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Psychopathy and Brain Function: Empirical Findings and Legal Implications

Christopher J. Patrick
Florida State University, Tallahassee, FL, USA

Noah C. Venables
Florida State University, Tallahassee, FL, US

Jennifer Skeem
University of California, Irvine, CA, USA

Introduction

A major focus of interest in contemporary research on mental disorders consists of work aimed at identifying differences in brain systems and processes associated with particular disorders or symptomatic expressions of disorders. This interest arises from the view that knowledge of the structure and workings of the brain is crucial to an understanding of psychological processes underlying abnormal behavior, which in turn will contribute to the development of optimally effective methods of treatment (i.e., by directly targeting underlying, brain-based processing deviations; Dadds & Rhodes, 2008; Insel & Cuthbert, 2009). The emphasis on neuroscience-oriented research in recent years also reflects the increased availability of non-invasive brain measurement methods appropriate for use with human subjects – including functional neuroimaging and electrocortical (i.e., electroencephalographic, or EEG, and event-related potential, or ERP) recording techniques. This chapter focuses on findings from studies that have used techniques of these types to test for differences in brain reactivity in individuals identified as psychopathic, and discusses implications of these findings for legal practices and policies.

In reviewing findings from brain research on psychopathy, it is important to distinguish psychopathy from other conditions with which it has historically been confused (e.g., criminal or antisocial behavior, in particular violent behavior), and

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to recognize meaningful distinctions even within the diagnosis of psychopathy (i.e., separable subsets of symptoms; diagnostic variants or "subtypes"). With this in mind, our review begins with a section on diagnostic distinctions. We then provide a brief description of differing brain measurement techniques, followed by a review of findings from studies using these techniques to study psychopathy as defined by assessment instruments that provide coverage of core-affective interpersonal (Factor 1) features along with impulsive-antisocial ('Factor 2') features. Findings from structural neuroimaging studies are considered briefly, followed by a review of findings from functional imaging studies, and newer ERP studies that have yielded the most consistent findings. Next, we identify and critically evaluate some key assumptions that underlie research on brain function in psychopathy and discuss constraints on the interpretation of findings from research of this kind. A final major section is devoted to discussion of implications of research on psychopathy and brain function for legal practices and policy making.

Diagnostic Distinctions

There is general agreement among researchers in the psychopathy area that this diagnostic condition can be distinguished from other similar-appearing conditions (e.g., child conduct disorder, adult antisocial personality, and persistent violent behavior) by the presence of certain core *affective-interpersonal* features. However, there remains some disagreement in the field as to the exact nature of these core features. Some conceptions of psychopathy place emphasis on callous-aggressive or antagonistic tendencies involving disregard for and instrumental-predatory victimization of other people (e.g., Hare, 1993, 2003; Lynam & Derefinko, 2006; McCord & McCord, 1964). Other conceptions emphasize deficits in the capacity for emotional reactivity, in particular negative emotions such as anxiety or fear (e.g., Cleckley, 1976; Lilienfeld & Widows, 2005; Lykken, 1995). Conceptions of each type recognize certain core diagnostic features in common – including egocentricity, manipulativeness, shallow affect, and absence or guilt or empathy – but characterize the overt (i.e., phenotypic) expression of these features somewhat differently. A triarchic model was proposed recently to organize these differing perspectives (Patrick, Fowles, & Krueger, 2009). The triarchic model describes alternative perspectives on psychopathy in terms of three distinct phenotypic constructs: meanness, boldness, and disinhibition. Perspectives that highlight callous-aggressive tendencies focus more on the meanness construct, and those that emphasize lack of anxiousness or fear focus more on the boldness construct. Perspectives of each type also place emphasis on the construct of disinhibition (lack of impulse control).

The most widely used instrument for assessing psychopathy in correctional and forensic settings is Hare's (1991, 2003) Psychopathy Checklist – Revised (PCL-R). The PCL-R indexes psychopathy through 20 items, each rated on a 0–2 scale (resulting in an overall PCL-R score range of 0–40), on the basis of a diagnostic interview and review of institutional archival records. Factor analytic work on the structure of

the PCL-R has yielded evidence suggesting two (Harpur, Hare, Hakstian, 1989), or alternatively three (Cooke & Michie, 2001) or four (Hare, 2003; Hare & Neumann, 2006), somewhat correlated but distinguishable item subsets or "factors" underlying PCL-R scores. Although there is accumulating evidence for the discriminant validity of PCL-R scores based on three (Hall, Benning, & Patrick, 2004) and four (Kennealy, Hicks, & Patrick, 2007; Hare & Neumann, 2006) factor models, most research to date examining the validity of separable psychopathy dimensions has focused on the two-factor model (Hare, 1991; Harpur *et al.*, 1989). PCL-R Factor 1 represents the core affective-interpersonal features of psychopathy in terms of items such as callous/lack of empathy, deficient depth and breadth of emotional experience, failure to accept responsibility for actions, glibness and superficial charm, grandiosity, pathological lying, and conning/manipulativeness. Factor 2 indexes impulsive-antisocial tendencies through PCL-R items that focus on chronic impulsive and irresponsive behavior, stimulation seeking, poor behavioral controls, failure to establish a life plan, and antisocial behavior beginning in childhood and continuing into adulthood.

