

Psychopathy: cognitive and neural dysfunction

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Psychopathy is a developmental disorder marked by emotional deficits and an increased risk for antisocial behavior. It is not equivalent to the diagnosis Antisocial Personality Disorder, which concentrates only on the increased risk for antisocial behavior and not a specific cause—ie, the reduced empathy and guilt that constitutes the emotional deficit. The current review considers data from adults with psychopathy with respect to the main cognitive accounts of the disorder that stress either a primary attention deficit or a primary emotion deficit. In addition, the current review considers data regarding the neurobiology of this disorder. Dysfunction within the amygdala's role in reinforcement learning and the role of ventromedial frontal cortex in the representation of reinforcement value is stressed. Data is also presented indicating potential difficulties within parts of temporal and posterior cingulate cortex. Suggestions are made with respect to why these deficits lead to the development of the disorder.

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Introduction

The importance of a multiple levels of analysis for the understanding of psychiatric conditions is clear.¹ To understand a disorder we need to specify its behavioral profile (ie, its clinical description), the functional impairments that give rise to this behavioral profile (ie, cognitive psychology), the neural systems that mediate these functions (ie, systems neuroscience), the molecular-level factors that are impacting on the neural systems (ie, molecular neuroscience), and the genetic bases of these molecular-level factors. The aim of the current paper is to summarize the psychopathy literature on the first of these three levels. Currently, molecular neuroscience work on this disorder is in its infancy.

There has been recent concern regarding the heterogeneity in the findings, particularly the structural and functional imaging findings, on adults with psychopathy.² Indeed, an uncritical eye might consider most of cortex dysfunctional in this population. A recent review raised important methodological issues regarding the subject population, questioning, for example, whether findings from patient/forensic populations where psychopathy might be indexed by in-depth clinical interview are directly comparable with studies where psychopathic traits are measured by healthy subjects' self-report.² While studies on healthy individuals are important (they allow dimensional work that is particularly useful for

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genetic analyses), the concern is that if we are unconfident about the neurobiological basis of the disorder, studies in healthy individuals may simply confuse the field. Considering this, they will not be considered in the current review.

Three other constraints should be mentioned regarding papers included in this review. First, a striking number of the published magnetic resonance imaging (MRI) studies did not match groups for IQ. Such matching is typical in the neuropsychological literature, but is not consistent in MRI studies with this population. A failure to match for IQ can lead to some misleading results (see also the structural MRI [sMRI] section below). At the very least, it means that it is impossible to conclude that a result reflects the disorder rather than simply the impact of IQ on brain structure or function. Consequently, studies where IQ was not clearly matched will not be considered in the current review (one exception is made for some recent provocative data, however).^{3,4}

Second, this review considers adults with psychopathy. As such, studies with youth with psychopathic traits will not be extensively reviewed.

Third, only results replicated in at least one other paper will be considered. For example, isolated findings of a reduction in cortical volume in a particular area, not replicated in at least one other paper, will not be considered.

Psychopathy: the behavioral profile

Psychopathy is a disorder characterized by pronounced emotional deficits, marked by reduction in guilt and empathy, and involves increased risk for displaying antisocial behavior.⁵ The disorder is developmental. Psychopathic traits, particularly the emotional component, are relatively stable from childhood into adulthood.^{6,7} One reason for the attention this classification receives is its strong predictive utility for institutional adjustment and recidivism (ie, reoffending).⁸ Individuals with psychopathy are approximately three times more likely to reoffend than those with low psychopathic traits, and four times more likely to reoffend violently.⁹ Admittedly, it is the past antisocial behavior, indexed by psychopathy assessments, that is particularly important in predicting future criminal activity.⁸ However, it is the emotional component that characterizes psychopathy; high levels of antisocial behavior can develop from other neurobiological and socio-environmental risk factors.¹⁰

Psychopathy is not equivalent to the *DSM-IV* diagnosis of conduct disorder or antisocial personality disorder (ASPD) or their *ICD-10* counterparts. The psychiatric diagnoses focus on antisocial behavior rather than underlying causes; ie, the emotion dysfunction seen in psychopathy.¹¹ As a consequence, individuals meeting the criteria for antisocial personality disorder are more heterogeneous in their pathophysiology than individuals meeting criteria for psychopathy.¹²

Psychopathy: the cognitive profile

Before continuing it is worth noting that the term “cognitive” is being used to refer to all relevant computations conducted by the brain. Sometimes the term “affective” is used with respect to emotional processes.¹³ However, for the purposes of this paper, affective processing will be considered as simply another form of cognitive processing.

With respect to cognitive dysfunction in psychopathy, the disorder is particularly interesting given the selectivity in the impairments seen. Thus, for example, executive functioning,¹⁴ Theory of Mind,¹⁵ and episodic memory (as long as it does not rely on augmentation by emotional content¹⁶) are intact in individuals with this disorder. Indeed, the two main classes of model of psychopathy concentrate on only two forms of dysfunction: attentional¹⁷ and emotional processing.^{18,19}

Psychopathy as a disorder of attention: the response set modulation hypothesis

According to the response modulation hypothesis, the difficulty faced by individuals with psychopathy relates to a problem in reallocating attention to secondary information when engaged in goal-directed behavior.^{17,20} This difficulty in balancing the demands of goal-directed processing and secondary information processing creates a bias whereby psychopathic individuals are less responsive to affective information unless it is a central aspect of their goal-directed focus of attention. It is argued that “psychopathic individuals initially perceive and identify both primary and secondary information, but are particularly adept at using higher-order processes to resolve the competition between goal-relevant and secondary demands on attention” (p 227).⁴ The authors argue that these higher-order processes create an “early attention bottleneck” that limits the processing of secondary infor-

mation. Typically, an early attention bottleneck has implied that only physical and not abstract properties of a secondary stimulus are processed; the bottleneck occurs within the visual stream, with “early” processing corresponding to physical feature as opposed to abstract feature processing.²¹ However, Newman and colleagues use the term in a temporal sense; processing by higher order processes of the first stimulus in a sequence of stimuli acts as a bottleneck for processing the second stimulus in a sequence.

