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Review

The neurobiology of antisocial behavior in adolescence; current knowledge and relevance for youth forensic clinical practice

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Abstract

Antisocial behavior in adolescents is generally seen as a neurodevelopmental problem; however, in spite of increasing knowledge on the neurobiology of persistent antisocial behavior, conduct disorders, and psychopathic traits, this knowledge is hardly used in clinical practice.

The aim of this review is to give an overview of current research on the neurobiology of antisocial behavior in adolescents and to discuss how this knowledge can be translated to youth forensic clinical practice.

First, an overview of recent literature on genetics, neuroimaging, neuropsychology, neurophysiology/neuroendocrinology, and antisocial behavior in adolescents is given. Second, implications for diagnostics, risk taxation, and treatment are discussed. Finally, an integrated biopsychosocial approach for future research regarding translational forensic child and adolescent psychology and psychiatry is advocated.

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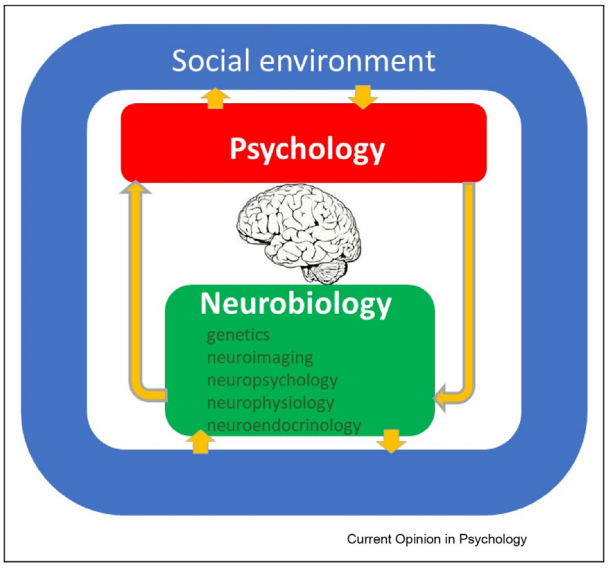
Introduction

Exploring boundaries and displaying risk-taking behavior are part of adolescence. Many adolescents will display antisocial behavior (such as aggression, rule-breaking, delinquency, and other types of conduct that violate the basic rights of another person) at some point, usually limited to a single minor incident or offense. However, some adolescents display a persistent, pervasive pattern of antisocial behavior that is often already present in early adolescence or even childhood [1–3]. Many of these persistent antisocial adolescents that habitually violate the rights of others and will not conform their behavior to the law or social norms are diagnosed with a conduct disorder (CD) [4]. Moreover, it has been shown that the most severe and persistent forms of CD include the presence of psychopathic traits in specific callous-unemotional (CU) traits [5,6]. CU traits are characterized by lack of empathy, guilt or remorse, and a shallow or deficient affect, which are fairly stable until adulthood [7]. In order to develop effective interventions to prevent the persistence of antisocial behavior and associated mental health problems, it is of main importance to gain more insight into the specific mechanisms involved in the development of this most severe type of antisocial behavior in youth.

Antisocial behavior is generally seen as a neurodevelopmental problem resulting from an interplay between neurobiological deficits, psychological and cognitive problems, and social adversity [8**]. This is reflected in the current biopsychosocial model for the development of antisocial behavior (see Figure 1). Based on this model, Popma and Raine (2006) already suggested that neurobiology should have a prominent part in the assessment and treatment of antisocial behavior [9]. Moreover, neurobiology may provide more insight into the different subtypes of antisocial behavior. According to the neurobiological model of Blair, impulsive antisocial behavior is thought to be related to reactive aggression and impaired decision making, mainly reflecting impairments in prefrontal functioning, while the more severe and persistent form of antisocial behavior with CU traits is related to intentional/proactive aggression and reduced responses to distress and unemotionality, reflecting reduced amygdala functioning [5]. However, in spite of an enormous increase in research on neurobiological correlates of antisocial behavior since then, current youth forensic assessment and interventions still mainly focus on psychological, social, and environmental risks and protective factors.

Figure 1



Schematic representation of the biopsychosocial model.

Therefore, the aim of the current review is to give an overview of the current knowledge on the neurobiology of antisocial behavior in adolescents and to discuss how this knowledge can be translated to youth forensic clinical practice.

Neurobiology of antisocial behavior

Genetics

There is a wealth of heritability studies that have analyzed empirical estimates of the relative contributions of genes and environment to the development of antisocial behavior. Recent analyses show that persistent delinquency has a substantial genetic origin (heritability 67%), aggressive behavior has a moderate heritability (39–46%) [10*], while conduct disorder in adolescence is about 50% genetic [11].