In support of the idea that the affective-interpersonal features of psychopathy demarcate a condition distinct from other impulse-related disorders, the two broad factors of the PCL-R show differing relations with a broad range of criterion variables – particularly after controlling for their shared variance, which can be viewed as indexing callous-aggressiveness (Patrick *et al.*, 2009; Venables & Patrick, in press) or antagonism (Lynam & Derefinko, 2006). In particular, variance specific to Factor 1 shows positive relations and negative relations, respectively, with trait measures of social dominance (Harpur *et al.*, 1989; Verona, Patrick, & Joiner, 2001) and anxiety or fearfulness (Hicks & Patrick, 2006; Kennealy *et al.*, 2007). By contrast, variance specific to Factor 2 shows *positive* relations with measures of anxiety and distress-proneness (Hicks & Patrick, 2006), as well as with measures of anger and hostility (Hicks & Patrick, 2006), impulsivity (Kennealy *et al.*, 2007; Verona *et al.*, 2001), substance abuse (Patrick, Hicks, Krueger, & Lang, 2005; Reardon, Lang, & Patrick, 2002; Kennealy *et al.*, 2007), and suicidality (Douglas *et al.*, 2008; Verona *et al.*, 2001; Verona, Hicks, & Patrick, 2005). From the standpoint of the triarchic model (Patrick *et al.*, 2009), scores on Factor 1 of the PCL-R can be viewed as indexing meanness along with boldness and to a lesser degree disinhibition, whereas scores on Factor 2 reflect disinhibition in conjunction with meanness.

Not surprisingly, given the contrasting (in some cases opposing; e.g., Hicks & Patrick, 2006; Verona *et al.*, 2005) external correlates of the two PCL-R factors, individuals scoring high on the PCL-R do not comprise a homogeneous group in terms of trait characteristics as indexed by measures other than the PCL-R. For example, a study by Hicks, Markon, Patrick, Krueger, & Newman (2004) that used model-based cluster analysis to classify the personality profiles of male offenders with high overall PCL-R scores ($\geq$30) identified two subgroups with markedly different profiles: (1) an "aggressive" subgroup with high scores on negative emotional traits (including anxiousness, alienation, and aggression) and low scores on traits reflecting planfulness and restraint, and (2) a "stable" subgroup low in anxiousness and

high on traits reflecting agency (well-being, social dominance, and achievement). A subsequent study (Hicks, Vaidyanathan, & Patrick, 2010) that classified personality profiles of female offenders with high overall PCL-R scores (>25)[1] yielded findings consistent with this: two subgroups were identified, distinguished by low versus high negative emotional traits and high versus low impulsiveness. Consistent with this, a study by Skeem, Johansson, Andershed, Kerr, and Eno Louden (2007) that classified high PCL-R (≥29) male offenders using scores of the PCL-R three-factor model (Cooke & Michie, 2001) and a measure of trait anxiety identified distinctive "primary" and "secondary" psychopathy subgroups differentiated most strongly by low versus high anxiousness. In turn, these findings dovetail with studies by Newman and colleagues (e.g., Lorenz & Newman, 2002; Newman. Schmitt, & Voss, 1997) reporting markedly different patterns of performance on laboratory tasks for low- versus high-anxious subgroups of high-PCL-R offenders. The clear implication of these findings is that the PCL-R criteria for psychopathy do not capture a homogenous diagnostic condition; individuals identified as psychopathic by the PCL-R comprise at least two markedly different subgroups,[2] one characterized by high anxiousness in particular, possibly in conjunction with heightened trait aggression and impulsivity, and another by low anxiousness and perhaps elevated levels of dominance and efficacy. This point is important to bear in mind when interpreting results from brain measurement studies focusing on high PCL-R scoring groups.

Parallel distinctions are evident in other inventories for the assessment of psychopathy. The dominant instrument for diagnosing psychopathy in children and younger adolescents, the Anstisocial Process Screening Device (APSD; Frick & Hare, 2001), consists of 20 items patterned after the PCL-R criteria, each rated on 3-point (0–2) scale by informants (e.g., parents, teachers) familiar with the target individual. Factor analyses of the APSD have revealed two (REF), or alternatively three distinctive item subsets or factors. The more extensively studied two-factor model distinguishes between *callous-unemotional* (CU) and *impulsive-conduct problem* (I/CP) features within the APSD. Although correlated, these two symptomatic components of APSD psychopathy (like the two PCL-R factors) exhibit diverging relations with external criterion variables (Frick & Dickens, 2006; Frick & Marsee, 2006). The dominant self-report inventory for psychopathy, the Psychopathic Personality Inventory (PPI, or PPI-R; Lilienfeld & Andrews, 1996; Lilienfeld & Widows, 2005), also measures psychopathy in terms of two distinctive higher order factors with contrasting external correlates – one labeled *fearless dominance*, and the other *self-centered impulsivity* (or impulsive-antisociality; Benning, Patrick, Blonigen, Hicks,

[1] The use of a lower cutoff level in this study was based on prior research supporting a lower PCL-R total score threshold for a diagnosis of psychopathy in female offenders (Bolt et al., 2004; Kennealy et al., 2007).

