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Recent neuro-imaging findings with respect to conduct disorder, callous-unemotional traits and psychopathy

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Abstract

Purpose of review: To review recent neuro-imaging findings with respect to conduct disorder (CD) and callous-unemotional (CU) traits in childhood and comparable psychopathy in adulthood that deepen the literature in important ways.

Recent findings: Recent structural findings particularly bring clarity to the literature. First, they reinforce previous work indicating that severity of psychopathy is positively associated with extent of cavum septum pellucidum. This suggests psychopathy is associated with early neurodevelopmental disruption within limbic structures; Second, they clarify the direction of the association between CD and particularly CU traits and white matter tract abnormalities even if it remains less transparent exactly which tracts are disrupted. However, conclusions based on recent functional imaging studies are more equivocal with inconsistencies in direction of emotional (albeit with notably more work confirming the previous reports of hypo-responsiveness in limbic regions) and reward responsiveness.

Summary: The recent data are, for the most part, consistent with a view that CU traits/ psychopathy represents an early appearing neuro-developmental disorder particularly associated with compromised emotional (limbic) functioning. However, some patients presenting with severe antisocial behavior may also show hyper-threat sensitivity, perhaps reflecting trauma exposure, and require different clinical interventions.

Keywords

MRI; conduct disorder; callous-unemotional traits; psychopathic traits

Introduction

The term *psychopathy* characterizes an increased risk for antisocial behavior coupled with pronounced emotional deficits reflecting reduced guilt, remorse and empathy [1,2]. In children, this emotional component is typically referred to as callous-unemotional (CU) traits [1]. Children and youth with CU traits are at notably increased risk for meeting criteria for psychopathy as adults [3]. Psychopathic traits are a source of considerable concern as

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Conflicts of interest

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they are associated with particularly heightened levels of aggression that may be less amenable to treatment than other factors increasing the risk for violence [1,2].

In this brief review, recent neuro-imaging work (January 2018 to June 2019) is reviewed. Studies to be considered were identified via two PubMed searches ("MRI and Psychopathy" and "MRI and callous unemotional traits"). A few were then excluded from review as they did not fit well within the topic areas considered given the word length constraints. In brief, the review will consider both structural (particularly those focusing on the Cavum septum pellucidum and diffusion tensor imaging [DTI]) and functional neuro-imaging studies (particularly those focusing on functions such as emotional processing, reinforcement processing and response control). Implications of these findings for conceptualizations of psychopathy are briefly discussed.

Structural Neuro-Imaging Studies

Findings on the Cavum septum pellucidum (CSP)

The CSP is a relatively common neuro-anatomical variant of the septum pellucidum, the thin triangular membrane between the right and left lateral ventricles in the human medial frontal lobe [4]. The extent to which the CSP persists during development is considered a marker of fetal maldevelopment that primarily reflects abnormal growth of limbic structures [5].

Because of suggestions that the core emotional dysfunction component of psychopathy (CU traits in youth) reflects atypical limbic system functioning/development [e.g., 6,7], some prior attention has been paid to the CSP. However, findings had been somewhat conflicted. One study, involving male and female adults from the community (temporary employment agencies), reported that those with CSP had higher scores of antisocial personality disorder and psychopathy, as well as more criminal charges and convictions when compared to controls [8]. A second reported that adolescents with large CSP have a higher risk for aggression, psychopathic traits, and a disruptive behavior disorder (DBD) diagnosis, including conduct disorder (CD) and oppositional defiant disorder (ODD) [9]. However, a third reported no significant differences between violent male offenders and non-incarcerated healthy controls in the incidence of CSP [10].