Specific genes have been associated with antisocial behavior (mainly dopaminergic, serotonergic, and oxytocin related), specifically in those with a history of child maltreatment [12–15]. However, a meta-analysis of Genome-Wide Association Study (GWAS) data did not indicate robust and reproducible genetic variants associated with antisocial behavior [16,17]. Antisocial behavior is most likely determined by many different genes, all of which have, at best, modest predictive value and are highly influenced by the heterogeneity of the phenotype of antisocial behavior and environmental influences [18]. One of the new approaches to overcome this problem is the study of polygenic risk score (PRS), a technique to estimate the effect of many genetic variants together on a specific phenotype or behavioral characteristic [19]. Indeed, recent analyses show that polygenic risk score explained the differences between stable low and high aggressive behavior throughout adolescence, as well as confirmed involvement of glutamatergic, dopaminergic, and neuroendocrine genetic variation in aggression and CU-traits, explaining up to 2% of explained variance in uncaring and unemotional behavior [20,21*].

Neuroimaging

Structural and functional magnetic resonance imaging (MRI) studies have resulted in a wealth of knowledge on brain development during adolescence, showing that (part of) the normative peak in risk behaviors that many typical-developing adolescents display can be explained by a relative protracted development of frontal cortical cognitive control systems, combined with fast maturity of subcortical socio-affective systems [22,23]. As stated above, for most youths, this behavior is incidental and limited to adolescence. However, studies in adolescents with severe and persistent antisocial behavior, including those with CD and/or CU traits, showed specific structural and functional deficits in brain development, mainly in prefrontal and subcortical (para)limbic areas and the connectivity between those areas.

First, structural brain alterations in (familial risk for) CD include smaller volumes of the frontal lobe, superior temporal gyrus, (inferior) parietal lobe, and occipital lobe [24], as well as smaller cingulate cortex volumes [25]. In addition, some evidence is found for specific structural gray matter alterations in frontal and limbic regions related to a history of childhood maltreatment in CD [26]. Although minimal evidence for structural abnormalities was found for CU-traits [5,27,28], some studies show specific structural and functional abnormalities in limbic and paralimbic structures [29**,30]. As for structural connections, i.e., white matter tracts, aggression has been related to diminished white matter density in pathways connecting subcortical and cortical regions [31], while CD and specifically CU traits have been related to alterations in additional, key subcortical-cortical and cortico-cortical connections (e.g., cingulum in CD males [32]; CU-traits: corpus callosum, anterior thalamic radiation, uncinate fasciculus [29**,33,34].

With respect to functional MRI, severe antisocial behavior has also been related to aberrant subcortical socio-emotional activation. This is reflected in differences in reward-related striatum and orbitofrontal cortex (OFC) functioning compared to the typical developing youth [35,36] and alterations in amygdala activity related to the processing of emotional faces, empathy, and threat acquisition, particularly in youth with high CU traits [37**,38–40]. Finally, studies on functional connectivity, i.e., resting-state brain activity,

suggest that CD is characterized by aberrant connectivity mainly in default mode, sensorimotor networks, and limbic system [41,42]. Moreover, proactive aggression and CU traits were related to specific connectivity patterns involving areas associated with emotion, empathy, morality, and cognitive control. (e.g. amygdala-precuneus coupling, frontal, parietal, and cingulate areas) [43].

Neuropsychology

Overall, offending youth show impairments in neurocognitive functioning. Adolescents who show antisocial and psychopathic behaviors tend to have lower IQs; specifically, low verbal IQs, have been found [44,45].

As for specific neuropsychological deficits, altered patterns of cognitive functioning in antisocial behavior largely overlap with deficits in structural and functional brain abnormalities in prefrontal and subcortical limbic structures. The most empirical support refers to the existence of problems or deficits in Executive Functioning (EF). Executive functioning is an umbrella term for mental top-down brain processes necessary to adapt behaviors to novel situations. Deficits in executive functions such as response inhibition, working memory, and mental flexibility have been found in CD [46*] and in psychopathic traits in young adults [47]. Dysfunctions in EF may also be the mediating factor between traumatic brain injury and antisocial behavior [48]. Executive functions such as (social attention, cognitive flexibility, working memory, and social planning) are also the basis of many emotional and social skills. At the level of emotion processing, specific deficits in emotion recognition, emotional learning, and emotion regulation have been found in youth with CD, which may be related to CU traits [49,50*]. However, another study found no specific relation with CU traits in CD [51].

Neurophysiology and neuroendocrinology

The autonomic nervous system (ANS) is among the most studied systems in antisocial behavior. According to the low-arousal theory, antisocial behavior is related to a low ANS activity, which subsequently may lead to sensation-seeking behavior, as well as fearlessness. An extensive meta-analysis showed that low resting heart rate is the most stable correlate of antisocial behavior throughout adolescence and early adulthood, with the strongest effects among the more serious antisocial groups, such as serious offenders and subjects with psychopathic traits [52**]. However, not all studies could replicate this finding [53,54]. This is most likely due to heterogeneity within CD, as adolescents with high CU traits and proactive aggressive behavior have low arousal levels, while adolescents with more anxiety and reactive aggressive behavior show high arousal levels [55,56].