[2] A recent cluster analytic study by Poythress et al. (2010), utilizing a much larger sample of male offenders ($N = 691$) than in prior subtyping studies, reported evidence for three rather than two high PCL-R scoring subgroups. However, this study focused on subgrouping of participants diagnosed with DSM-IV antisocial personality disorder rather than psychopathy as defined by overall PCL-R scores.

& Iacono, 2005). Unlike the two broad factors of the PCL-R or APSD, these two PPI factors are uncorrelated. From the standpoint of the triarchic model, the PPI fearless dominance factor is purely indicative of boldness, whereas the PPI self-centered impulsivity factor indexes disinhibition (deficient impulse control) and to a lesser extent meanness (callous-aggressiveness).[3] By contrast, the CU and I/CP factors of the APSD can be viewed as preferentially indexing meanness and disinhibition, respectively.

Brain Measurement Techniques

Neuroimaging Measures

The main neuroimaging method that has been used in studies of psychopathy to date is magnetic resonance imaging (MRI). MRI measures variations in the alignment of endogenous subatomic particles within a magnetic field to index anatomic details of the brain (structural MRI) or variations in blood flow and blood oxygenation (i.e., hemodynamic, or blood level– and oxygen level–dependent [BOLD] response) associated with neuronal activity in specific brain regions (functional MRI, or fMRI). Computerized tomography (CT), a structural imaging method that measures regional density of neural tissue using X-ray beams passed through the brain, was used in some older studies of individuals identified as violent. However, studies to date that have examined anatomic differences in psychopathic individuals have used structural MRI, or in one instance (described below), the MRI-based technique of diffusion tensor imaging (DTI) – which provides information about the integrity of neural (e.g., white matter tract) connections among brain structures of interest. Besides fMRI, the other functional imaging techniques that have been used in studies of psychopathy are single photon emission computerized tomography (SPECT) and positron emission tomography (PET). SPECT and PET both rely on the injection of radioactive tracer isotopes into the blood in small amounts; particles emitted by the isotope from brain regions of interest (photons in the case of SPECT, positrons in the case of PET) can be used to index either neuronal activity or neurotransmitter function in those regions.

Electrocortical Measures

The most commonly used electrocortical measurement technique in human research is electroencephalography (EEG), which measures voltage oscillations over the cortical surface through sensors attached to differing sites on the scalp. Older studies

[3] The PPI contains eight subscales, seven of which are represented in the two-factor model. The subscale not strongly associated with either factor, Coldheartedness, can be viewed as indexing meanness (in reverse).

focusing on psychopathy (and, relatedly, on antisociality and violence) assessed for differences in EEG activity at rest (i.e., while sitting quietly, with eyes open or closed) – typically quantified as relative amount of oscillatory activity within differing frequency bands (e.g., delta, theta, or alpha) during the period of rest. However, more recent studies evaluating responses of psychopathic individuals to discrete stimuli of particular types or in relation to behavioral responses have operationalized cortical reactivity in terms of event-related potential (ERP) response. The current review focuses on more recent studies of this type.

ERP response reflects average changes in voltage at scalp recording sites across time (e.g., millisecond by millisecond) following the presentation of a stimulus or the emission of a response, relative to a pre-stimulus baseline. By averaging EEG signal activity over multiple trials, positive or negative deflections in activity that occur systematically in relation to the event of interest are revealed, as trial-by-trial fluctuations unrelated to the event of interest drop out. The ERP response is commonly quantified in terms of "components," that is, positive- or negative-polarity peaks evident in the average signal waveform within particular windows of time following the event of interest. Positive-going and negative-going components are designated "P" and "N," respectively, and are numbered to reflect the approximate latency of their peak (e.g., P300, N400) or relative point of occurrence across time (e.g., P1, N1, P2). Earlier ERP components are presumed to reflect more elemental, "automatic" processes related to registration or detection of an event, whereas later components are presumed to reflect more elaborative or "controlled" processing of events. Two ERP response components of particular interest in studies of psychopathy and related phenomena, discussed further below, are the P3 (or P300) response and the error-related negativity (ERN) response.