Two recent studies somewhat clarify the situation. Both investigated the relationship between CSP and psychopathic traits in two separate large forensic samples [N=355 [female] and 1742 [male] respectively; 11*,12**]. Consistent with Toivonen et al. (2013), both found no significant difference in CSP size or CSP presence/absence between inmates and non-incarcerated controls. However, CSP length was positively correlated with Hare Psychopathy Checklist-Revised (PCL-R) total and Factor 1 (the interpersonal/ affective facets) in males and with facet 1 (interpersonal) and facet 4 (antisocial behavior) in females. In short, these findings extend previous work [8,9] and are consistent with suggestions that increased psychopathy is associated with limbic abnormalities. However, it is important to note, as much of the previous literature has [9,11*,12**], that these abnormalities are seen in many psychiatric conditions and clearly do not just relate only to psychopathy level.

DTI Findings

The suggestion that psychopathy related to limbic abnormalities motivated the first DTI studies. These studies examined the integrity of the white matter tracts, specifically the uncinate fasciculus; a bidirectional, long-range tract of white matter that connects ventromedial/orbital frontal cortex and the amygdala/ anterior temporal lobes [13]. Early work relatively consistently indicated reduced fractional anisotropy (FA; i.e., reduced white matter integrity) of this tract in *adults* with psychopathy [14–16]. But studies with youth were relatively inconsistent. Some also reported decreased FA of the uncinate fasciculus and/or frontal/ temporal tracts in youth with CD/conduct problems [e.g., 17,18,19]. However, others reported *increased* FA of the uncinate fasciculus in males with CD [e.g., 20,21].

Recent work has broadened the focus with respect to white matter tracts and concentrated in adolescent samples. One study did examine tract integrity in two relatively small groups of adult male offenders; those with impulse control problems (N=15) and those without (N=10) [22]. This study reported no group differences in FA or significant correlations between psychopathy severity and FA in the whole sample. However, within the 15 impulsive offenders, interpersonal-affective traits (PCL-R Factor 1) were negatively correlated with FA in the anterior and posterior temporal lobe and orbitofrontal cortex.

Three studies with patients with CD and comparison individuals produced relatively consistent results regarding direction of effect even if not tract implicated. Participants with CD, relative to controls, showed reduced dorsal default-mode network (DMN) radial diffusivity [23], lower FA in the retrosplenial cingulum tract [24*] and higher axial diffusivity in the corpus callosum and lower radial diffusivity and mean diffusivity in the anterior thalamic radiation relative to typically developing youth [25*]. All three of these studies indicated that these effects might be more severe in the youth with CD and callous-unemotional traits. This conclusion complements a large sample (N>2000) of predominantly healthy and younger (8–11 years) participants [26**]. They found callous traits were associated with lower global mean diffusivity with multiple individual tracts, including the uncinate and cingulum, contributing to this global association. Notably, two of the studies, in somewhat overlapping samples, indicated that the effects reported might be more marked in males with CD rather than females with CD [24*,25*].

Functional Data

Response control

Here response control tasks are defined as those involving participants responding to some stimuli and withholding responses to others. They can be classic response control tasks such as the Go/No-Go task where participants respond to common “Go” stimuli (e.g., white Xs; 84% of trials) but withhold responses to rare “No-Go” stimuli (e.g., white Ks; 16% of trials) [27]. Alternatively, they can be odd-ball or continuous performance tasks where participants respond to rare targets (e.g., 10% frequency) while withholding responses from common (80%) non-target stimuli or rare (10%) “novel” non-targets [28].

One contrast that can be derived from the Go/No-Go task is between false alarms (incorrect responses to No-Go stimuli) and hits (correct responses to Go stimuli); activity may represent error related activity. Maurer et al. (2019) conducted Region-of-Interest (ROI) analyses concentrating on several subregions of the basal ganglia previously shown to function anomalously in youths with psychopathic tendencies (caudate, putamen, globus pallidus, and nucleus accumbens) as well as two additional ROIs which have never been previously investigated in relation to adolescent psychopathy scores: the subthalamic nucleus and substantia nigra. Only within these additional two ROIs was there a significant inverse relationship between total Hare Psychopathy Checklist: Youth Version (PCL-YV) score in 182 male incarcerated adolescents and responses to false alarms vs. hits. Neither Factor 1 or Factor 2 showed a relationship with responsiveness to this contrast (though there were some relationships with individual Facets of these factors).