As for ANS reactivity, Respiratory Sinus Arrhythmia (RSA) has been most extensively studied as an indicator of emotion regulation. Several studies show a decreased RSA responsivity in reaction to diverse emotional stimuli, although results are less consistent than for resting heart rate [56,52**,54,57,58].

Several studies have specifically focused on stress reactivity in antisocial behavior, mostly including heart rate and/or the so-called stress hormone cortisol. These studies also showed a decreased responsivity in adolescents with antisocial disorders, with the main effects in those with CU traits [59,60]. Furthermore, dorsal striatum activity as part of the mesolimbic system, known to be sensitive to environmental adversity, seems to play a role in externalization-specific cortisol stress responses [59,61*,62]. However, a recent review on the association of basal and reactivity cortisol levels with the development of delinquent behavior did show inconsistent results [63*].

Finally, sex hormones, specifically testosterone in males, have been related to aggressive behavior and CD [56,61*].

A recent multisample, multimethod study of our own group has integrated neurophysiological and neuroendocrinological assessments over several antisocial and normal developing cohorts. This large study confirms the importance of both neurophysiology and neuroendocrinology: both are related to antisocial behavior, such as psychopathic traits, and aggressive and impulsive behavior; moreover, these relations showed to be consistent throughout adolescence and early adulthood [64**].

Translation of neurobiological knowledge to youth forensic clinical practice

Diagnostics and risk taxation

Based on the current knowledge described above, using neurobiological knowledge to make a distinction between antisocial behavior with or without psychopathic traits and CU traits, in specific, may be most valuable for clinical forensic practice. Neurobiological assessments may provide additional indicators of CU traits that are more objective than self-report only. Based on the current literature, the most promising and practical assessments to differentiate between antisocial youth with or without CU traits are neurophysiological (heart rate, heart rate variability/RSA) and neuroendocrinological (cortisol, testosterone) measures that are related to stress and emotion processing, as well as neuropsychological functions such emotion recognition, emotional learning, and emotion regulation, which are also related to structural and functional deficits in subcortical limbic structures such as the amygdala in antisocial youth with CU traits. Assessment of executive

functioning, which is the basis of many emotional and social skills, is also relevant in this respect.

Moreover, in line with the biopsychosocial model, it is important to stress that neurobiological assessments should be integrated with psychosocial assessments, as several studies have found an association between parental antisocial behavior, harsh parenting, and maltreatment and lower heart rate and altered basal RSA levels in antisocial youth with our without CU traits. This may indicate potential physiological pathways through which genetics and child maltreatment may impact the development of antisocial behavior and CU traits [65,66,67**], as was also posed in Blair's neurobiological model of the development of psychopathic traits [5].

Finally, as for risk taxation, recent studies by our own groups have shown significant additional value of neurophysiological and neuroendocrinological measures to standard psychosocial risk assessment for the prediction of (violent) reoffending in severe antisocial and delinquent youth [68*,69**,70].

Treatment and treatment evaluation

Currently, the main challenge lies in translating neurobiological knowledge into effective interventions for antisocial youth.

First, neurobiological knowledge is important for the psychoeducation of youth and parents. Increasing their knowledge regarding the neurobiological processes that underlie the development may help youth to better understand their behavior. It should, however, be stressed that, although antisocial behavior has a relatively high heritability, which is related to deficits in brain development and functioning, current knowledge does not support the idea that people are 'determined by their brains to commit crimes'. A 50–60% heritability still leaves a large contribution to the environment. Moreover, specifically during adolescence, the brain is still in development and flexible, which forms a window of opportunity for interventions to steer away from further antisocial development.

Second, neurobiological findings may guide specific interventions to change the developmental trajectory of antisocial behaviors [71**]. For severe delinquent youth, neurobiological insights on antisocial development may help to promote effective interventions within the juvenile justice system [72–74].

As for specific neurobiologically informed interventions, pharmacologic interventions that target dopaminergic, noradrenergic, and serotonergic activity, including psychostimulants, alpha-2 agonists, atomoxetine, and risperidone, -have shown benefits [75]. Specifically for methylphenidate, functional brain imaging studies show that methylphenidate may normalize subcortical, specifically amygdala functioning, as well as resting-state functional connectivity of mesolimbic seed regions with areas involved in moral decision making, visual processing, and attention in adolescents with conduct disorder that have been related to antisocial behavior and CU traits [76,77*].