It is important to recognize that these alternative measurement techniques provide contrasting types of information that allow for differing inferences about brain function. Structural MRI and DTI provide information about the size, shape, and relative anatomic location of particular brain structures and the neural pathways that connect them. However, data of this type are not directly informative about brain processes that might be dysfunctional in individuals with psychopathy. For example, the finding of an average reduction in volume of the subcortical amygdala cannot be taken as evidence for deficient fear or affect-driven attention in psychopathy; at best, it can only be viewed as *consistent with* such possibilities (i.e., given evidence from other work pointing to a role for the amygdala in fear reactivity and attention-allocation in emotional contexts), with other interpretations needing to be considered as well.

To permit more direct inferences about brain processing differences, measures of online activation during relevant task procedures are needed. For research of this type, functional MRI is advantageous because it offers fine-grained spatial resolution (in the order of 2–3 mm), permitting signal activity to be precisely localized within specific regions of the brain. However, the temporal resolution of fRMI is limited by the gradual nature of the hemodynamic (BOLD) response. By contrast, EEG (including ERP) measurement provides fine-grained resolution in the temporal

domain and also in the spectral (frequency) domain, but the spatial resolution and regional specificity of EEG is limited in comparison to fMRI (i.e., because brain activity is recorded only from the surface of the scalp). However, the spatial resolution of EEG can be improved through multi-electrode, dense-array recording, which provides for more precise estimation of the underlying sources of surface-recorded signals. Beyond this, the resolution of EEG can be further improved by referencing EEG data to structural or functional neuroimaging data collected from the same participant, either concurrently or in separate test sessions. In conjunction with continuous measurement of activity along dimensions of time and frequency, this approach provides for fine-grained localization of underlying sources of brain activity (with high temporal resolution) because EEG source models can be constrained to accommodate specific anatomic locations or regions of activation as defined by MRI. However, to date, approaches of this type that provide for stronger inferences about underlying sources of EEG or ERP activity have not been used in studies of psychopathy.

Neuroimaging Studies of Psychopathy

Structural Imaging Studies

Structural MRI studies have reported evidence for neuroanatomic abnormalities in differing brain regions in individuals high as compared to low in in psychopathy as defined by the PCL-R, including reduced volume of gray matter in frontal and temporal regions of cortex (Müller *et al.*, 2008; Yang *et al.*, 2005); reduced volume bilaterally of the amygdala (Yang, Raine, Narr, Colletti, & Toga, 2009); reduced volume bilaterally of the posterior hippocampus (particularly in relation to scores on PCL-R Factor 1; Laakso *et al.*, 2001), left–right hippocampal volume asymmetry (Raine *et al.*, 2004), or abnormalities in hippocampal shape (Boccardi *et al.*, 2010); increased volume of white matter in the corpus callosum (Raine *et al.*, 2003); and increased volume of the striatum (with increased volume of the lenticular nucleus in particular predicted by overall PCL-R scores, and increases in caudate body and caudate head volumes exhibiting preferential relations, respectively, with scores on PCL-R Factor 1 and scores on the impulsive-antisocial ["lifestyle"] facet of PCL-R Factor 2; Glenn, Raine, Yaralian, & Yang, 2010). In addition, a recent study by Craig *et al.* (2009) that used the MRI-based method of diffusion tensor imaging reported evidence for reduced structural integrity of the uncinate fasciculus, a neural pathway connecting the ortbitofrontal cortex and the amygdala, in a sample of nine forensic patients scoring high ($\geq$25) on the PCL-R compared with a nonforensic control group. Notably, the one study to date that tested specifically for differences in the anterior cingulate and its dorsal and ventral subregions found no associations with PCL-R psychopathy, either in comparisons of high- versus low-PCL-R total score groups or in correlational analyses utilizing continuous PCL-R total and factor scores.

Taken together, these studies implicate structural abnormalities in various frontal and temporal regions of the brain – including cortical and subcortical grey matter structures and white-matter pathways connecting certain structures – as potentially relevant to psychopathy.

Functional Imaging Studies

As noted in the section on neuroimaging procedures, functional imaging studies provide detailed information about activity in specific brain regions within the context of a particular processing task. Table 3.1 lists published functional imaging studies to date that have examined brain activation differences in relation to PCL-R defined psychopathy in adult participants, as well a smaller number of studies that have examined differences associated with psychopathy in adult or child samples as defined by scores on the PPI and the APSD, respectively.

Of the nine functional imaging studies to date that have focused on PCL-R defined psychopathy, all but one (Kiehl, Smith, Mendrick, Forster, Hare, & Liddle, 2004, which apparently utilized the same participant sample as Kiehl *et al.*, 2001) have examined brain reactivity in experimental procedures involving emotional processing of differing types, including viewing of affective and neutral text, face, or other pictorial stimuli under conditions of simple presentation or performance of a concurrent task (e.g., discrimination of text or face stimuli for some nonaffective parameter such as word/nonword or gender; encoding/rehearsal/retrieval of word stimuli); impact of a preceding mood manipulation on subsequent cognitive/reaction time performance; processing of CS+ and CS− stimuli in an aversive conditioning context; and processing of moral dilemmas entailing more or less emotion provocation, and anticipation of punishment to oneself or viewing delivery of punishment to an opponent in a competitive interaction context.

