI measures an individual's expression of PDD constellation core features, which include questions for each feature of the constellation, such as lying, callousness, and manipulation (Larsson et al., 2006). The commonly used self-report APSD is a 20-item rating scale regarding the psychopathic features of CU, narcissistic, and impulsive traits (Brammer et al., 2006).

Regarding the genetics of psychopathy, trait development has been mostly studied through twin studies, such as the Twins Early Development Study that uses same-sex pairs.

Considering that sex has no notable impact on acquiring psychopathic traits (Viding et al., 2005), this factor should not pose a limitation to study variation. Genetic information in such studies may be obtained by laboratory procedures such as Polymerase Chain Reaction (PCR). Here, DNA is collected in saliva samples using cotton swabs, then amplified in equipment that extracts the short (484-base-pair (bp)) or long (528-bp) fragments of the focus gene region, 5-HTTLPR (Brammer et al., 2006). This is placed into agarose gel electrophoresis that divides the genotype into l/l, s/s or s/l (Sadeh et al., 2010). Most importantly, neuroimaging techniques such as functional magnetic resonance imaging (fMRI) can be paired with genetic identification for optimal scientific support.

## II. Epigenetics of Psychopathy

Although Karpman's psychopathy subtypes are similar through behavior, their core differences lie within genetic composition and environmental motivation. AB in primary psychopathy is less particular to specific categories of influence, while secondary traits are known to be susceptible to environmental influences, perhaps for adapting or surviving in a particular environment (Lee et al., 2009).

In an adult male twin study for factors initiating psychopathic traits, all dimensions of psychopathy in the Psychopathic Personality Inventory (PPI) scale were affected by genetic and nonshared environmental influences, with genes composing 29-56% of variation and shared environments showing no consequences in any PPI dimension. In a self-report twin study on male adolescents, though, 40% of the genetic effects have been found to specifically affect CU and impulsive/antisocial traits of a "psychopathic personality constellation," with remaining variance resulting from nonshared environments (Larsson et al., 2006). Consistent with the adult

study, there were no notable effects of shared environments on psychopathic trait variance. Following these studies, an article reviewed YPI findings on 1,090 16- to 17-year-old monozygotic and dizygotic twin pairs, finding nonshared environmental factors accounting for 37% of psychopathic personality variance (Larsson et al., 2006). Thus, it has been suggested that these nonshared environmental factors may be due to the high susceptibility to peer influence during this developmental period. Studies further exploring the gene-environment (GxE) interactions concluded that this may also influence narcissistic traits of psychopathy alongside CU-traits (Sadeh et al., 2010). Thus, one genetic factor that is said to strongly initiate a CU personality may not be isolated in specific psychopathic feature triggers.

Animal studies helped establish relationships between social status and serotonin (5-HT) functional outcomes in unstable environments (Sadeh et al., 2010). A human study further identified that interactions between the 5-HTT allele for serotonin expression and socioeconomic status (SES) is related to CU-trait outcomes, with CU-traits having an inverse relationship with SES (Sadeh et al., 2010). In fact, this study interpreted that SES may influence both callous and narcissistic subcategories of psychopathy. Specifically to long-allele homozygotes of the 5-HTTLPR region, both of these categories of psychopathy showed an inverse association with family income (Palma-Gudiel & Fañanás, 2017). Such traits emerging from this context could be possible consequences of disadvantaged youth having to utilize this for survival, conditioning them into prioritizing their own well-being and survival regardless of its impact on others in dire situations (Sadeh et al., 2010).

The 5-HTTLPR region can be seen as a moderator of environmental impact on emotional and behavioral responses to stressors (Canli & Lesch, 2007). Interestingly, different 5-HTTLPR polymorphisms have been discovered to interact uniquely to adverse environmental conditions.

For instance, individuals carrying the short-allele here have an increased amygdala fear-response to environmental threats than for homozygous long-alleles (Palma-Gudiel & Fañanás, 2017). Rhesus monkey studies examining maternal separation found that the resulting depleted social adaptation was due to altered serotonergic system functioning.