Previous event related potential studies have indicated that individuals with psychopathy show compromised responses *to rare target and novel stimuli* on odd ball tasks [see, for a review, 29]. However, a recent fMRI study with 168 incarcerated adult males reported that Factor 1 scores on the PCL-R were inversely related to responsiveness within a broad array frontal, parietal, temporal, limbic, occipital, subcortical, and cerebellar regions *to the common non-target stimuli* [28]. The reason for this inconsistency with previous findings is unclear though it may represent reduced motivation to perform the task as a function of PCL-R.

Responding to reinforcements

There has been some debate regarding the relationship between reinforcement processing (particularly reward processing) and CD and/or psychopathic traits. One view considers that *hyper-responsiveness to reward* is a risk factor for CD and/or psychopathic traits [30]; the suggestion is that hyper-reward responsiveness means that rewarding actions will be chosen even if they harm other individuals. An alternative view is that reduced reward sensitivity/responsiveness, particularly within regions critical for the representation of long-term goals, should result in an individual who makes poorer decisions (response choices will be less well guided by goal-modifiable reward expectations) and is thus more likely to be impulsive/become frustrated and aggressive as a function of their frustration [31]. Most of the previous literature with respect to adolescents with CD/psychopathic traits has been consistent with the second view. However, the data are considerably more equivocal with adults and psychopathic traits. Recent work has done little to settle this debate.

Two studies looked at responsiveness to drug cues. Substance abuse is associated with a heightened response to drug reward cues within regions including dorsomedial frontal, anterior cingulate and anterior insula cortices, the amygdala and striatum [for a review, see 32]. If psychopathy is associated with heightened reward responsiveness, one might predict heightened responsiveness to drug cues in addicted individuals with psychopathy. In contrast, if psychopathy is associated with *reduced* reward responsiveness, one might predict that individuals with psychopathy should show *reduced* responsiveness to drug cues. One study with 54 incarcerated male adolescents reported a negative correlation between psychopathic traits and neural response to drug versus neutral images within anterior

cingulate cortex and the amygdala [33**]. This was consistent with an earlier study with adult offenders [34]. However, the second study with 105 adult probationers/parolees reported that psychopathic traits were positively correlated with drug > food reactivity within the right insula and left amygdala [35].

A third study with 37 boys (aged 8–11 years) with conduct problems and 27 typically developing comparison boys examined responses to monetary rewards and punishments and reported that conduct problems were related to reduced responsiveness but only to *punishment* [36*]. There were no group differences in responsiveness to reward. Moreover, level of CU traits was unrelated to the response to punishment (or reward).

Emotional responsiveness

There has long been a view that CD/antisocial personality disorder (ASPD) is associated with reduced neural responses to threat and during moral processing. Moreover, both forms of neural response are inversely related to CU/psychopathic traits [cf. 6,7,37,38]. Recent work has mostly been consistent with this view – albeit with some qualifications.

Studies consistent with the majority of previous work reported: (a) reduced responsiveness to looming threats within acute threat circuitry (the amygdala and periaqueductal gray) as well as temporal, lateral frontal, and parietal cortices in youth with Disruptive Behavior Disorders (CD and ODD) relative to comparison youth [N=31 & 27 respectively; 39*]. Level of CU traits were also inversely related to threat responsiveness to looming stimuli within lateral frontal and parietal cortex (though not the amygdala); (b) reduced responses within the amygdala to emotional expressions in adolescents as a function of CU traits [N=72] but only in participants who had *not* experienced significant abuse. This association did not hold in those who had experienced significant abuse [40*]; (c) reduced responses within the amygdala to emotional expressions in adolescents with CD relative to controls [N=46 & 25 respectively; 41]. Level of CU traits did not moderate this amygdala responsiveness. However, psychopathic traits were inversely related to amygdala-ventral anterior cingulate connectivity during angry expression processing; (d) reduced responses when *passively viewing* negative relative to neutral images within ventromedial, ventrolateral, angular and occipital cortices (though not the amygdala) in high psychopathy (N=15, PCL-R>30) relative to mid and low scoring psychopathy groups [N=29 & 23, PCL-R=21 to 29, <21 respectively; 42*]. However, this study reported *no* group differences when viewing negative pictures following instruction to maximize the intensity of the experienced emotional response relative to the passively viewing these negative images; (e) reduced reactive times and reduced dorsal anterior cingulate responses during opportunities for dishonest gain as a function of PCL-R in an incarcerated sample (N=67) of male adults [43*]. These findings were interpreted as indicated that increasing psychopathy was associated with reduced response conflict when behaving dishonestly.