Although no two of these PCL-R studies have used the same experimental procedure, some have used similar procedures. Both Intrator *et al.* (1997) and Kiehl *et al.* (2001) examined brain reactivity to emotional versus neutral words, within discrimination (word vs. nonword) and memory (encoding, rehearsal, and/or recall) contexts, respectively. The first of these studies reported *increased* activation bilaterally for emotional versus neutral words in high (as compared to low) PCL-R participants in frontal-temporal cortex and "contiguous" subcortical regions (regions of interest in this study, which used SPECT, consisted of eight crude, lobe-based subdivisions of cortex, together with eight adjacent subcortical regions), whereas the second reported *decreased* activation in multiple a priori–defined limbic-subcortical regions, along with (in post hoc analyses) increased activation in right and left inferior lateral-frontal regions of cortex. Both Schneider, Habel, Kessler, Posse, Grodd, and Muller-Gartner (2000) and Birbaumer *et al.* (2005) examined brain reactivity to CS+ and CS− stimuli during sequential phases of a differential aversive condition procedure, using foul odor and painful tactile-pressure stimuli as USs, respectively. The first of these studies reported *increased* activation in amygdala and dorsolateral

Table 3.1 Functional Neuroimaging Studies of PCL-R/PCL:SV, PPI, or APSD Diagnosed Psychopathy

Authors (Year)	*Imaging Method*	*Psychopathy Sample*	*Control Sample(s)*	*Major Findings for High versus Low Psychopathy*
PCL-R/PCL:SV Studies				
Intrator *et al.* (1997)	SPECT	Male substance abuse treatment inpatients, PCL-$R_{tot} \geq 25$ ($M = 29.9$), $n = 8$	(1) Male substance abuse treatment inpatients age-matched to psychopathy sample (M for combined samples = 36.8), PCL-$R_{tot} < 17$ ($M = 9.1$), $n = 9$; (2) "Normal control group," M age = 31.1, $n = 9$	*Increased* activation for emotional versus neutral words during discrimination from pseudowords in 4 of 16 ROIs examined: R/L frontal-temporal cortex and contiguous R/L subcortical regions
Schneider *et al.* (2000)	fMRI	Males consisting of offenders from forensic treatment facilities or general psychiatric inpatients, diagnosed with antisocial personality disorder (but no other DSM-IV disorder except substance abuse), M age = 31.5, PCL-$R_{tot} \geq 24$ ($M = 28.6$), $n = 12$	Male "healthy controls" recruited from the community, M age = 27.6	*Increased* activation for CS+ versus CS− during latter part of acquisition phase of differential aversive conditioning task in 2 of 13 ROIs: bilateral amygdala, bilateral dorsolateral prefrontal cortex

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Table 3.1 (*Continued*)

Authors (Year)	*Imaging Method*	*Psychopathy Sample*	*Control Sample(s)*	*Major Findings for High versus Low Psychopathy*
Kiehl *et al.* (2001)	fMRI	Male prisoners, M age = 33.9, PCL-$R_{tot} \geq 28$ ($M = 32.8$), $n = 8$	(1) Male prisoners, M age = 37.1, PCL-$R_{tot} \leq 23$ ($M = 16.6$), $n = 8$; (2) Male "healthy control participants," M age = 31.9, $n = 8$	(1) *Decreased* activation for emotional versus neutral words during encoding/rehearsal/ recall in 10 of 10 limbic subcortical ROIs (frontal: rostral and caudal anterior cingulate, L inferior frontal gyrus, posterior cingulate gyrus; temporal: R/L amygdala/ hippocampus, L parahippocampus, R/L anterior superior temporal gyrus, ventral striatum); (2) *increased* activation in R/L inferior lateral frontal cortex evident in post hoc tests
Müller *et al.* (2003)	fMRI	Male offenders from a forensic psychiatric facility, M age = 33.0, PCL-$R_{tot} \geq 34$ (M = 36.8), $n = 6$	Male "healthy volunteers" without any neuropsychiatric history, M age = 28.0, $n = 6$	(1) *Decreased* activation for unpleasant versus neutral picture stimuli in some regions as determined by whole-brain analysis (frontal—L paracentral lobule, L/R cingulate gyrus, R subgenual cingulate; temporal—L hippocampal gyrus, R medial temporal gyrus; occipital—L cingulate gyrus, R fusiform gyrus), along with (2) *increased* activation in others (frontal—L precentral, R inferior frontal, R medial frontal, and R cingulate gyri; temporal—L/R medial and L superior temporal gyri, R amygdala, R insula; parietal—L precuneus, R inferior parietal lobe; occipital—L/R occipital cortex); (3) *decreased* activation for pleasant versus neutral picture stimuli in one of the regions that showed a decrease for unpleasant versus neutral (R medial temporal gyrus) and also in some regions different from these