It is clear that regions implicated in top-down attentional control (ie, higher order attentional processes), such as lateral frontal, dorsomedial, and parietal cortices, impact the amygdala’s response to emotional stimuli. Increased priming of task-relevant representations by these regions is thought to reduce the representational strength of emotional stimuli within temporal cortex, following representational competition,²² and consequently reduce amygdala responses to these stimuli.^{23,24} In short, the reduced emotional responsiveness of individuals with elevated psychopathic traits could be a secondary consequence of heightened top-down attentional control to non-emotional stimulus features.²⁵

In recent studies in adults with psychopathy, Newman and colleagues manipulated attention either towards the threat-relevant component of a stimulus array or away from this component and examined fear-potentiated startle (FPS).^{3,4} In each of these studies, psychopathy scores were significantly inversely related to FPS under conditions that required participants to focus on a threat-irrelevant dimension of stimuli. In contrast, psychopathy scores were unrelated to FPS when attention was focused on the threat-relevant dimension.

These studies provide important support for the suggestion that it is an attentional abnormality, rather than a problem in emotional responding, that is central to an understanding of psychopathy. Given the literature on the interaction of top-down attentional control and emotional responding,^{23,24} these data should suggest that psychopathy is related to enhanced recruitment of regions implicated in top-down attentional control (ie, dorsomedial and lateral frontal and parietal cortices²⁶). The stronger these are recruited (as a function of psychopathy), the stronger the priming of threat irrelevant stimulus dimensions, the weaker the representation of threat relevant stimulus dimensions following representational competition, and the weaker the emotional response. However, there are at least five reasons to be cautious.

First, while these are correlational studies within a forensic sample, and thus studies where IQ could not be matched across groups, it remains critical to show that IQ did not correlate with psychopathy level. Otherwise the results might reflect the influence of IQ rather than psychopathy. However, this matching was not done.

Second, only the individuals with psychopathy showed an impact of the attentional manipulation. Individuals low in psychopathy showed no differentiation in their fear-potentiated startle as a function of whether attention was directed towards or away from threat-relevant stimulus features. It is currently unclear why this paradigm contrasts with other work showing that manipulations of attention do have an impact on emotional responding in healthy individuals.^{23,24}

Third, while superior recruitment of top-down attentional control systems would result in reduced emotional responses to emotional stimuli that are not the focus of attention, there are no indications of increased recruitment of such systems in the studies showing reduced amygdala responses to emotional stimuli in adults with psychopathy.

Fourth, several studies have shown reduced FPS in individuals with psychopathy to environmental threats in the absence of task demands to attend to other stimulus features.^{27,28} It is unclear what early stimuli are blocking the processing of the threat prime in these studies.

Fifth, if higher-order processing of the first stimulus in a sequence of stimuli acts as a bottleneck for processing the second stimulus in a sequence, why is the attentional blink apparently decreased in individuals with psychopathy? In attentional blink experiments, two targets are embedded within a stream of distracters in a rapid serial visual presentation with the second (T2) appearing at different temporal “lags” in relation to the first (T1). The classic pattern of results identified in the attentional blink task reflects a participant’s reduced ability to report the identity of T2 if it is presented between approximately 100 ms and 600 ms after onset of T1.²⁹ One might have considered that the “bottleneck” created by the first target stimulus should prevent the processing of later stimuli in the sequence. However, the data indicates that targets presented after the target (at least at lag 4 [320 ms] and greater) are more likely to be recognized in individuals with psychopathy relative to controls.³⁰ The authors make reference to an interpretation of the attentional blink as reflecting the conflict between consolidating one’s perception of T1 and real-

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locating attention in response to a lag-1 distracter.³¹ They argue that because of reduced representation of the lag-1 distracter, less conflict is generated and there is more possibility of allocating attention to stimuli greater than lag-1 after the target. The difficulty for this explanation is that it would predict reduced accuracy for the lag-1 distracter (reflecting its reduced representation), and this was not seen.³⁰

In summary, 20 years after its development, the response set modulation hypothesis remains highly influential. We have not attempted a full critique here,²⁵ but instead have concentrated on the newest version of the model suggesting an early attentional bottleneck. Irrespective of the difficulties, it has been highly successful in generating a wide array of paradigms for understanding the disorder, with some of the data from these paradigms proving challenging for emotion based views of psychopathy.