In contrast, one study reported widespread increased activity during an affective Stroop task in a sample of 39 adolescents with CD relative to 39 healthy comparison adolescents [44]. This included increased amygdala responses to emotional stimuli in the adolescents with CD relative to the healthy adolescents during conditions when this response should have been suppressed as a function of task demands (incongruent trials). A second involved 100 multi-

problem young adults (individuals lacking a stable income, without the prerequisites to get a job and with a high probability of a criminal conviction) and 22 healthy controls [45]. Participants were asked to rate the morality of images that were: (i) immoral and negative (e.g., a person threatening another person with a knife); (ii) non-moral and negative (e.g., people shouting at each other); or (iii) neutral (e.g., people sitting next to each other). The multi-problem young adults made significantly less of a differential morality rating response to immoral relative to non-moral items relative to the healthy controls. However, morality ratings were not moderated by level of psychopathy as assessed by the Youth Psychopathy Inventory – Short Version (YPI-SV). Total YPI-SV score and the affective component of this score were positively related to responses to immoral relative to non-moral items in the areas of left ventromedial prefrontal cortex, left superior temporal gyrus, and left cingulate.

Summary and Conclusions

Findings over the past 18 months have served to clarify some areas of the literature even if others may have been further obfuscated. The studies on the CSP at least temporarily settle the issue and reinforce the idea that this is a feature associated with higher psychopathy levels [as well as other psychiatric conditions] [11*,12**]. Similarly, the DTI findings in adolescents, like those previously published in adults, clarify and indicate reduced structural connectivity (as indexed by *reduced* FA) in white matter tracts in CD and related to CU traits [23,24*,25*]. Consistent with the CSP literature they indicate abnormalities in structural connections between limbic areas but also suggest that white matter tracts may be far more broadly compromised in psychopathy/CU traits. This may indicate that psychopathy/CU traits are associated with impairment beyond emotional processing. Alternatively, the effects may be secondary developmental consequences of the primary condition with relatively minimal *direct* impact on symptom presentation.

The functional neuro-imaging data was less helpful in bringing clarity to the literature. The findings with the Go/No-Go and oddball tasks were not immediately interpretable within previous findings and will need to be followed up [27, 28]. Similarly, while previous work with adolescents with CD had typically indicated reward neural responsiveness in this population, of the recent work, one study was consistent [33**] but another was not [36*]. This latter study indicated *reduced* punishment responsiveness instead. Moreover, in contrast to the studies with adolescents, the study with adults indicated *increased* reward responsiveness in adults with psychopathy [35]. The emotional processing studies were mostly consistent with previous work indicating reduced responsiveness in CD/psychopathy [39*, 41,42*,43*]. However, two of the seven studies indicated *increased* responsiveness [44, 45]. Moreover, there are indications that the emotional impairment can be removed by increasing the salience of the emotional stimulus via attentional manipulations [42*].

In short, more functional work is needed to clarify whether there might a developmental transition from decreased reward responsiveness in adolescent samples to increased reward responsiveness in adulthood or whether effectively different psychiatric populations are being studied in the adolescent vs. adult literatures. With respect to the emotional processing literatures, there already are strong indications of at least two forms of CD – one marked by increased and the other decreased responsiveness to threat stimuli [46, 47]. The form marked

by increased responsiveness to emotional stimuli may be more common in individuals who have been exposed to abuse [40*].

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