

The Neurobiology of Psychopathy:  
A Neurodevelopmental Perspective

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Deposited 06/08/2021

Citation of published version:

Gao, Y., Glenn, A., Schug, R., Yang, Y., Raine, A. (2009): The Neurobiology of Psychopathy: A Neurodevelopmental Perspective. *Canadian Journal of Psychiatry*, 54(12).

This is an accepted manuscript. The fully published version can be found at:

DOI: <https://doi.org/10.1177/070674370905401204>

# The neurobiology of psychopathy: A neurodevelopmental perspective

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We provide an overview of the neurobiological underpinnings of psychopathy. Cognitive and affective–emotional processing deficits are associated with abnormal brain structure and function, particularly the amygdala and orbitofrontal cortex. There is limited evidence of lower cortisol levels being associated with psychopathic personality. Initial developmental research is beginning to suggest that these neurobiological processes may have their origins early in life. Findings suggest that psychopathic personality may, in part, have a neurodevelopmental basis. Future longitudinal studies delineating neurobiological correlates of the analogues of interpersonal–affective and antisocial features of psychopathy in children are needed to further substantiate a neurodevelopmental hypothesis of psychopathy.

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## Highlights

- People with psychopathic personality are characterized by a constellation of traits including interpersonal–affective features (for example, superficial charm, manipulativeness, and lack of affect and emotion) and antisocial features (for example, impulsivity and aggression).
  - Cognitive and affective–emotional processing deficits associated with brain abnormalities, particularly structural and functional impairments in the amygdala and orbitofrontal–ventromedial prefrontal cortex, have been found in people with psychopathy.
  - Psychopathy may have a neurodevelopmental basis, and future molecular genetic studies identifying genes’ coding for early brain abnormalities, together with longitudinal imaging studies, are needed to further substantiate this neurodevelopmental hypothesis.
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People with psychopathic personality are characterized by a constellation of traits including interpersonal–affective features (for example, superficial charm, manipulativeness, and lack of affect and emotion) and antisocial features (for example, impulsivity and aggression).<sup>1</sup> The search for the neurobiological basis of psychopathy began more than 150 years ago, when a railway construction worker, Phineas Gage, suffered severe damage to the PFC and subsequently developed a radical change in his personality and became psychopathiclike.<sup>2</sup> Cleckley’s book, *The Mask of Sanity*,<sup>3,4</sup> provided the first and classic description and interpretation of psychopathy and theorized that this form of PD may be due to a biological deficit.

The aim of our review is to present neurobiological evidence for a disruption in the cognitive and emotional processing in people with psychopathy. Findings from key areas of neurobiological research on psychopathy, including brain imaging, neurological, neuropsychological, psychophysiological, and hormone studies, will be outlined and discussed in the context of psychopathic personality as a neurodevelopmental disorder.

## Brain Imaging

Most structural brain imaging studies have focused on the PFC, and findings suggest that psychopaths exhibit impairments in this region. For example, Raine et al<sup>5</sup> showed significant prefrontal grey matter volume reductions in

patients with ASPD who also scored high on psychopathy. Similarly, Yang et al<sup>6</sup> found significant prefrontal grey reductions in criminal psychopaths compared to control subjects. Two recent studies using voxel-based morphology have also found reduced grey matter volume in the PFC in psychopaths.<sup>7,8</sup> Overall, prefrontal deficits have been argued to contribute to the poor decision-making, emotional dysregulation, and impaired moral judgment in psychopathic people.

Evidence linking structural impairments in brain regions beyond the PFC with psychopathy has also been found. Laakso et al<sup>9</sup> found reduced posterior hippocampus volumes in antisocial alcoholics with high psychopathy scores. Psychopaths also show volume reductions in the bilateral amygdala, particularly the basolateral and superficial nuclei groups.<sup>10</sup> Deficits in the amygdala–hippocampal complex have been associated with emotional deficits including shallow affect and lack of remorse in psychopaths, as well as social dysfunctions including pathological lying and superficial charm. Additionally, Raine et al<sup>11</sup> found significant increased callosal white matter volume, increased callosal length, and increased functional interhemispheric connectivity in psychopaths. Callosal volume was significantly related to the Deficient Affect factor of psychopathy, and to a lesser extent the Impulsive–Irresponsible factor, but not the Arrogant–Deceptive factor. Overall, findings indicate that structural impairments, particularly in the amygdala, hippocampus, and corpus callosum, may contribute to the emotional deficits found in psychopaths.