### D. 5-HTTLPR Polymorphism and the SCL6A4 Gene

5-HT is expressed by the SLC6A4 serotonin transporter protein gene, specifically in the 5-HTTLPR region (Sadeh et al., 2010), or the serotonin transporter. Psychopathic traits are derived from 5-HTTLPR polymorphisms, or different versions of one gene sequence, altering the function of genes coding for serotonergic proteins. Resulting depleted serotonin levels ultimately lead to antisocial and aggressive behavior of psychopathy (Sadeh et al., 2010). Thus, since psychopathic traits are proven to be a susceptible consequence from serotonin neurotransmission disruptions, this confirms using 5-HTTLPR as a reliable psychopathy biomarker (Brammer et al., 2016).

Among the various SLC6A4 gene alterations, it is uncertain which precise genotype has the most powerful influence. However, its repeat polymorphism is most popularly studied due to its prominent impact on 5-HTTLPR through deletion or insertion of 44-bp (Sadeh et al., 2010), respectively referred to as the short-allele and long-allele.

In this article, we will be exploring 5-HTTLPR polymorphism's specific association with the callous-unemotional trait of psychopathy. This brings the question: How is callous-unemotional behavior in psychopathic adolescents affected by specific polymorphisms in the 5-HTTLPR region of the SLC6A4 gene? Based on the presented information, the long-allele

alone may be involved in CU adolescent psychopathy because its 44-bp insertion leads to consistently decreased serotonin production.

## Methods

This review began with a general idea of adolescent psychopathy (Figure 1), searching phrases on Google Scholar including "*psychopathic risk factors*," "*psychopathy in adolescents*," and "*psychopathic development*." Along with repetitive mentions of CU-traits in 14 selected sources, frequent comments regarding 5-HTTLPR polymorphisms for these traits were correspondingly observed within. Consequently, the phrase "*5-HTTLPR polymorphisms CU-traits*" was investigated, finding its prominent involvement of short- and long-alleles, then saving 2 sources. With this genetic variance becoming the focus, four from the original set of sources were simultaneously disregarded. Since the SLC6A4 gene was often acknowledged in these, "*SLC6A4 psychopathy*" was searched, and one article was extracted from the results. This source (Palma-Gudiel & Fañanás, 2017) officially inspired the hypothesis formation, additionally based on the frequent associations with 5-HTTLPR polymorphisms and CU-traits.

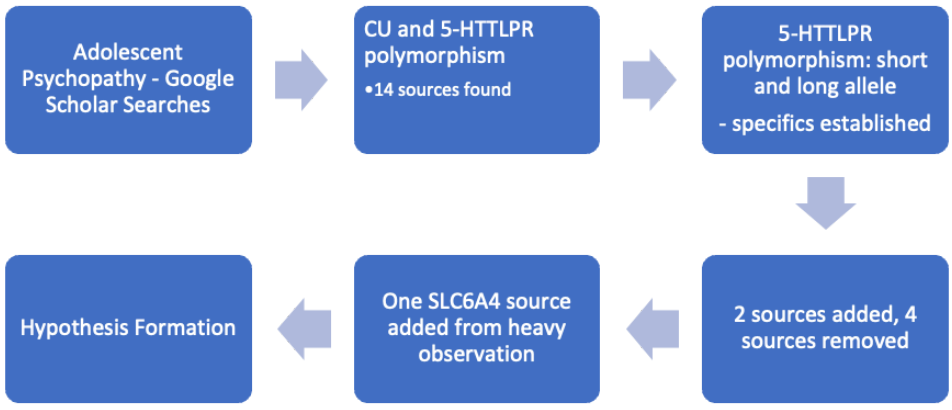

*Figure 1: Hypothesis/Topic Formation*

Looking at Figure 2, two Google Documents ("*Layout*" and "*Notes*") were created to progressively organize the collected information. *Layout* was initially only the planned structure, establishing subcategories within the Introduction, Results, and Discussion sections. *Notes* included 15 pages of bullet-points of all seemingly relevant information extracted from included sources, then narrowing down the most necessary information into what successfully relates into corresponding *Layout* categories. These compartmentalized data allowed for organized synthesization and clear comparisons.