Emotion-based accounts

Adults with psychopathy show a variety of emotional processing impairments. For example, they show:

- (i) Reduced autonomic responses to the pain and distress of others³²⁻³⁴
- (ii) Reduced recognition of emotional expressions (for meta-analytic reviews of this literature, see refs 35,36). Interestingly, this impairment is relatively selective. Recognition of fearful, sad, and happy expressions is clearly reduced, while the recognition of disgusted and angry expressions remains intact^{35,36}
- (iii) Reduced aversive conditioning; they are less likely to show autonomic activity to stimuli associated with shock³⁷
- (iv) Pronounced difficulties with reinforcement based decision-making.³⁸

These are seen in:

- (a) Extinction: where the participant learns to respond to a stimulus for reward but, after a set number of trials, this responding must be extinguished because the reinforcement contingencies have changed and the response is no longer rewarded³⁹
- (b) Reversal learning: where the participant learns to make one form of response to a pair of stimuli to gain a reward but, after a set number of trials, this response must change, due to a change in reinforcement contingency, in order to gain the reward⁴⁰
- (c) Economic decision-making paradigms: the

Ultimatum game involves the participant and another individual. The participant has to decide whether to accept the offer of a share of resources made by the individual. This can be fair (eg, making a 50:50 split on \$20 so each gains \$10) or progressively unfair (eg, only \$4 is offered to the participant). Individuals with psychopathy show increased rejection of unfair offers, even at cost to themselves, relative to comparison individuals⁴¹

- (d) Moral judgment: Individuals with psychopathy show reduced responsiveness to what can be termed “care-based” transgressions (ie, transgressions involving harm to another; eg, one person hitting another¹⁰). This has been seen using a variety of paradigms.^{18,42-45} Again this impairment in transgression processing is selective. Care-based transgressions are reliant on appropriate responsiveness to the pain and distress of others.¹⁰ As noted above, this is dysfunctional in adults with psychopathy.³²⁻³⁶ In contrast, conventional transgressions (reliant on authority; eg, talking in class) are reliant on appropriate responsiveness to other individual’s anger while disgust-based transgressions (that can cover aspects of sexual behavior) are reliant on appropriate responsiveness of other individual’s disgust.¹⁰ Adults with psychopathy show intact processing of these emotional expressions.^{35,36} They also show intact processing of these forms of transgression.^{18,42,44}

Given these data, a variety of authors have suggested that an emotional dysfunction underpins the deficits seen in individuals with psychopathy.^{18,19,28,46-49} The oldest of these positions suggested that punishment processing was dysfunctional while reward processing was intact or even possibly superior.^{18,28,46-48} It is now clear that the situation is considerably more complicated.¹⁰

Three critical data points are important to note. First, the expression impairment is not seen for all aversive expressions; it is seen for fear and sadness but not anger and disgust. This is inconsistent with a general impairment in processing aversive stimuli. Second, the expression processing impairment is also seen for happy expressions. This suggests that the processing of rewarded stimuli is also disrupted. Third, the immediate response to punishment is intact in adults with psychopathy.

To consider the last point in more detail, when the participant is punished on a task such as the reversal learning paradigm, they are likely to change their response on

the next trial. If this new response is then rewarded, they are more likely to stay with the new response. Punishment signals that a change in response should occur. If punishment processing was the principle problem in psychopathy, then adults with psychopathy should not change their responding following punishment. Yet adults with psychopathy are as likely to change their response following punishment as comparison adults.⁴⁰ The idea is that the individual's choices are determined by the relative reward values of the responses available to them. The individual is more likely to stay with a new response following its reward because the expected reward value of this new response is now stronger than the expected reward value of the old response.⁵⁰ If there is deficient representation of expected value, the individual's decision-making will be poorer; they should be more likely to return to an old, now punished, response rather than stay with the new rewarded response. This exact behavioral profile is seen in adults with psychopathy; they are significantly more likely to change their response following a reward than comparison individuals.⁴⁰

In other words, models of psychopathy stressing only impairment in punishment processing are insufficient. From a cognitive perspective, it appears that individuals with psychopathy face two core difficulties with respect to emotional processing.¹⁰

First, they show impairment in stimulus-reinforcement learning (associating a reward or punishment value with a stimulus). This is most clearly manifested in their difficulty on aversive conditioning tasks.³⁷ But it is also relevant to their impairment in processing both the distress (their fear, sadness, and pain) as well as the happiness of others.^{35,36} Emotional expressions can be considered to be reinforcers allowing humans to rapidly transmit valence information on objects and actions between one another; you regard actions resulting in fear and pain as bad and actions resulting in happiness as good.⁵¹ Indeed, it is argued that care-based transgressions come to be regarded as "bad" because of the association of representations of these transgressions with the aversive feedback of the distress of the victims of these transgressions.¹⁰ In line with the position here, adults with psychopathy regard care-based transgressions as less bad than comparison adults.^{18,42-45}

Second, they show impairment in the representation of reinforcement outcome information.¹⁰ As noted above, impaired representation of reinforcement outcome information allows an explanation of why individuals

with psychopathy are more likely to change their response following a *reward* for that response. The value of the new response is updated and represented more poorly resulting in another response being chosen, leading to an increased probability that the subject will change their response. Similarly, on the Ultimatum game, individuals with psychopathy will be more likely to reject offers,⁴¹ even though this will cost them money, because they less well represent the reward value of this money. There is also likely a third difficulty in prediction error signaling. If an individual receives more or less reward than expected or more or less punishment than expected, this generates a prediction error; the greater the difference between prediction and reality, the greater the prediction error. Prediction errors are critical for reinforcement-based learning. The greater the prediction error, the faster the system will attempt to learn the new value of the stimulus or action.⁵² However, this third impairment will not be considered in any further detail here as the data supporting its existence is obtained with youth with psychopathic traits.⁵³ The relevant studies have yet to be done in adults with psychopathy.