Specific structural abnormalities have been found for subgroups of psychopaths. By separating psychopaths with criminal convictions (unsuccessful psychopaths) from those without convictions (successful psychopaths), studies have found deficits specifically to unsuccessful psychopaths. Raine et al<sup>12</sup> reported an exaggerated anterior hippocampal volume asymmetry (right greater than left) in unsuccessful psychopaths, but not in successful psychopaths or controls. Using the same sample, Yang et al<sup>6</sup> reported a significant 18% to 23% reduction in the prefrontal grey matter volume in unsuccessful (but not successful) psychopaths. Findings suggest that neuropathological characteristics such as abnormal hippocampal asymmetry and reduced prefrontal grey matter volume may contribute to the emotional dysregulation and poor fear conditioning in unsuccessful psychopaths, and consequently render these people less sensitive to environmental cues predicting danger and capture.

Functionally, psychopaths show abnormal activation in the frontal-temporal circuit. Using single-photon emission computed tomography, Soderstrom et al<sup>13</sup> found significant negative correlations between psychopathy scores (particularly the interpersonal factor) and frontotemporal perfusion. In an fMRI study using a semantic task, Kiehl et al<sup>14</sup> found that psychopaths failed to show the appropriate neural differentiation between abstract and concrete stimuli in the right superior temporal gyrus, left ventrolateral PFC, middle temporal cortex, and anterior cingulate cortex. Using affective pictures as stimuli, several other fMRI studies have reported abnormal affect-related activation in the dorsolateral PFC, ventrolateral PFC, anterior and posterior cingulate cortex, amygdala, hippocampus, and parahippocampus gyrus in psychopaths.<sup>15–19</sup> Finally, in a recent study of moral decision-making, psychopathic people demonstrated less amygdala activity when making decisions about moral dilemmas that were particularly emotional in nature.<sup>20</sup> People who scored high on the interpersonal factor demonstrated reduced functioning in regions previously implicated in moral decision-making (that is, the medial PFC, posterior cingulate, angular gyrus, and amygdala), providing initial evidence of reduced functioning in psychopaths in regions that may be critical to behaving morally.

Additional studies have examined the neural correlates of the clustered psychopathy traits, specifically the affective–interpersonal factor and antisocial lifestyle factor of psychopathy. Yang et al<sup>6</sup> found negative correlations between prefrontal grey volumes and scores on both these factors. One functional imaging study found reduced blood flow to be associated with high affective–interpersonal psychopathy scores,<sup>13</sup> although no such correlation was found in a group of alcoholics with ASPD.<sup>21</sup> Several recent studies found people who scored high on psychopathic features of conning and manipulative have significantly increased white matter volume and reduced grey matter in the PFC, particularly in the ventral and lateral regions of the PFC.<sup>6,10</sup> It was argued that the increased prefrontal white matter may lead to faster sharing of information which facilitates lying and malingering. These findings echo those of Glenn et al<sup>20</sup> described above on moral decision-making, and suggest that disturbed frontal function–structure may in part contribute to impaired moral judgment. A facet-based approach holds the promise of breaking down the complexity of the psychopathy construct and obtaining greater understanding of psychopathic subfeatures, which are greatly underresearched and poorly understood.

Overall, brain imaging studies have suggested that: 1) the orbitofrontal, ventromedial prefrontal, and the cingulate cortex are crucial in decision-making, behavioural control, and emotional regulation, and that deficits in these regions may contribute to features such as impulsivity and impaired moral judgment in psychopaths; and 2) the medial temporal regions, particularly the amygdala and hippocampus, are critical for emotional processing, and thus when impaired predispose to a shallow affect and lack of empathy in psychopaths. Findings also suggest that no one single region, when impaired, will result in psychopathy. Although some strong initial evidence has been presented suggesting brain

abnormalities in psychopaths, inconsistencies among findings raise an important question regarding whether brain impairments are restricted to a particular subgroup of psychopaths, specifically criminal (unsuccessful) psychopaths. Several questions also remain unanswered, including whether brain deficits lead to the development of psychopathy, or whether a psychopathic lifestyle renders these people more prone to brain dysfunction. Further studies are needed to shed light on these issues.