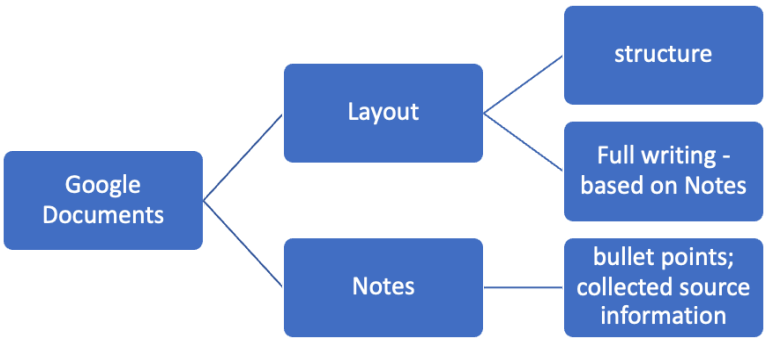


*Figure 2: Synthesis/writing process.*

## Results

### I. 5-HTTLPR Variants

Encoded by SLC6A4, the serotonin transporter protein (5-HTT) is crucial in serotonin regulation by removing excess 5-HT from the synaptic cleft (Canli & Lesch, 2007). SLC6A4 methylation resulting in polymorphism in the 5-HTTLPR promoter region through either homozygous or heterozygous forms alters 5-HTT expression and function that affects serotonin's amount correspondingly, creating behavioral differences presented between the short- and long-allele (Brammer et al., 2016; Canli & Lesch, 2007; Palma-Gudiel & Fañanás, 2017).

Regarding the variant mechanisms, long-alleles are suggested to cause faster removal of serotonin from the synaptic cleft due to its observed higher 5-HT transporter mRNA concentrations, depleting 5-HT availability in the cleft (Canli & Lesch, 2007). This polymorphism is more common among African-Americans than European-Americans, and only the homozygous-long (l/l) genotype shows a negative correlation between SES and CU traits. A sample of healthy l/l-genotype adults displayed lower prosocial empathetic responses than s/s adults (Brammer et al., 2016).

In comparison, as detected through human blood platelets, short-alleles lead to reduced 5-HT reuptake, increasing 5-HT synaptic cleft availability (Palma-Gudiel & Fañanás, 2017; Sadeh et al., 2010). This is due to the reduced production of 5-HTT mRNA and protein (Canli & Lesch, 2007). The short-allele has a 42% prevalence in the Caucasian population (Palma-Gudiel & Fañanás, 2017). Its effect on serotonin availability has been linked to an increased risk for affective dysregulation-based psychiatric diagnoses and intensified amygdala activation in response to negative emotional triggers (Sadeh et al., 2010). This increased synaptic serotonin does not mimic selective-serotonin-reuptake-inhibitors (SSRIs), supported by a study finding that s-carriers have higher rates of suicidal tendencies (Palma-Gudiel & Fañanás, 2017).

Comparing l/s and s/s genotypes, the brain activity of those without a short-allele polymorphism related to outcome behavior of lower emotional distress, better emotional regulation, and overall lower amygdala and hippocampus resting levels (Sadeh et al., 2010). Family studies also found that the short-allele is more related to anxiety and neuroticism than the long-allele, while other studies found no relationship with 5-HTTLPR variants (Canli & Lesch, 2007).

These polymorphisms have been particularly associated with antisocial personality disorder (ASPD) in women containing the s/s allele, while ASPD symptoms were unnotable among l/l women (Palma-Gudiel & Fañanás, 2017). When an unpredictable acute-stressor task was done on women, there were significant activations in this network that includes the amygdala, thalamus, and putamen, exclusively among s-carriers. Moreover, this study showed long-alleles having an inverse relationship with insula activation and emotional regulation, upholding that the long-allele has lower reactivity to emotional stimuli. One neuroimaging study using the Go-NoGo task examined the relationship between 5-HTTLPR and excitability between the prefrontal cortex and limbic system, finding that those with at least one short-allele copy demonstrated higher ACC activity than homozygous long-allele carriers. Ultimately, an fMRI study confirmed that the variations' neural effects lie within the amygdala, aligning with its key function for emotional regulation. Increased 5-HT availability from short-alleles have been directly linked to psychopathy, disrupting the amygdala's circuitry for appropriate emotional reactions (Sadeh et al., 2010).

5-HTTLPR's functioning in emotional regulation and fear extinction of CU-traits has been found by one study to occur through the amygdala and anterior cingulate cortex (ACC) neural pathway. Short-allele carriers were found to have reduced gray matter in the ACC and amygdala and reduced interconnectivity, resulting in emotional dysregulation (Canli & Lesch, 2007). This serotonergic pathway is particularly responsive to environmental factors that increase susceptibility of such trait expressions (Sadeh et al., 2010). Thus, this amygdala-ACC pathway could be a neurological vessel in works with environmental adversity towards these PDD subcategories. However, the hippocampus has been briefly noted to also be important via 5-HT regulation.