Psychopathy: the neural profile

Both structural and functional magnetic resonance imaging studies can inform an account of psychopathy. We will briefly consider the current state of the literature regarding these studies. Note though that only studies where groups were matched for IQ will be considered. The importance of appropriate matching can be seen from the data presented in a recent sMRI study.⁵⁴ This study reported a 30% reduction across much of cortex in adults with psychopathy relative to healthy comparison individuals.⁵⁴ However, these results were only seen when comparing individuals with psychopathy with healthy comparison individuals. The IQ and, for that matter, the substance dependence rates of these comparison individuals, was not reported but it is likely, given their job descriptions (students, hospital staff, and skilled workers), that their average IQ was significantly higher and their average substance dependence rate was significantly lower than those of the patients. These findings may have driven the findings. This suggestion is supported from the authors' data on only the patients. Groups of patients with high psychopathy vs low psychopathy scores, matched for IQ, showed very minimal differences in cortical volume.⁵⁴

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sMRI studies

A series of findings, reported across labs where appropriate IQ comparisons have been made, are worth noting. Not all studies have reported reduced volumes in these regions in psychopathy but none (at least involving IQ matched samples) have reported increased volumes in these regions. Thus, three studies have reported reduced amygdala volumes in adults with psychopathy⁵⁵⁻⁵⁷ including the largest structural imaging study of this population to date (N=296).⁵⁵ Similarly, four studies have reported reductions in temporal pole^{55,58-60} and two in STS.^{58,61} Three studies have reported reductions in orbitofrontal cortex.^{55,58,61} Moreover, and interestingly given the extensive connections between the amygdala and orbitofrontal cortex though the uncinate fasciculus white matter tract, all three DTI studies examining the structural integrity of this tract in individuals with psychopathy have reported reduced structural integrity relative to comparison individuals.⁶²⁻⁶⁴

Functional MRI studies

Regrettably, again, many of the functional MRI (fMRI) studies of psychopathy, even when IQ was assessed (as an IQ<80 was exclusory), did not report that groups were matched for IQ making their interpretation problematic. Consequently, the data from such studies will not be considered here. However, studies where appropriate IQ matching was conducted include investigations of moral judgment,^{65,66} expression processing,^{67,68} emotional memory,⁶⁹ processing abstract and concrete words,⁷⁰ emotional Theory of Mind,⁷¹ and connectivity mapping.^{64,72}

Several of these studies support the sMRI findings of core dysfunction in the amygdala. Thus, individuals with psychopathy have been reported to show amygdala activity during moral judgment⁶⁶ and also a weaker positive association between amygdala activity and severity ratings of transgressions than is seen in healthy individuals.⁶⁵ In addition, violent schizophrenic patients with psychopathy show reduced amygdala responses to fearful expressions⁶⁸—though a relationship between psychopathic traits in aggressive individuals and amygdala responsiveness was not seen in another study.⁶⁷ In addition, a reduction in amygdala activity was seen during an emotional memory paradigm.⁶⁹ Currently, though the literature with respect to orbital/ventromedial frontal cor-

tex (vmPFC) is less convincing. One study reported a reduction in the differential responsiveness of vmPFC to moral and nonmoral images.⁶⁵ However, a second study reported *increased* vmPFC responses in individuals with psychopathy when performing a task involving the identification of other individual's emotional responsiveness (this increased vmPFC responsiveness did not relate to the emotional content as it was also seen in the non-emotional control condition).⁷¹ Notably, though, studies have shown weaker functional connectivity between vmPFC and the amygdala⁶⁴ and between vmPFC and posterior cingulate cortex.⁷²

Given the findings of reductions in the temporal pole, it is interesting to note that studies have reported reduced responsiveness within this region to moral transgressions⁶⁵ and abstract words.⁷⁰ There have also been two reports of reduced posterior cingulate cortex responsiveness: during the processing of moral transgressions⁶⁶ and emotional memory.⁶⁹ In addition, posterior cingulate cortex shows reduced connectivity with vmPFC and regions of posterior cortex engaged in visual representation and attention priming.⁷² Two studies have also observed anomalous responsiveness within rostral medial frontal cortex. Thus, one study showed reduced activity within this region during moral judgment with increasing psychopathic traits.⁶⁶ A second showed *increased* activity within this region relative to comparison individuals to judgments concerning vignette character's emotional states.⁷¹

The implications of these data for models of psychopathy

From a neurobiological perspective, there are two main accounts of psychopathy.^{11,49} Kiehl's model, the paralimbic hypothesis, has been driven by suggestions that specific brain regions share similar cytoarchitectonic features regarding neuronal type, structure and density.^{49,73} On the basis of cytoarchitectonic information, Kiehl has argued that the amygdala, orbital frontal cortex, all of cingulate cortex, parahippocampal area, and insula are all dysfunctional in individuals with psychopathy.^{49,73} Regions of temporal cortex are also implicated, with superior temporal sulcus stressed in the earlier review⁴⁹ in contrast to temporal pole in the more recent review.⁷³ The strength of this model are that it can easily account for indications of dysfunction outside of the three main areas, amygdala, vmPFC, and striatum, stressed by

Blair.^{10,74} However, there are two main difficulties faced by this model.

First, how to handle the empirical data. Consider the Ermer et al (2011) sMRI study, for example. It is striking in that the reduced grey matter was confined to posterior cingulate cortex - not all of cingulate cortex as the cytoarchitectonic-based model would predict. Should this be considered simply a Type II error? But if it is not, what does it mean for the model that one region appears untouched while other regions, with the same cytoarchitectonic properties, show dysfunction?