### ***Neurodevelopmental Considerations***

Despite the increasing number of empirical studies on adult psychopaths, brain imaging research on psychopathiclike children and adolescents is rare. Preliminary evidence linking brain dysfunction with psychopathic traits in children and adolescents has started to emerge. For example, using fMRI, Finger et al<sup>22</sup> found abnormal ventromedial PFC function in children and adolescents with CU traits and disruptive behaviour disorders during a reversal learning task. Using the same sample, Marsh et al<sup>23</sup> reported reduced amygdala response to fearful expressions in psychopathiclike youths compared to healthy controls. In addition, studies on youth with antisocial and aggressive behaviour have indicated both structural and functional deficits in the brain regions similar to those reported in adult psychopaths.<sup>24-28</sup> Further, Raine et al (unpublished observation) reported a relation between psychopathy and *cavum septum pellucidum*, a marker of prenatal limbic and septal neural maldevelopment, indicating an early neurodevelopmental basis to psychopathy. Taken together, these findings provide some evidence supporting the speculation that the condition of psychopathy may in part be a result of neurodevelopmental abnormalities.

### **Neurology**

Neurological conditions include brain damage that has occurred as a result of trauma by an external force or an internal disease such as a tumour or neurodegenerative disease. The study of patients who have developed impairments in specific brain regions and have subsequently demonstrated psychopathiclike traits or behaviours has helped to elucidate how impairments in these regions may contribute to psychopathy.

The neurological condition that most closely resembles psychopathy comes from damage to the ventromedial region of the PFC. Damage to this region has been found to result in numerous psychopathiclike characteristics, and has thus been referred to as “acquired sociopathy.”<sup>29</sup> One of the earliest cases of this condition is that of Phineas Gage, as stated above,<sup>30</sup> and a few similar cases have also been reported.<sup>2,31</sup> Common features following damage to the frontal lobe in these cases include lack of empathy, difficulties with emotion regulation, impulsivity, disinhibited behaviour, poor planning, and blunted emotions. When making moral judgments, people with ventromedial PFC damage, compared to control subjects, have been found to be more likely to endorse actions that involve highly emotionally aversive harm. This suggests that the ventromedial PFC mediates emotions that are important for certain types of moral judgment.<sup>32</sup>

People with FTD have also shown signs of psychopathiclike characteristics. FTD is a progressive neurodegenerative disorder that involves the frontal lobes, temporal lobes, or both. Patients with FTD have demonstrated characteristics such as frequent violations of social norms, a lack of empathy, loss of insight for the consequences of their behaviour and its effect on others, and a failure to respond to the needs of others. People with FTD have also been found to demonstrate moral decision-making patterns to hypothetical scenarios similar to those of people with ventromedial PFC damage described in the Koenigs et al<sup>32</sup> study above.<sup>33</sup>

People with lesions to the amygdala have also demonstrated some of the same impairments that are observed in psychopaths, including impairments in aversive conditioning,<sup>34</sup> augmentation of the startle reflex to visual threat primes,<sup>35</sup> and recognizing fearful facial expressions.<sup>36</sup> However, patients with lesions to the amygdala do not closely resemble people with psychopathy. In psychopathic people, many of the functions of the amygdala appear to still be intact, or are only mildly impaired, suggesting that the amygdala-related deficits observed in psychopathy may be more specific.

### ***Neurodevelopmental Considerations***

The idea that psychopathy may represent a neurodevelopmental deficit is supported by evidence that when brain impairments occur early in life, psychopathiclike effects appear to be even more pronounced. Anderson et al<sup>37</sup> found that patients who incurred damage to the ventromedial PFC before the age of 16 months developed irresponsible and criminal behaviour, abusive behaviour towards others, and a lack of empathy or remorse. These antisocial characteristics and behaviours were more severe than those observed in patients who suffered damage in adulthood. It has been suggested that intact functioning of the ventromedial PFC is important for moral development.<sup>37</sup> When this region is damaged very

early in life, the process of moral socialization may be disrupted. Indeed, the study found that these people exhibited an immature stage of moral reasoning.

Although damage to any specific brain region does not entirely replicate the disorder of psychopathy, studies of people with neurological impairments are useful in helping to understand the result of impaired functioning of certain brain regions that may be implicated in psychopathy. In particular, the study of patients who have incurred brain damage very early in life may be especially useful, as it demonstrates how deficits in brain functioning may impair social and moral development in the individual. Future research particularly in child patients with brain damage may be helpful in gaining a more precise understanding of the specific impairments that result from abnormal functioning in specific regions.