## II. 5-HTTLPR for CU in Adolescents

CU traits are considered to be less stable among children compared to adolescents, meaning that CU traits may become clearer in later development (Palma-Gudiel & Fañanás, 2017). In order to uncover a relationship between SES and SLC6A4 in psychopathy in early adolescence, a self-report APSD was used to measure CU, narcissistic, and impulsive subcategories. They found that significant levels of both CU and narcissism were expressed the most among adolescents containing the l/l genotype and grew up in low-SES environments, while s/s was highest for impulsivity (Sadeh et al., 2010).

These presented APSD outcomes may clash with previous associations between short-allele absence and better emotional regulation compared to l/s and s/s genotype individuals (Sadeh et al., 2010). However, results still showed that the short-allele absence leaves individuals susceptible to AB through callous traits (Sadeh et al., 2010), supported by multiple other analyses showing a positive correlation between long-alleles and CU traits, as well as narcissism (Palma-Gudiel & Fañanás, 2017).

Considering the long-allele's expression of CU and narcissistic traits, this polymorphism may also be involved in sensitivity to disadvantaged environments. Opposed to the short-allele, the long-allele's biological function results in suppressed emotionality (Sadeh et al., 2010). This goes under the differential susceptibility hypothesis, a psychological interpretation that different individuals are each uniquely susceptible to a range of environmental conditions (Sadeh et al., 2010). In this case, CU-trait vulnerability would be strongly affected by the presence and expression of the long-allele, and whether it is homozygous or heterozygous, combined with an adverse environment.

## III. Psychopathy Treatment

Developing through various social experiences with the expected guidance of teachers and parents, our trajectory in achieving appropriate behavior is considered reaching a normal behavioral "feedback" that we learn as children. However, one could be identified with CU-traits if there is a chronic lack of ability to maintain or comprehend this feedback (Bjørnebekk & Mørkrid-Thøgersen, 2021).

Treating CU at an early age decreases the risk of developing psychopathic traits, so CU in childhood can be seen as a precursor for psychopathy in adulthood. However, studies have found that the majority of children with high CU scores (determined by maternal judgment) do not develop psychopathy later in life. CU trait scores have been found to be highest among 14 to 15 year olds. For example, in a sample of 13 year olds, about 50% those with significant levels of CU had psychopathic diagnoses at 24 years old, while those with lower scores typically did not develop psychopathic traits by this age (Bjørnebekk & Mørkrid-Thøgersen, 2021). Therefore, it is important to consider the degree of CU when using CU as a predictor of psychopathy or related behaviors, and can be used for more organized categorization.

As a major trait of CU individuals is solely caring about themselves by lack of remorse (Bjørnebekk & Mørkrid-Thøgersen, 2021), numerous studies confirmed that the optimal treatment methods involve positive encouragement. Through positive encouragement, the CU individual is inspired to like the people around them more, but primarily by self-interest (Bjørnebekk & Mørkrid-Thøgersen, 2021). Positive encouragement can generally be applied through "parental warmth" through praise and affection. Studies have found that for children with high CU scores, parental warmth reduces their conduct problems, establishing a negative correlation with CU degree (Bjørnebekk & Mørkrid-Thøgersen, 2021). Parental training

programs, such as CU-specific Parent/Child Interaction Therapy (PCIT-CU), exist to alleviate such behavioral challenges by praising youth towards understanding others' boundaries and displaying appropriate behavior. In a study comparing children with high and low CU-traits, both groups equally improved when treated with parental prosocial attitudes, as opposed to the uncooperative parents (Bjørnebekk & Mørkrid-Thøgersen, 2021). These recent treatments as early psychopathy-development prevention, including stimulant pharmacological interventions, have been suggested to successfully reduce CU and narcissistic traits, along with improving their deficient emotional recognition (Palma-Gudiel & Fañanás, 2017).

While supportive parental behavior reduces CU behaviors, unstable households intertwine in CU development (Bjørnebekk & Mørkrid-Thøgersen, 2021). Punishment-based treatment is logically inefficient if CU adolescents are unable to comprehend the meaning of negative consequences. Furthermore, an important risk factor in severe CU trait development among adolescents is relatively frequent conflict in the household (Bjørnebekk & Mørkrid-Thøgersen, 2021).