				(frontal—R medial frontal gyrus; occipital— L/R occipital cortex), along with (4) *increased* activation in some of the regions that showed increases for unpleasant versus neutral (frontal—L precentral; temporal—L medial temporal gyrus) and also in some regions different from these (frontal—R precentral and left inferior frontal gyri; temporal—L superior and R medial temporal gyri; parietal—R supermarginal and L angular gyri; occipital—L/R fusiform gyrus; L/R cerebellum)
Kiehl *et al.* (2004)	fMRI	Same as Kiehl *et al.* (2001)	Male "healthy control participants," M age = 27.9, $n = 8$	Lack of increased activation for abstract words (relative to ITI baseline) during discrimination from pseudowords in 3 of 19 ROIs: R superior temporal gyrus and contiguous cortex, left fusiform gyrus)
Birbaumer *et al.* (2005)	fMRI	Male offenders awaiting trial or on parole, M age = 35.3, PCL-$R_{Factor1} \geq 10.5$ ($M = 11.6$; PCL- R_{tot} $M = 24.9$), $n = 10$	Male "healthy control subjects" matched for age ($M = 31.5$) and education, $n = 10$	*Decreased* activation for CS+ versus CS− during acquisition phase of differential aversive conditioning task in 5 of 13 ROIs: secondary somatosensory cortex, left amygdala, right insula, rostral anterior cingulate cortex, ventromedial orbitofrontal cortex
Deeley *et al.* (2006)	fMRI	Male offenders recruited through forensic mental health services, M age = 36, PCL-R_{tot} ≥ 25 ($M = 29.3$), $n = 6$	Male "healthy" individuals from the general population, M age = 27, $n = 9$	*Decreased* activation for fearful versus neutral face stimuli, when discriminating faces for gender, in selected regions (R cerebellum, R fusiform gyrus, postcentral gyrus) as determined by whole-brain analysis; *decreased* activation for happy versus neutral face stimuli in one of these same regions (R fusiform gyrus) and two distinct others (R lingual gyrus, middle occipital gyrus)

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Table 3.1 (*Continued*)

Authors (Year)	*Imaging Method*	*Psychopathy Sample*	*Control Sample(s)*	*Major Findings for High versus Low Psychopathy*
Müller *et al.* (2008)	fMRI	Male offenders from a forensic psychiatric facility, M age = 33.1, PCL-$R_{tot} \geq 28$ ($M = 30.5$), $n = 10$	Male "healthy volunteers" without any neuropsychiatric history, M age = 32.2, $n = 12$	Lack of moderating impact of a prior negative emotion induction (viewing of unpleasant pictures) on performance or activation in distinct brain regions (R medial and L inferior frontal gyri, R superior temporal gyrus) within a subsequent reaction time task
Glenn *et al.* (2009a, b)	fMRI	Community participants (age and gender unspecified) with PCL-R_{tot} scores ranging from 7 to 32; $N = 17$	Lower versus higher continuous PCL-R scores (correlational analyses)	Higher PCL-R scorers (versus lower scorers) showed *decreased* activation in one of five a priori ROIs (L amygdala) during moral decision-making about emotional dilemmas, along with *increased* activation in one other post hoc region (R dorsolateral prefrontal cortex); those highest on PCL-R Factor 1 also showing reduced activity in other 'moral circuit' regions (medial prefrontal cortex, posterior cingulate cortex, R angular gyrus)
Veit *et al.* (2010)	fMRI	Male offenders from two forensic psychiatric facilities with PCL:SV_{tot} scores ranging from 9 to 21 ($M = 16.1$); $N = 10$	None: Results for psychopathy group were compared impressionistically, rather than quantitatively, with results from a prior published study of "healthy volunteers" (Lotze *et al.*, 2007)	Lack of expected bilateral activation in pain processing regions (L/R anterior cingulate cortex, amygdala, hypothalamus, and insula), as determined by whole brain analysis, during anticipation of physical punishment to self in a competitive reaction time task; higher PCL:SV*factor2* scorers (versus lower scorers) showed increased activation in dorsal and ventral medial prefrontal cortex when viewing delivery of punishment to their opponent