## Neuropsychology

Psychopathy has not traditionally been associated with generalized cognitive or intellectual dysfunction,<sup>38</sup> but rather with circumscribed deficits in specific neuropsychological domains such as attention, language, and executive functioning. Evidence suggests that psychopaths fail to shift attentional resources to accommodate secondary or unattended information while engaged in goal-directed behaviour (that is, response modulation). For example, while some studies have shown that psychopaths demonstrate normal interference on both conventional colour–word and modified Stroop tests,<sup>39–41</sup> other studies have suggested that psychopaths show reduced interference on other Stroop-like paradigms such as picture–word<sup>40,42,43</sup> and spatially separated Stroop tasks<sup>40</sup>—findings that have been interpreted as superior selective attention.<sup>42</sup> However, psychopaths have shown reduced attentional functioning on other neuropsychological tasks,<sup>44</sup> failed to demonstrate normative attentional narrowing when presented with aversive images,<sup>45</sup> and failed to demonstrate superior selective attention on visuospatial attention tasks using auditory and linguistic cues.<sup>45</sup> Neuropsychological paradigms used in other studies<sup>47–54</sup> (that is, dual tasks, divided visual field tasks, and cued reaction time tasks) have also shown attentional abnormalities in psychopaths, which may reflect (in some findings but not others) more effortful, top-down attention processing, left hemispheric response modulation deficits, or other cognitive processing abnormalities.

Clinical descriptions of the discordant expression and experience of emotions among psychopaths, along with their characteristic glibness and verbal fluency,<sup>4</sup> have led to neuropsychological research into the language abilities of psychopaths. On lexical–decision tasks, psychopaths have failed to show reaction time facilitation for affective, relative to neutral, words<sup>55</sup> (as have low-anxious psychopaths in left hemispheric processing conditions<sup>56</sup>); and it has also been reported in one study that psychopathic people make more errors processing negative emotionally valenced words in both lexical–decision and negative word decision tasks.<sup>57</sup> Psychopaths demonstrate significantly reduced affective, but not semantic, priming,<sup>58</sup> and reduced performance on an emotional metaphor sorting task despite literal understanding of the metaphors.<sup>59</sup> On word identification tasks, psychopaths have been found to make more errors identifying abstract words than concrete words<sup>60</sup>; and on verbal grouping tasks, psychopaths group words by denotation and literal meaning, whereas nonpsychopaths group words by connotations.<sup>61</sup> Additionally, studies have shown that the speech of psychopaths is characterized by less cohesion,<sup>62</sup> lower volume with acoustically undifferentiated affective content,<sup>63</sup> and content-incongruent language-related hand gestures.<sup>64</sup> Further, psychopaths demonstrate left-hemispheric language processing errors on divided visual–verbal categorization tasks<sup>65</sup> and on some verbal–dichotic listening tasks,<sup>66</sup> but not others.<sup>67</sup> These abnormal cerebral asymmetries have been interpreted as psychopaths having fewer left hemisphere resources available for complex language processing.

Findings from studies using broadly operationalized executive functioning or frontal tasks have been disparate, with some showing deficits in psychopathic people<sup>68–72</sup> and others not.<sup>68,73–79</sup> Recently, more region-specific neuropsychological investigations (that is, involving purported dorsolateral prefrontal measures such as the Wisconsin Card Sorting Test, and orbitofrontal measures such as the Porteus Mazes Q-score, and the go–no-go and Stroop colour word tasks) have identified in psychopathic people’s deficits on orbitofrontal, but not dorsolateral prefrontal, tasks,<sup>43,80,82,83</sup> or on orbitofrontal, but not classical frontal–general, executive function measures (for example, Trail-Making Test or COWAT).<sup>83–85</sup> Studies using the Iowa gambling task and similar card playing tasks also suggest orbitofrontal deficits in psychopathic people,<sup>86,87</sup> though group differences may be specific to poor attention,<sup>88</sup> immediate response feedback,<sup>89</sup> or attributable to reduced anxiety rather than psychopathy.<sup>90</sup> Additionally, though dorsolateral prefrontal (that is, Wisconsin Card Sorting Test) deficits in psychopaths have recently been reported, these may be population-specific (that is, among female parolees, inmates assessed with psychopathy screening instruments, and in unsuccessful, relative to successful, psychopaths).<sup>84,91,92</sup> Overall, findings are consistent with clinical descriptions of psychopathy that appear similar to orbitofrontal pathologies but somewhat incompatible with dorsolateral prefrontal deficits.<sup>81</sup>