Life-persistent AB is typically an outcome of AB displayed in early childhood, between ages 3-10. However, ABs showing up in adolescence tend to stay confined in teenage development, meaning that it would be unlikely for traits here to persist into adulthood. Still, this limit may vary upon disorder severity, circumstances, drug addiction, and peer influence (including further poor encouragement from others in prison), which all may lead to chronic, violent conduct problems originating in the adolescent phase (Bjørnebekk & Mørkrid-Thøgersen, 2021).

Emotionality measurement is considered to be the most important predictor of psychopathy in youth, which can be determined by Limited Prosocial Emotions (LPE) criteria: a

lack of remorse or empathy and shallow affect. One LPE examination found that a significant portion of a 5-16 year-old sample had high scores for CU-traits (Bjørnebekk & Mørkrid-Thøgersen, 2021). Children diagnosed with CU-specific CD displayed obstacles in emotional cognition and motivation, with socially deviant goals that were justified with violence and unnecessary blame on others. These justifications were in fact supported by their positive views on such actions (Bjørnebekk & Mørkrid-Thøgersen, 2021). They do not acknowledge others' vulnerable states or emotions such as pain and fear. These altered perceptions in moral tests present their difficulties to comprehend social rules that should guide appropriate behaviors in the given situations, as well as which action path would ultimately harm others (Bjørnebekk & Mørkrid-Thøgersen, 2021).

Studies lack direct evidence of 5-HTTLPR genotypes' neural impact on social interaction. However, there is evidence of facial emotional stimuli associating gray matter structure and brain region activation from 5-HTTLPR function, finding that structures such as the striatum, anterior cingulate, insula, and inferior frontal gyrus are all involved in communication, social cognition, and mirrored learning (Canli & Lesch, 2007). Studies on SLC6A4 and its environmental interaction have documented that brain regions in the mirror neuron systems (frontal and parietal regions) are involved in social cognition abilities through imitation and bonding functions (Canli & Lesch, 2007).

## Discussion

### I. Consistent Results

From the extensive psychopathy research accumulated thus far, there was an abundance of steady findings, starting with the notion that CU-traits of psychopathy can be identified in early life. This can persist into adulthood and is most commonly observed among violent criminal offenders (Brammer et al., 2016; Gacono, 2000; Tiihonen et al., 2019). CU's definition of lacking empathy is notably consistent in study measures, and appears to be generalized across all age groups (Brammer et al., 2016; Viding et al., 2005).

Serotonin appears to be a fundamental biological feature of CU-trait genetics, especially in studies comparing SES status (Sadeh et al., 2010). Compelling research on genetic differences targeting the 5-HTTLPR regions found polarizing outcomes of short- versus long-allele polymorphisms, with the long-allele repeatedly associated with CU-traits across studies. Long-alleles are critically associated with lowered amygdala activity by decreased serotonin availability in the synaptic cleft, resulting in fear extinction (Canli & Lesch, 2007; Palma-Gudiel & Fañanás, 2017; Sadeh et al., 2010). Short-alleles are more tied to anxious, over-emotional aspects of psychopathy. This could imply that short-alleles could also be a major risk factor for emotional mental health issues, or that long-alleles are associated with lower reactivity that increases risk of acquiring callous traits in adverse environmental conditions (Canli & Lesch, 2007).

Adding on, this may further suggest that GxE interactions may have different trigger categories for each polymorphism type. Thus, these findings strongly associate the long-allele with CU-dimension of psychopathy, possibly excluding the short-allele from significant

influence. This would consequently mean that brain structure also changes, but more research must be done to elaborate on this vague implication.

Narcissism and callousness were often compartmentalized together in numerous studies, both resulting from GxE interactions (Palma-Gudiel & Fañanás, 2017; Sadeh et al., 2010), with psychopathy predominantly affected by genetics and nonshared environments (Larsson et al., 2006; Viding et al., 2005). Overall, this suggests that risk factors of CU personalities are not exclusive to this one trait in the psychopathic dimensions, also recognizing that a key characteristic for both is the isolated concern for themselves (Palma-Gudiel & Fañanás, 2017).