PPI Studies

Gordon *et al.* (2004)	fMRI	Male college students, subdivided (median split) into high versus low scorers on each factor of the PPI-187, *M* age = 23.5, *N* = 20	Lower versus higher PPI factor scores (median split on each factor)	High PPI-1 (fearless dominance) scorers, relative to low scorers, showed *decreased* activation during affective discrimination of fearful, angry, sad, and joyful faces in three of five ROIs (right amygdala, medial prefrontal cortex, right inferior temporal cortex) along with *increased* activation in the other two ROIs (visual cortex, right dorsolateral prefrontal cortex); high PPI-2 (self-centered impulsivity) scorers, relative to low scorers, showed *increased* activation in one of five ROIs (right amygdala)
Rilling *et al.* (2007, 2010)	fMRI	College students, continuous PPI-56 total and factor scores, *M* age = 21.2, *N* = 30 (15 female)	Lower versus higher PPI total and factor scores (correlational analyses)	Males with higher PPI scores (versus males with lower scores), in particular those highest on PPI-1, showed *decreased* activation in one of an unspecified number of ROIs (rostral anterior cingulate cortex) for outcomes of a Prisoner's Dilemma game in which their cooperation was not reciprocated
Harenski *et al.* (2009)	fMRI	Adult females, continuous PPI-56 total and Coldheartedness scale scores; *N* = 10	Lower versus higher continuous PPI total and Coldheartedness scores (correlational analyses)	Higher PPI scorers (versus lower scorers) showed *decreased* activation in one of seven a priori ROIs (medial prefrontal cortex) during simple viewing of unpleasant pictures depicting moral violations, and *increased* activation in two of seven ROIs (superior prefrontal cortex, ventrolateral prefrontal cortex) during efforts to suppress reactions to unpleasant pictures as a whole; participants higher (versus lower) on PPI Coldheartedness showed reduced activation in one ROI (L amygdala; for R amygdala, $p = .086$) during simple viewing of unpleasant pictures depicting moral violations

(*Continued*)

Table 3.1 (*Continued*)

Authors (Year)	*Imaging Method*	*Psychopathy Sample*	*Control Sample(s)*	*Major Findings for High versus Low Psychopathy*
Buckholtz *et al.* (2010)	PET, fMRI	Adults, continuous PPI-187 factor scores; $N = 30$ (15 female)	Lower versus higher continuous PPI scores (correlational analyses)	Higher PPI-2 (self-centered impulsivity) scorers, relative to lower scorers, showed *increased* dopamine release following amphetamine administration, and *increased* activation during anticipation of monetary reward, in major ROIs targeted for analysis (R and L nucleus accumbens); Higher PPI-2 scorers also showed *increased* dopamine response to amphetamine in one other post hoc region of the striatum (ventrolateral putamen).
APSD Studies				
Marsh *et al.* (2008)	fMRI	Children/adolescents (M age = 14.5) diagnosed with conduct disorder or oppositional defiant disorder, with $APSD_{tot} \geq 20$ ($M = 29$) and $PCL:YV_{tot} \geq 20$ ($M = 24$), $n = 12$ (5 female)	(1) Children/adolescents (M age = 13.8) *without* conduct disorder or oppositional defiant disorder, but diagnosed with attention deficit hyperactivity disorder (M $APSD_{tot} = 11$), $n = 12$ (4 female); (2) Male and female "healthy comparison subjects" (M age = 14.2) *without* conduct disorder, oppositional defiant disorder, or attention deficit hyperactivity disorder (M $APSD_{tot} = 7$), $n = 12$ (6 female)	Relative to control groups of two types ("healthy" and ADHD), high callous-unemotional participants showed (1) d*ecreased* activation for fearful versus neutral face stimuli, when discriminating faces for gender, in R amygdala (with effects for other temporal/parietal regions unclear, because follow-up group contrasts were done for R amygdala region only); along with (2) *decreased* covariation ('functional connectivity') between activation in the R amygdala for fearful versus neutral faces and activation in certain other regions (R ventromedial prefrontal cortex, L posterior cingulate gyrus, L anterior insula/claustrum, L/R inferior temporal gyrus/fusiform gyrus); and (3) *increased* covariation between amygdala activation and activation in four additional regions (R cingulate gyrus, L/R middle frontal gyrus, thalamus)

Finger *et al.* (2008)	fMRI	Children/adolescents (M age = 13.8) with $APSD_{tot} \geq 20$ ($M = 29$) and $PCL{:}YV_{tot} \geq 20$ ($M = 24$); $n = 14$ (5 female)	(1) Children/adolescents (M age = 13.4) *without* conduct disorder or oppositional defiant disorder, but diagnosed with attention deficit hyperactivity disorder (M $APSD_{tot} = 9$), $n = 14$ (4 female); (2) Male and female "healthy volunteers" (M age = 13.6) *without* conduct disorder, oppositional defiant disorder, or attention deficit hyperactivity disorder (M $APSD_{tot} = 7$), $n = 14$ (5 female)	*Increased* activation within a probabilistic reversal-learning task for punished reversal errors versus rewarded correct responses in selected regions as determined by whole-brain analysis (R/L medial frontal gyrus, R caudate); within the high psychopathy group, $APSD_{callous\text{-}unemotional}$ scores uniquely predicted degree of increased activation for punished errors versus rewarded responses
Jones *et al.* (2009)	fMRI	Boys (ages 10–12 years; $M = 11.9$) from a large community sample, with $APSD_{callous\text{-}unemotional}$ and $SDQ_{conduct\text{-}problem}$ ratings $\geq 10^{th}$ percentile; $n = 17$	Boys (ages 10–12 years; $M = 11.3$) from the same large community sample, scoring within ± 1 *SD* of the sample M for $APSD_{callous\text{-}unemotional}$ and $SDQ_{conduct\text{-}problem}$ ratings; $n = 17$	*Decreased* activation for fearful versus neutral face stimuli, when discriminating faces for gender, in two of two a priori ROIs (R amygdala, anterior cingulate cortex)