Heterogeneity of the neuropsychological findings may be partly due to the existence of subgroups of psychopaths. For example, Ishikawa et al<sup>91</sup> found that unsuccessful psychopaths drawn from temporary employment agencies showed the

expected executive functioning deficits as would be predicted by Morgan and Lilienfeld,<sup>71</sup> whereas successful psychopaths failed to show this impairment. Indeed, successful psychopaths even outperformed control subjects on executive functioning. These findings suggest that better executive functioning may protect a subgroup of psychopaths from being detected and arrested while allowing them to perpetrate significant harm to others in the community. Such findings may provide an initial basis for the design of future studies on even more successful industrial psychopaths on whom we currently know little.

### ***Neurodevelopmental Considerations***

Similar neuropsychological abnormalities in selective attention, emotional processing, and behavioural inhibition have also been found in psychopathiclike children and adolescents. One of the first studies on juvenile psychopaths demonstrated reduced asymmetry on a verbal dichotic listening task,<sup>93</sup> replicating findings in adult psychopaths.<sup>65</sup> Psychopathiclike juveniles also showed passive avoidance learning deficits,<sup>94</sup> as observed in adult psychopaths,<sup>95</sup> indicating reward dominance in this population. Adolescents with psychopathic traits and low anxiety have shown less interference than control subjects on picture–word Stroop tasks<sup>96</sup>; and adolescents with CU traits have been associated with slower reaction times to negative emotional words, while those characterized by impulsivity demonstrated faster reaction times to negative words in a lexical decision task paradigm.<sup>97</sup> Additionally, psychopathiclike juvenile delinquents have demonstrated deficits on orbitofrontal tasks indexing response inhibition (that is, go–no-go and stopping tasks) but not dorsolateral prefrontal–diffuse frontal tasks in comparison to nonpsychopathic delinquents.<sup>82</sup> These findings are consistent with those found in adult psychopathic populations, and may speak to specific neurodevelopmental trajectories associated with psychopathy.

### **Psychophysiology**

A relatively large number of psychophysiological studies have been conducted on psychopathy. Most of this research has assessed autonomic and central nervous system functioning at baseline level or in response to neutral or emotional stimuli using electrodermal, cardiovascular, startle reflex, and electrocortical indicators.

Electrodermal activity is controlled exclusively by the sympathetic nervous system, and reflects both arousal (for example, levels and number of nonspecific responses) and responsivity (for example, reactivity to novel or emotionally valenced stimuli). Heart rate reflects both sympathetic and parasympathetic nervous system activity. In general, studies have shown that adult psychopathic, relative to nonpsychopathic, offenders tend to be electrodermally less responsive both when anticipating and reacting to aversive stimuli.<sup>98–101</sup>

Another line of research has focused on an abnormal startle reflex response in the context of emotional stimuli in psychopaths. In control subjects, presentation of pleasant stimuli is found to attenuate and unpleasant stimuli to potentiate the startle response, compared with presentation of neutral stimuli.<sup>102</sup> Psychopathic people fail to show potentiation of the startle blink when presented with unpleasant (for example, fearful) stimuli,<sup>103–106</sup> indicating emotional information processing deficits in psychopaths.

The ERP refers to averaged changes in the electrical activity of the brain in response to specific stimuli. Studies examining the association between psychopathy and the P300 (a positive-going waveform occurring about 300 milliseconds after a stimulus, thought to represent deployment of neural resources to task-relevant information) have yielded mixed results, with some showing a negative association,<sup>107,108</sup> others a positive association,<sup>109,110</sup> and still others no association.<sup>111–114</sup> A recent meta-analysis aggregating the studies on P300 amplitude and latency and psychopathy has shown a nonsignificant correlation between P300 and psychopathy, suggesting somewhat intact information-processing in this subgroup (Gao & Raine, unpublished communication). It has also been suggested that reduced P300 amplitude may be specifically associated with the impulsivity or externalizing vulnerability of psychopaths.<sup>115,116</sup> Other ERP components besides P300 have also demonstrated relations with psychopathy. For example, studies have reported reduced frontal N275 amplitudes (thought to reflect response inhibition) during the go–no-go task<sup>115</sup> and reduced N300 amplitudes (thought to be particularly sensitive to affective features of stimuli) while processing positively and negatively valenced emotional faces.<sup>116</sup> Additionally, psychopathic offenders show abnormal late negativity, maximal over frontocentral scalp regions, within various stimulus-processing and decision-making tasks (for an overview of this work, see Kiehl et al<sup>108</sup>). Finally, ERN is a negative-polarity scalp potential that peaks within about 100 milliseconds following an incorrect response in a speeded reaction time paradigm. A reduced ERN has been observed in people with low scores on the Socialization scale (reflecting antisocial features of psychopathy)<sup>117</sup> and in psychopathic offenders,<sup>118</sup> although Brazil et al<sup>119</sup> did not replicate these findings. Nevertheless, it has been suggested that reduced ERN may indicate either a deficit in error detection<sup>117</sup> or conflict monitoring impairments in people with psychopathy.<sup>118</sup>