Lastly, our knowledge of core features of CU-traits and narcissism can successfully be transferred onto treatment focused on positive reinforcement involving parental affection (Bjørnebekk & Mørkrid-Thøgersen, 2021). This contradicts previous attempts at punishing and guilting CU-specific psychopathic patients, as CU-individuals do not have adequate neural functioning towards intense negative emotions. Since adolescents are highly susceptible to peer influence by heightened mirror cognition, the treatment efforts in this phase may be reversed by poorly-influencing surroundings. While high concentrations of studies were confident about effectiveness of CU-prevention in childhood, the adolescent treatment aftermath is still vague and should be studied more, despite CU scores being highest among 14-15 year-olds (Canli & Lesch, 2007). Still, with emotion comes the consideration of those around oneself, therefore instilling this behavioral treatment could be seen as a loophole around this biological obstacle to express emotions.

## II. Varying Results

Despite repetitive associations between short-allele presence and higher serotonergic functioning via amygdala networks, one study contrastingly found that short-allele carriers had reduced connectivity in the ACC-amygdala pathway (Canli & Lesch, 2007). Although this is one contradiction against persistent findings, it nonetheless confirms that the amygdala is highly involved in psychopathic emotional dysregulation, while the true function of short-alleles is still in exploration. Psychopathy's serotonergic pathways are prominently uncertain, with another network proposal involving the hippocampus (Sadeh et al., 2010). Along with pathways that emerge CU-traits, the overall socializing role of 5-HTTLPR also stays unclear, but the amygdala's consideration in these networks remains constant.

It is possible that these contrasts may be due to a number of factors, with one being the use of numerous data-collection methods across these studies. Though the CU-trait definition remained consistent, there was immense variance among measure and questionnaire types for the same focus. Techniques were especially diverse in non-genetic methods, such as maternal judgment, potentially drawing these different conclusions. Furthermore, in CU development, one study claimed that early AB expression is often life-persistent, while another assured that most high-scoring CU children do not develop psychopathy later (Bjørnebekk & Mørkrid-Thøgersen, 2021). This reinforces the importance of distinguishing specific traits from broad diagnoses, as CU traits particularly may have a completely separate progression from antisocial disorders.

**Conclusion: Study Implications & Future Research**

Our hypothesis on the long allele's involvement in CU with decreased serotonin was only partially correct. The error lies within how exactly the long allele is associated with this serotonin amount, as we hypothesized that it decreases production. Instead, the long-allele causes the 5-HTT to rapidly clear out the synaptic cleft. There was also no direct evidence of any impact on serotonin amount from the 44-bp variance, nor how this could lead to faster clearance. Perhaps there could be an association with production levels with other SLC6A4 polymorphisms, but none were found from this 5-HTTLPR research. There also seems to be an effect on 5-HT transporter mRNA amount from long-alleles, as there was a higher quantity observed in the long-allele's presence. Thus, although our hypothesis was not entirely correct, it brings the new question of the long allele's effect on increased production of this mRNA that could result in CU-traits. Despite these reconfirmed biological outcomes for the long-allele, interpretations of mechanisms within are still left debatable. There must be more research on the long-allele individually since much of its functional assumptions were based indirectly by the short-allele's absence. Additionally, it was established by numerous studies of the 5-HTTLPR's serotonergic function in psychopathic development, but no studies provided explanations for during adolescence itself. Studies should also be more consistent with variables, methods, and age group categorization.

It is quite remarkable that this presented research from only the past 23 years has uncovered about the genetics of specific psychopathic traits, helping ongoing and rapidly accumulating studies narrow down genetic focus and accumulate optimal information. However, there is a continued exclusion of certain demographics in studies, as far too few articles here were found that included specifically females and adolescents. In fact, only one study provided

individual information on women (Palma-Gudiel & Fañanás, 2017), with multiple others only focusing on males only. Future studies should consider emphasizing these two factors, which can help with comparisons and exploring the roots of potential differences. Research should also continue to look into twin studies because until 2006, only two have been done on small samples, both exclusively on males. Moreover, psychopathic studies are disproportionately Caucasian-concentrated, even in mixed-race studies. Sadeh (2010) admitted that most participants were European-American, with the least among Asian-Americans (2.5%) while Asian-Americans make up 7% of the U.S. population (Budiman & Ruiz, 2021). Such demographic gaps inaccurately represent diverse communities, thus providing less reliable data.

Building off of the discussed various methods of collecting and combining meaningful data, from self-reports to biological techniques of just the past two decades, these continued recent studies instill confidence of continued and improved discoveries in psychopathy genetics. Along with a hopefully heightened consideration of underrepresented demographics, this new knowledge will ultimately strengthen our understanding of adequate treatments, improving both the individual's quality of life and the public's security.

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