Second, the neuropsychological literature does not support the idea of dysfunction in several of the regions implicated by the paralimbic hypothesis. For example, the hippocampus is critical for episodic memory. While individuals with elevated CU traits may show a failure in the augmentation, by the amygdala, of emotional memory, they show no significant general episodic memory impairment that parahippocampal dysfunction would predict.¹⁶ Similar arguments can be made for the roles of anterior cingulate cortex in conflict monitoring (if anything superior in psychopathy) and superior temporal cortex and temporal pole in Theory of Mind, consistently found to be intact in psychopathy.¹⁵ Of course, the question then becomes why are some regions showing indications of reduced gray matter when functions mediated by these systems remain intact? One possible answer is that the gray matter reduction in some of these regions is a developmental consequence of consequence of reduced input from regions that are dysfunctional in psychopathy such as the amygdala.¹⁰ A second possibility is that only some of the functions these regions are implicated in *are* dysfunctional (though what these might be needs to be specified for hippocampus and temporal pole, for example). Either possibility suggests that the paralimbic hypothesis requires greater detail.

A contrasting view, termed the Integrated Emotion Systems (IES) model, will be briefly developed here.¹⁰ This model takes a cautious approach when considering which regions might be dysfunctional in individuals with psychopathy. Not only must the fMRI data indicate aberrant activity within a region but also the functions mediated by these regions must be shown to be disrupted (and putatively related to the development of the disorder). An fMRI study might identify reduced activity in an area. But this need not reflect dysfunction in the integrity of that area. Instead, it may reflect reduced input to this area from another region that is dysfunc-

tional in psychopathy. A different study, using a task that does not rely on the integrity of the dysfunctional region(s) might show no reduced activity in the area.

The IES model follows Patrick's seminal work stressing the importance of the amygdala.²⁸ The amygdala is critical for stimulus-reinforcement learning; both for aversive and appetitive reinforcements.^{75,76} Stimulus-reinforcement learning, as indexed by aversive conditioning, is impaired in psychopathy.³⁷ Indeed, adults with psychopathy show reduced amygdala responses during aversive conditioning (though, it should be noted, it is unclear whether the groups were matched for IQ in this study).⁷⁷ The emotional expressions of fear, sadness, and happiness are thought to initiate stimulus-reinforcement learning; they allow the individual to learn the value of the object or action to which they are displayed.⁵¹ The amygdala is important for processing these expressions (particularly fear).⁷⁸ In line with the amygdala dysfunction hypothesis, violent patients with psychopathy show reduced amygdala responses to fearful expressions.⁶⁸ According to the IES model, care-based transgressions come to be regarded as "bad" because of the association of representations of these transgressions with the aversive feedback of the distress of the victims of these transgressions.¹⁰ Amygdala dysfunction, and consequent impaired stimulus-reinforcement learning and responsiveness to the distress of others, should result in a deficient response to care-based transgressions. At the neural level this should be partly manifested as a reduced amygdala response to care-based transgressions. The data is consistent with this suggestion.^{65,66}

During instrumental learning tasks, where the individual is attempting to learn an action to gain reward or avoid punishment, the amygdala and/or striatum feeds reinforcement expectancy information to ventromedial frontal cortex where this information is represented.⁵⁰ Given the diffusion tensor imaging data showing reduced integrity of the white matter tracts between the amygdala and vmPFC in psychopathy,⁶²⁻⁶⁴ it is likely that this feed-forward of reinforcement information occurs less successfully. This suggestion is also consistent with data showing reduced amygdala-vmPFC functional connectivity in adults with psychopathy.⁶⁴ The representation of expected outcome information (how good or bad the action is) within vmPFC is also thought to be dysfunctional.¹⁰ This is consistent with the data from Harenski and colleagues' moral judgment task.⁶⁵ However, formal fMRI modeling work that would

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directly address the issue has only been done in youth with psychopathic traits,⁵³ not adult samples. Similarly, studies demonstrating dysfunction in the role of striatum in prediction error signaling have not been conducted in adults with psychopathy, only youth with psychopathic traits.⁵³

Conclusions

Psychopathy is a serious developmental disorder marked by pronounced emotional dysfunction and an increased risk for aggression. It is not equivalent to antisocial personality disorder from *DSM-IV-R*. Individuals meeting criteria for psychopathy with gold standard assessment techniques will also meet criteria for antisocial personality disorder. However, many other individuals with antisocial personality disorder will not meet criteria for psychopathy.⁵⁹

It is argued here that the emotion dysfunction relates to three core functional impairments: in the association of stimuli with reinforcement, the representation of expected value information and in prediction error signaling. These impairments are thought to relate to the observed dysfunction seen in both sMRI and fMRI studies within the amygdala, vmPFC, and (currently only in work with youth samples) striatum. Other regions of temporal cortex (temporal pole and superior temporal sulcus) may also be dysfunctional—though whether this reflects primary pathology or the secondary, developmental impact of dysfunction in the core regions is

unclear. It is also unclear whether any functions reliant on these regions are detrimentally affected in individuals with psychopathy. Finally, there is sMRI and fMRI evidence of posterior cingulate cortex dysfunction. This is interesting given the extensive connectivity of this region with vmPFC and also its shared overlap in function. Both regions are implicated in the representation of expected value.⁷⁹ However, as yet, no studies have formally investigated the representation of expected value within posterior cingulate cortex in adults with psychopathy.