Adult psychopathic offenders do not show reliable differences in heart rate reactivity to aversive or stressful stimuli, or baseline level differences in heart rate or electrodermal arousal.<sup>100</sup> There may be at least 2 reasons for this divergence in findings. First, the different features of psychopathy have a distinct etiology and it is the affective–interpersonal features that are associated with abnormal autonomic reactivity.<sup>103,120</sup> Second, autonomic impairments may be specific to the unsuccessful psychopaths. For example, Ishikawa et al<sup>91</sup> found reduced heart rate stress reactivity in unsuccessful psychopaths, whereas successful psychopaths showed heightened reactivity. An important challenge for future research will be to delineate the nature of psychophysiological impairments that underlie antisocial features of psychopathy, compared with interpersonal–affective features, and to assess whether successful and unsuccessful psychopaths can be differentiated at a psychophysiological level.

Findings of diminished autonomic (in particular electrodermal and startle reflex) reactivity to stressful and aversive stimuli in psychopaths are consistent with theories that have emphasized insensitivity to punishment or reduced capacity for fear in psychopathy,<sup>121</sup> especially in relation to its affective–interpersonal features.<sup>104,122</sup> Based on the somatic marker hypothesis,<sup>2,123</sup> impairments in brain regions including the amygdala and orbitofrontal cortex impede autonomic responses to aversive stimuli, which in turn predispose to persistence of risky behaviours and impairment in real-life decision-making in psychopaths.

### ***Neurodevelopmental Considerations***

Diminished autonomic reactivity has also been found in psychopathiclike adolescents<sup>124</sup> and conduct-disordered children with CU traits.<sup>97,125,126</sup> Prospective studies have indicated that abnormal electrodermal responses (that is, longer electrodermal half-recovery time) to aversive stimuli as early as age 3 years predisposes to psychopathic personality in adulthood.<sup>127</sup> Further, impaired electrodermal fear conditioning at age 3 years has been found to be associated with aggressive behaviour at age 8 as well as criminal behaviour 20 years later at age 23 (Gao et al, unpublished communication). Specifically, while nonaggressive children show a marked increase in fear conditioning from ages 3 to 8 years, aggressive children show a weaker developmental profile, suggestive of retarded maturation of the amygdala. Thus there is evidence for an early psychophysiological predisposition to the development of aggressive and antisocial behaviour, features that characterize the childhoods of psychopaths. These findings provide further support for a neurodevelopmental perspective on psychopathic personality.

### **Hormones**

Associations between psychopathy and common hormones such as cortisol and testosterone have also been explored. Cortisol is a glucocorticoid hormone that is released by the HPA axis. Cortisol functions to provide energy during times of stress<sup>128</sup> and is also involved in potentiating the state of fear,<sup>129</sup> sensitivity to punishment, and withdrawal behaviour.<sup>130</sup> Testosterone is a product of the hypothalamic–pituitary–gonadal axis and is associated with approach-related behaviour, reward sensitivity, and fear reduction.<sup>131</sup> It has been hypothesized that features of psychopathy such as hyporesponsivity to stressors, reduced fearfulness, reduced sensitivity to punishment, and enhanced sensitivity to reward may be a result of reduced cortisol levels and increased testosterone levels.<sup>132</sup>

A few studies have found evidence of reduced cortisol in psychopathy. In adults, Cima et al<sup>133</sup> reported that psychopathic offenders showed lower cortisol levels than nonpsychopathic offenders. Holi et al<sup>134</sup> found a negative correlation between serum cortisol levels and psychopathy in young adult male offenders with a history of violence. In undergraduates, O’Leary et al<sup>135</sup> found that males scoring higher in psychopathy showed less cortisol reactivity to a social stressor than lower-scoring males.