However, neurobiologically informed interventions do not necessarily have to involve interventions at the pharmacological level. Interventions aimed at improving the neuropsychological functioning of antisocial youth, such as cognitive training and improving cognitive control, have also been found to be promising [46*,78]. Specific training in executive functioning in combination with parental training in perseverance may reduce proactive aggression [79]. Recently, a specific intervention program for high-risk children, based on individual neuropsychological profiles, has been shown to be effective in reducing antisocial behavior [80].

As for aggression and emotion regulation, it has been shown that aggression may be reduced by changing self-control using Triple P, Aggression Replacement Therapy (ART) etc. [81*]; moreover, ART has also been shown to be able to actually normalize neuroendocrine functioning, also in antisocial youth with CU traits [82].

Finally, at the neurophysiological level, a promising approach may be biofeedback using wearables to improve awareness of physiological signals preceding aggressive outbursts and stimulate emotion and aggression regulation [83,84].

Translational research agenda

Although, as we have seen above, there is ample knowledge available on the neurobiology of antisocial behavior, and some promising neurobiologically informed interventions have already been tested, there are some gaps in knowledge that hamper full translation to clinical practice.

First, we need more knowledge on the interplay between neurobiological, psychological, and biological characteristics. Current neurobiological research has mainly focused on one or two neurobiological factors, and in some cases, on the interaction with one or two environmental factors; however, from a biopsychosocial perspective, it is of main importance to integrate neurobiological assessments with the mainly psychosocial assessments that are currently used in clinical practice. Our previous work has shown that such an approach does have enormous power in improving the prediction of reoffending [69**]; moreover, this may also provide more insight in the underlying mechanisms

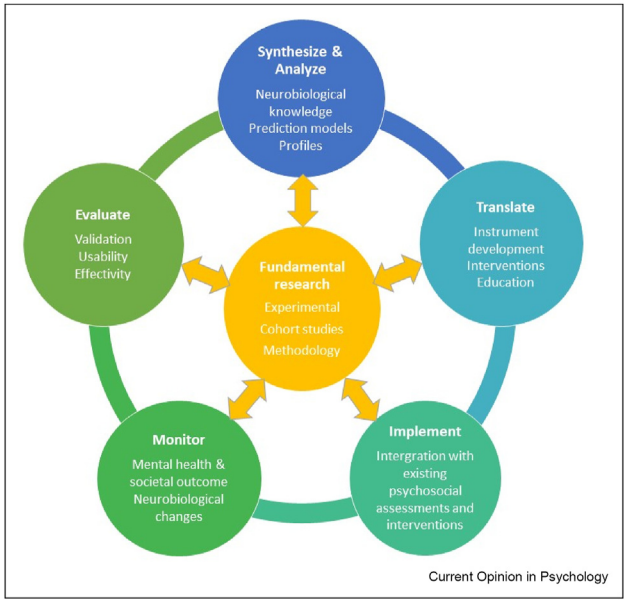
involved in the different subtypes of antisocial behavior, such as the group with severe and persistent antisocial behavior that also display CU traits [5].

Second, most findings are on the group level and therefore difficult to translate to interventions at the individual level. Through structural biopsychosocial assessments in clinical practice, longitudinal data will become available that can be used to create open-source models and algorithms that can be utilized to predict individual treatment outcomes [69**].

Third, although there are some indications that interventions do change neurobiological characteristics, we need more knowledge on the changeability of neurodevelopmental and neurobiological characteristics of antisocial youth in response to treatment. This fundamental knowledge is essential to determine whether there is still enough neuroplasticity to steer an initial antisocial development in a positive direction.

In conclusion, this review has shown that there is a wealth of knowledge available already on the genetic, neuroimaging, neuropsychological, neurophysiological, and neuroendocrinological correlates of antisocial behavior in adolescents; however, it also shows that, in order to move the field forward and create direct clinical relevance, the main goal of future neurobiological research in antisocial behavior should be to better integrate neurobiological research in clinical practice in order to study individual biopsychosocial profiles and the changeability thereof in relation to treatment. To achieve this goal, we need a translational, iterative approach in which we not only observe but also intervene in clinical practice in collaboration with clinical partners [85]. Together, we have to engage in a translational research cycle consisting of consolidation of (existing) knowledge; translation of knowledge in integrated assessments, interventions, and education; implementation of integrated knowledge; monitoring of the use of this knowledge; and evaluation of validity, usability, and affectivity. Importantly, this cycle is dynamic, meaning that fundamental knowledge is constantly updated, and information flows both toward as well as back from clinical practice (Figure 2). Eventually, this will help us to translate fundamental neurobiological research into personalized treatment programs that are based on the individual biopsychosocial profiles of antisocial youth.

Figure 2



Translation research cycle.

Author contribution

Lucres MC Jansen did the Conceptualization, Reviewing of literature, and Writing of this paper.

Conflict of interest statement

Nothing declared.

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