Importantly, by specifying the computational and neural systems level impairments that are associated with this disorder, we now have available biomarkers of dysfunction. Such biomarkers are not only of potential use in diagnostic classification—the functional impairments in one aggressive patient may be very different from those of another—but also for assessing treatment efficacy. Currently, this disorder is regarded as extremely difficult to treat. Moreover, treatment studies are difficult when the outcome measure may be reoffending or incidence of aggressive episodes. However, with appropriate biomarkers it becomes possible to use these to determine treatment efficacy. The field is currently at this exciting stage. Now we need to identify effective treatments. □

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REFERENCES

1. Cicchetti D, Dawson G. Multiple levels of analysis. *Dev Psychopathol.* 2002;14:417-420.
2. Koenigs M, Baskin-Sommers A, Zeier J, Newman JP. Investigating the neural correlates of psychopathy: a critical review. *Mol Psychiatry.* A2011;16:792-799.
3. Newman JP, Curtin JJ, Bertsch JD, Baskin-Sommers AR. Attention moderates the fearlessness of psychopathic offenders. *Biol Psychiatry.* 2010;67:66-70.
4. Baskin-Sommers AR, Curtin JJ, Newman JP. Specifying the attentional selection that moderates the fearlessness of psychopathic offenders. *Psychol Sci.* 2011;22:226-234.
5. Hare RD. *Hare Psychopathy Checklist-Revised (PCL-R)*. 2nd Ed. Toronto, Canada: Multi Health Systems; 2003.
6. Munoz LC, Frick PJ. The reliability, stability, and predictive utility of the self-report version of the Antisocial Process Screening Device. *Scand J Psychol.* 2007;48:299-312.
7. Lynam DR, Caspi A, Moffitt TE, Loeber R, Stouthamer-Loeber M. Longitudinal evidence that psychopathy scores in early adolescence predict adult psychopathy. *J Abnorm Psychol.* 2007;116:155-165.
8. Walters GD. Predicting institutional adjustment and recidivism with the psychopathy checklist factor scores: a metaanalysis. *Law Hum Behav.* 2003;27:541-558.
9. Hemphill JF, Hare RD, Wong S. Psychopathy and recidivism: a review. *Legal Criminol Psychol.* 1998 1998;3:139-170.
10. Blair RJR. The amygdala and ventromedial prefrontal cortex in morality and psychopathy. *Trends Cogn Sci.* 2007;11:387-392.
11. Blair RJR, Mitchell DGV, Blair KS. *The Psychopath: Emotion and the Brain*. Oxford, UK: Blackwell; 2005.
12. Karnik NS, McMullin MA, Steiner H. Disruptive behaviors: conduct and oppositional disorders in adolescents. *Adolesc Med Clin.* 2006;17:97-114.
13. Davidson RJ. Affective neuroscience and psychophysiology: toward a synthesis. *Psychophysiology.* 2003;40:655-665.
14. Morgan AB, Lilienfeld SO. A meta-analytic review of the relation between antisocial behavior and neuropsychological measures of executive function. *Clin Psychol Rev.* 2000;20:113-136.
15. Blair RJR, Sellars C, Strickland I, et al. Theory of Mind in the psychopath. *J Forensic Psychiatry.* 1996;7:15-25.
16. Christianson SA, Forth AE, Hare RD, Strachan C, Lidberg L, Thorell LH. Remembering details of emotional events: a comparison between psychopathic and nonpsychopathic offenders. *Pers Individ Diffe.* 1996;20:437-443.

Psicopatía: disfunción cognitiva y neural

La psicopatía es un trastorno del desarrollo caracterizado por déficit emocionales y un riesgo aumentado de conductas antisociales. No es equivalente al diagnóstico de Trastorno de Personalidad Antisocial, el cual se centra sólo en el riesgo aumentado de conducta antisocial y no en una causa específica, como por ejemplo la empatía reducida y la culpa que constituyen el déficit emocional. Esta revisión examina datos de adultos con psicopatía respecto a las principales consideraciones cognitivas del trastorno, poniendo énfasis en el déficit primario de atención o el déficit primario de las emociones. Además se incluyen datos sobre la neurobiología de este trastorno. Se destaca la disfunción del papel de la amígdala en el refuerzo del aprendizaje y el papel de la corteza frontal ventromedial en la representación del valor del refuerzo. También se presentan datos que señalan posibles dificultades en partes de la corteza cingulada temporal y posterior. Se plantean sugerencias acerca del por qué estos déficit llevan al desarrollo de este trastorno.

La psychopathie : une dysfonction neurale et cognitive

La psychopathie est un trouble développemental marqué par des déficits émotionnels et un risque accru de comportement antisocial. Il est différent du Trouble de la Personnalité Antisociale, diagnostic qui repose sur le risque augmenté de comportement antisocial et non sur une étiologie spécifique, par exemple une empathie et une culpabilité diminuées qui constituent le déficit émotionnel. L'exposé présenté ici analyse les données issues d'adultes psychopathes concernant les principales perturbations cognitives de la maladie qui mettent en évidence soit un déficit primaire d'attention soit un déficit primaire d'émotion ; de plus, cette revue étudie les données neurobiologiques de ce trouble. La dysfonction du rôle de l'amygdale dans l'apprentissage du renforcement et du rôle du cortex frontal ventromédian dans la représentation du renforcement est soulignée. Des problèmes éventuels au niveau de certaines parties du cortex cingulaire temporal et postérieur sont aussi présentés. Des explications sont proposées pour expliquer comment ces déficits aboutissent au développement de la maladie.