It has long been hypothesized that testosterone may be involved in aggressive behaviour because the large sex differences in testosterone levels parallel the large sex differences in aggressive–antisocial behaviour. Several studies have explored this link, yet very few have examined the relation between testosterone levels and psychopathy specifically. Stalenheim et al<sup>136</sup> found that testosterone levels were positively related to the lifestyle and antisocial features of psychopathy, although it is possible that the results may be confounded by comorbid substance abuse and other psychiatric disorders. Higher testosterone levels have been found in young criminals,<sup>137–139</sup> and have been associated with various antisocial behaviours including difficulties on the job, law breaking, marriage failures, drug use, alcohol abuse, and violent behaviour.<sup>140</sup> Future studies are necessary to elucidate the relation between testosterone and psychopathy specifically.

It has been proposed that the combination of reduced cortisol and increased testosterone underlies the emotional deficits observed in psychopathy.<sup>132</sup> Testosterone and cortisol have been shown to have mutually antagonistic properties; cortisol diminishes testosterone production and inhibits its effects,<sup>141</sup> whereas testosterone inhibits activity of the HPA axis and

consequently reduces the production of cortisol.<sup>142</sup> Van Honk and colleagues have found that injections of testosterone reduce fearfulness,<sup>143</sup> promote responding to angry faces,<sup>144</sup> and shift the balance from punishment to reward sensitivity.<sup>145</sup> In the latter study, Van Honk et al<sup>145</sup> found that a single administration of testosterone led participants to show decreased sensitivity to punishment and increased sensitivity to reward in the Iowa gambling task; thus, by manipulating the balance between cortisol and testosterone, critical changes can be observed in a person's decision-making behaviour, which may predispose to psychopathy.

### ***Neurodevelopmental Considerations***

There is some evidence that differences in hormone levels may be present at an early age in youth with psychopathic traits. Low cortisol levels have been observed in adolescents with CU traits, which are thought to be similar to psychopathic traits in adults.<sup>146</sup> This suggests a neurodevelopmental basis for psychopathy, as lower levels of cortisol in childhood may significantly impair social development by reducing responsivity to stressors and thus decreasing fear of negative consequences such as potential punishment. In youth, Loney et al<sup>147</sup> failed to find associations between testosterone levels and CU traits in boys. However, in other antisocial youth, higher testosterone levels have been found in girls with conduct disorder<sup>147</sup> and adolescent boys with externalizing behaviours.<sup>148</sup> Testosterone levels change greatly during puberty, so the link between psychopathy and testosterone may vary with age. Additional studies examining testosterone and psychopathy in youth will be needed to further elucidate this relation.

While early evidence suggests that dysregulation of hormone system may be involved in psychopathy, additional research is needed to explore this relation and its implications further. Hormones can affect the functioning of key brain regions to change behavioural patterns, and therefore may be especially important in our understanding of the underlying factors that may cause or maintain the neurobiological abnormalities observed in psychopathy. Future studies in youth may help to determine whether differences in hormone levels may exist early in life in people who become psychopathic in adulthood.

### **A Neurodevelopmental Hypothesis of Psychopathy**

Although evidence of neurobiological deficits in psychopathiclike adolescents and children (with CU traits) similar to those observed in adults has accumulated,<sup>93,124,127,149</sup> direct evidence from neuroimaging studies is rare (although see Finger et al<sup>22</sup> and Marsh et al<sup>23</sup>). Nevertheless, as indicated above, there is preliminary MRI evidence of an early neurodevelopmental abnormality (*cavum septum pellucidum*) in psychopaths (Raine et al, unpublished observation). We have previously hypothesized that prior findings of reduced lateralization both in juvenile and in adult psychopaths may arise from a disturbance in the normal neurodevelopmental processes of hemispheric specialization.<sup>150</sup> Later brain imaging evidence of structural abnormalities to the corpus callosum in psychopaths, together with evidence of functional interhemispheric connectivity, provides some support for this position.<sup>12</sup> The fact that morphological changes to the corpus callosum were complex and involved both thinning and lengthening, as well as an increase in white matter volume, tend to dictate against simple, nondevelopmental processes such as discrete trauma or degenerative disease processes. Corpus callosum abnormalities in psychopathic antisocial people may instead reflect atypical neurodevelopmental processes involving an arrest in early axonal pruning or increased white matter myelination.

A neurodevelopmental perspective of adult psychopathic, ASPD is consistent with the facts that such behaviour has its roots early in life,<sup>151,152</sup> unfolds relatively consistently over childhood and adolescence,<sup>153,154</sup> has a steady, progressive course that does not fluctuate markedly over time, is relatively impervious to conventional treatments,<sup>155,156</sup> and is in part genetically determined.<sup>157</sup> In addition, people who incur neurological damage at a very early age develop characteristics that most closely resemble psychopathy, suggesting that psychopathy is likely associated with impairments in brain functioning prior to moral socialization. These facts are broadly consistent with classic definitions of a neurodevelopmental disorder.<sup>158</sup> In addition, psychosocial, demographic, and head injury measures have not been found to account for the brain structural and functional impairments observed in psychopaths.<sup>6,11,12</sup>

Other brain imaging findings are also consistent with a neurodevelopmental hypothesis of psychopathy. The atypical anterior hippocampal asymmetries in unsuccessful psychopaths<sup>12</sup> have been hypothesized to reflect an underlying neurodevelopmental abnormality that disrupts hippocampal–prefrontal circuitry, resulting in affect dysregulation, poor contextual fear conditioning, and insensitivity to cues predicting capture. Atypical brain asymmetries are thought to in part reflect disrupted neurodevelopmental processes.<sup>159</sup> Such disruption probably occurs early in life because brain asymmetries first emerge during fetal development<sup>159</sup> and the overall degree of structural change attributable to environmental influences is limited by early morphogenesis.<sup>160,161</sup>



These early biological disruptions may underlie impaired information or emotion processing as indicated by abnormal psychophysiological functioning and neuropsychological performance, especially in the context of aversive stimuli. In turn, this could give rise to their insensitivity to punishment or reduced capacity for fear, and eventually predispose them to psychopathic behaviour. Regarding hormones, an imbalance in cortisol and testosterone levels early in life may impair social development. Low cortisol levels may reduce responsivity to stressors and decrease fear of punishment. Similarly, increased testosterone may reduce sensitivity to punishments and rewards, making effective socialization difficult and thus increasing the risk for future antisocial behaviour. Further empirical studies are clearly necessary to complete the picture of networking early brain disruption, the neurobiological deficits outlined above, and psychopathic behaviour.

Finally, neurodevelopmental disorders are typically viewed as having a significant genetic basis.<sup>158</sup> Evidence from behavioural genetic studies have indicated a significant influence of genes on psychopathy,<sup>162–164</sup> while molecular–genetic studies are starting to shape our understanding of psychopathic personality in identifying specific genes involved in brain structure and function<sup>165</sup> and which may be compromised in psychopaths. Future studies encapsulating neuroimaging and molecular genetics should be conducted to test a “genes to brain to psychopathy” hypothesis, to identify the genes coding for the early neurodevelopmental brain abnormalities that, in turn, predispose to psychopathic personality.<sup>166</sup>

## Conclusions

Summarizing the above findings, to date, on adult psychopathy, there is replicable evidence for neurocognitive and affective–emotional processing deficits in psychopaths, together with structural and functional brain abnormalities. On balance, although in some areas studies are limited, the most consistent findings, to date, are structural and functional abnormality in the amygdala and orbitofrontal–ventromedial PFC, deviant attention, language, and executive functions, diminished autonomic activity and responsivity to aversive stimuli, and reduced cortisol levels in psychopathic people. Future studies delineating different neurobiological correlates of the subfeatures of psychopathy and the successful and unsuccessful psychopathy distinction, as well as consideration of the possible confounding effects of other personality traits (for example, anxiety), are needed to further our understanding of the etiology of psychopathy. Finally, to examine the more subtle functional deficits in psychopathy, future functioning brain imaging studies are needed to use cognitive and affective paradigms activating the specific brain circuit(s) thought to be dysfunctional in psychopaths, together with assessment of the structural integrity of these structures.

Although it is clearly difficult to conduct longitudinal studies on psychopathy, examining the development of neurobiological measures for psychopathic personality from an early age is crucial to furthering our knowledge on etiology and testing a neurodevelopmental hypothesis of psychopathy. Continued efforts to identify and assess psychopathiclike children and adolescents using prospective longitudinal designs could have potentially important implications for the prevention and management of adult psychopathy. If psychopathic traits and serious offending are, in part, neurodevelopmentally determined, successful prevention and intervention efforts would be most effective if they begin in early childhood, infancy, or even prenatally.

## Funding and Support

The Canadian Psychiatric Association proudly supports the In Review series by providing an honorarium to the authors.

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