17. Newman JP, Brinkley CA, Lorenz AR, Hiatt KD, MacCoon DG. Psychopathy as psychopathology: Hare's essential contributions. In: Herve H, Yuille JC, eds. *The Psychopath: Theory, Research, and Practice*. Mahwah, NJ: Lawrence Erlbaum Associates; 2007:173-206.
18. Blair RJR. A cognitive developmental approach to morality: investigating the psychopath. *Cognition*. 1995;57:1-29.
19. Frick PJ, Viding E. Antisocial behavior from a developmental psychopathology perspective. *Dev Psychopathol*. 2009;21:1111-1131.
20. Patterson CM, Newman JP. Reflectivity and learning from aversive events: toward a psychological mechanism for the syndromes of disinhibition. *Psychol Rev*. 1993;100:716-736.
21. Broadbent DE. *Perception and Communication*. Oxford, UK: Oxford University Press; 1958.
22. Desimone R, Duncan J. Neural mechanisms of selective visual attention. *Ann Rev Neurosci*. 1995;18:193-222.
23. Mitchell DG, Nakic M, Fridberg D, Kamel N, Pine DS, Blair RJ. The impact of processing load on emotion. *Neuroimage*. 2007;34:1299-1309.
24. Pessoa L, Ungerleider LG. Neuroimaging studies of attention and the processing of emotion-laden stimuli. *Prog Brain Res*. 2004;144:171-182.
25. Blair RJR, Mitchell DG. Psychopathy, attention and emotion. *Psychol Med*. 2009;39:543-555.
26. Kastner S, Ungerleider LG. Mechanisms of visual attention in the human cortex. *Annu Rev Neurosci*. 2000;23:315-341.
27. Levenston GK, Patrick CJ, Bradley MM, Lang PJ. The psychopath as observer: Emotion and attention in picture processing. *J Abn Psychol*. 2000;109:373-386.
28. Patrick CJ, Bradley MM, Lang PJ. Emotion in the criminal psychopath: Startle reflex modulation. *J Abn Psychol*. 1993;102:82-92.
29. Raymond JE, Shapiro KL, Arnell KM. Temporary suppression of visual processing in an RSVP task: an attentional blink? *J Exp Psycho Hum Percept Perform*. 1992;18:849-860.
30. Wolf RC, Carpenter RW, Warren CM, Zeier JD, Baskin-Sommers AR, Newman JP. Reduced susceptibility to the attentional blink in psychopathic offenders: Implications for the attention bottleneck hypothesis. *Neuropsychology*. 2012;26:102-109.
31. Marois R, Chun MM, Gore JC. Neural correlates of the attentional blink. *Neuron*. 2000;28:299-308.
32. Aniskiewicz AS. Autonomic components of vicarious conditioning and psychopathy. *J Clin Psychol*. 1979;35:60-67.
33. House TH, Milligan WL. Autonomic responses to modeled distress in prison psychopaths. *Journal of Personality and Social Psychology*. 1976;34:556-560.
34. Blair RJR, Jones L, Clark F, Smith M. The psychopathic individual: a lack of responsiveness to distress cues? *Psychophysiology*. 1997;34:192-198.
35. Marsh AA, Blair RJ. Deficits in facial affect recognition among antisocial populations: a meta-analysis. *Neurosci Biobehav Rev*. 2008;32:454-465.
36. Dawel A, O'Kearney R, McKone E, Palermo R. Not just fear and sadness: meta-analytic evidence of pervasive emotion recognition deficits for facial and vocal expressions in psychopathy. *Neurosci Biobehav Rev*. 2012;36:2288-2304.
37. Rothemund Y, Ziegler S, Hermann C, et al. Fear conditioning in psychopaths: event-related potentials and peripheral measures. *Biol Psychol*. 2012;90:50-59.
38. Blair KS, Leonard A, Morton J, Blair RJR. Impaired decision making on the basis of both reward and punishment information in individuals with psychopathy. *Person Indiv Diff*. 2006;41:155-165.

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39. Newman JP, Patterson CM, Kosson DS. Response perseveration in psychopaths. *J Abnorm Psychol.* 1987;96:145-148.
40. Budhani S, Richell RA, Blair RJ. Impaired reversal but intact acquisition: probabilistic response reversal deficits in adult individuals with psychopathy. *J Abnorm Psychol.* 2006;115:552-558.
41. Koenigs M, Kruepke M, Newman JP. Economic decision-making in psychopathy: a comparison with ventromedial prefrontal lesion patients. *Neuropsychologia.* 2010;48:2198-2204.
42. Blair RJR, Jones L, Clark F, Smith M. Is the psychopath "morally insane"? *Person Individ Diff.* 1995;19:741-752.
43. Koenigs M, Kruepke M, Zeier J, Newman JP. Utilitarian moral judgment in psychopathy. *Soc Cogn Affect Neurosci.* 2012;7:708-714.
44. Aharoni E, Antonenko O, Kiehl KA. Disparities in the moral intuitions of criminal offenders: the role of psychopathy. *J Res Pers.* 2011;45:322-327.
45. Young L, Koenigs M, Kruepke M, Newman JP. Psychopathy increases perceived moral permissibility of accidents. *J Abnorm Psychol.* 2012;121:659-667.
46. Fowles DC. Psychophysiology and psychopathy: a motivational approach. *Psychophysiology.* 1988;25:373-391.
47. Lykken DT. A study of anxiety in the sociopathic personality. *J Abn Soc Psychol.* 1957;55:6-10.
48. Hare RD. Psychopathy. In: Venables PH, Christie MJ, eds. *Research in Psychophysiology.* New York, NY: Wiley; 1975:325-348.
49. Kiehl KA. A cognitive neuroscience perspective on psychopathy: Evidence for paralimbic system dysfunction. *Psychiatry Res.* 2006;142:107-128.
50. O'Doherty JP. Beyond simple reinforcement learning: the computational neurobiology of reward-learning and valuation. *Eur J Neurosci.* 2012;35:987-990.
51. Blair RJR. Facial expressions, their communicatory functions and neuro-cognitive substrates. *Philos Trans R Soc Lond B Biol Sci.* 2011;358:561-572.
52. Rescorla RA, Wagner AR. A theory of Pavlovian conditioning: variations in the effectiveness of reinforcement and nonreinforcement. In: Black AH, Prokasy WF, eds. *Classical Conditioning II.* New York, NY: Appleton Century-Crofts; 1972:64-99.
53. White SF, Pope K, Sinclair S, et al. Disrupted expected value and prediction error signaling in youth with disruptive behavior disorders during a passive avoidance task. *Am J Psychiatry.* 2013;170:315-323.
54. Boccardi M, Frisoni GB, Hare RD, et al. Cortex and amygdala morphology in psychopathy. *Psychiatry Res.* 2011;193:85-92.
55. Ermer E, Cope LM, Nyalakanti PK, Calhoun VD, Kiehl KA. Aberrant paralimbic gray matter in criminal psychopathy. *J Abnorm Psychol.* 2012;121:649-658.
56. Yang Y, Raine A, Colletti P, Toga AW, Narr KL. Morphological alterations in the prefrontal cortex and the amygdala in unsuccessful psychopaths. *J Abnorm Psychol.* 2010;119:546-554.
57. Yang Y, Raine A, Narr KL, Colletti P, Toga AW. Localization of deformations within the amygdala in individuals with psychopathy. *Arch Gen Psychiatry.* 2009;66:986-994.
58. Yang Y, Raine A, Colletti P, Toga AW, Narr KL. Abnormal temporal and prefrontal cortical gray matter thinning in psychopaths. *Mol Psychiatry.* 2009;14:561-562.
59. Gregory S, fytche D, Simmons A, et al. The antisocial brain: psychopathy matters. *Arch Gen Psychiatry.* 2012;69:962-972.
60. Ly M, Motzkin J, Philippi C, et al. Cortical thinning in psychopathy. *Am J Psychiatry.* 2012;169:743-749.
61. de Oliveira-Souza R, Hare RD, Bramati IE, et al. Psychopathy as a disorder of the moral brain: fronto-temporo-limbic grey matter reductions demonstrated by voxel-based morphometry. *Neuroimage.* 2008;40:1202-1213.
62. Sundram F, Deeley Q, Sarkar S, et al. White matter microstructural abnormalities in the frontal lobe of adults with antisocial personality disorder. *Cortex.* 2012;48:216-229.
63. Craig MC, Catani M, Deeley Q, et al. Altered connections on the road to psychopathy. *Mol Psychiatry.* 2009;14:946-953, 907.
64. Motzkin JC, Newman JP, Kiehl KA, Koenigs M. Reduced prefrontal connectivity in psychopathy. *J Neurosci.* 2011;31:17348-17357.
65. Harenski CL, Harenski KA, Shane MS, Kiehl KA. Aberrant neural processing of moral violations in criminal psychopaths. *J Abnorm Psychol.* 2010;119:863-874.
66. Glenn AL, Raine A, Schug RA. The neural correlates of moral decision-making in psychopathy. *Mol Psychiatry.* 2008;14:5-6.
67. Pardini DA, Phillips M. Neural responses to emotional and neutral facial expressions in chronically violent men. *J Psychiatry Neurosci.* 2010;35:390-398.
68. Dolan MC, Fullam RS. Psychopathy and functional magnetic resonance imaging blood oxygenation level-dependent responses to emotional faces in violence patients with schizophrenia. *Bio Psychiatry.* 2009;66:570-577.
69. Kiehl KA, Smith AM, Hare RD, et al. Limbic abnormalities in affective processing by criminal psychopaths as revealed by functional magnetic resonance imaging. *Biol Psychiatry.* 2001;50:677-684.
70. Kiehl KA, Smith AM, Mendrek A, Forster BB, Hare RD, Liddle PF. Temporal lobe abnormalities in semantic processing by criminal psychopaths as revealed by functional magnetic resonance imaging. *Psychiatry Res.* 2004;130:27-42.
71. Sommer M, Sodan B, Dohnel K, Schwerdtner J, Meinhardt J, Hajak G. In psychopathic patients emotion attribution modulates activity in outcome-related brain areas. *Psychiatry Res.* 2010;182:88-95.
72. Juarez M, Kiehl KA, Calhoun VD. Intrinsic limbic and paralimbic networks are associated with criminal psychopathy. *Hum Brain Mapp.* In press.
73. Anderson NE, Kiehl KA. The psychopath magnetized: insights from brain imaging. *Trends Cogn Sci.* 2012;16:52-60.
74. Finger EC, Marsh AA, Blair KS, et al. Disrupted reinforcement signaling in the orbital frontal cortex and caudate in youths with conduct disorder or oppositional defiant disorder and a high level of psychopathic traits. *Am J Psychiatry.* 2011;168:834-841.
75. LeDoux JE. The amygdala. *Curr Biol.* 2007;17:R868-R874.
76. Everitt BJ, Cardinal RN, Parkinson JA, Robbins TW. Appetitive behavior: impact of amygdala-dependent mechanisms of emotional learning. *Ann N Y Acad Sci.* 2003;985:233-250.
77. Birbaumer N, Veit R, Lotze M, et al. Deficient fear conditioning in psychopathy: a functional magnetic resonance imaging study. *Arch Gen Psychiatry.* 2005;62:799-805.
78. Murphy FC, Nimmo-Smith I, Lawrence AD. Functional neuroanatomy of emotions: a meta-analysis. *Cogn, Affect Behav Neurosci.* 2003;3:207-233.
79. Levy DJ, Glimcher PW. Comparing apples and oranges: using reward-specific and reward-general subjective value representation in the brain. *J Neurosci.* 2011;31:14693-14707.