(*Continued*)

Table 3.1 (*Continued*)

Authors (Year)	*Imaging Method*	*Psychopathy Sample*	*Control Sample(s)*	*Major Findings for High versus Low Psychopathy*
Finger *et al.* (2011)	fMRI	Children/adolescents (M age = 14.1) with $APSD_{tot} \geq 20$ ($M = 28.9$) and $PCL:YV_{tot} \geq 20$ ($M = 24.7$); $n = 15$ (6 female)	"Healthy volunteer" children/adolescents (M age = 13.2) *without* conduct disorder, oppositional defiant disorder, or attention deficit hyperactivity disorder ($M\ APSD_{tot} = 6.9$), $n = 15$ (6 female)	*Decreased* activation within a passive avoidance (reward/punishment) learning task to earlier versus later reinforced outcomes in selected regions as determined by whole-brain analysis (R orbitofrontal cortex, caudate), along with *decreased* activation to rewarded correct response presentations in one of these same regions (R orbitofrontal cortex); in addition, high psychopathy participants showed decreased activation in certain other brain regions (including amygdala, caudate, insula, and 'attention-related' regions of prefrontal and parietal cortex) across the task as a whole

Note: APSD = Antisocial Process Screening Device (Frick and Hare, 2001); PCL:SV = Psychopathy Checklist: Screening Version (Forth *et al.*, 2003); PCL:YV = Psychopathy Checklist: Youth Version (Forth *et al.*, 2003); PPI-187 = original 187-item version of the Psychopathic Personality Inventory (PPI; Lilienfeld and Andrews, 1987); PPI-56 = abbreviated, 56-item version of the PPI (Lee and Salekin, 2010); and SDQ = Strengths and Difficulties Questionnaire (Goodman, 1997).

prefrontal cortex regions to the CS+ versus the CS− for psychopathic participants during the latter part of acquisition, whereas the second reported *decreased* differential activation for high PCL-R participants in left amygdala and ventromedial prefrontal cortex regions, as well as in right insula, rostral anterior cingulate, and secondary somatosensory cortex. Two other studies by Müller *et al.* (2003, 2008) utilized emotional and neutral picture stimuli, but in quite different ways. Müller *et al.* (2003) examined reactivity to pictures as primary stimuli and reported a complex pattern of differences for psychopathic as compared to nonpsychopathic participants (i.e., decreased activation in some cortical and subcortical brain regions, but increased activation in others, for both pleasant and unpleasant pictures relative to neutral – with specific regions of decrease and increase for unpleasant pictures overlapping only partly with regions of decrease or increase for pleasant pictures). Müller *et al.* (2008) used unpleasant picture viewing as a mood induction and found that high-PCL-R offenders, in contrast with low-PCL-R controls, exhibited no impact of this induction on responding in a subsequent "cognitive" reaction time task, either behaviorally or in terms of activity in distinct brain regions (R medial and L inferior frontal gyri, R superior temporal gyrus) during this task. Commonalities in findings across these six emotion-processing studies include increased activation in regions of frontal/prefrontal cortex (Intrator *et al.*, 1997; Schneider *et al.*, 2000; Kiehl *et al.*, 2001; Müller *et al.*, 2003); increased activation in temporal-subcortical regions, including the amygdala in some studies (Intrator *et al.*, 1997; Müller *et al.*, 2003; Schneider *et al.*, 2000) along with decreased amygdala activation in others (Kiehl *et al.*, 2001; Birbaumer *et al.*, 2005); decreased activation in anterior cingulate (Kiehl *et al.*, 2001; Müller *et al.*, 2003; Birbaumer *et al.*, 2005) and posterior cingulate, hippocampal, and frontal gyrus regions (Kiehl *et al.*, 2001; Müller *et al.*, 2003); and decreased activation in inferior frontal and superior temporal gyri (Kiehl *et al.*, 2001; Müller *et al.*, 2008).

Findings in common between the foregoing six studies and the other three fMRI studies that have examined emotion processing in relation to PCL-R defined psychopathy are (1) increased activation in regions of prefrontal cortex (dorsolateral region, evaluated post hoc – Glenn *et al.*, 2010; and dorsal and ventral medial, selectively in relation to higher PCL-R Factor 2 – Veit, Lotze, Sewing, Missenhardt, Gaber, & Birbaumer, 2010); and (2) decreased activation in the anterior cingulate (Veit *et al.*, 2010), posterior cingulate (Glenn, Raine, & Schug, 2009), amygdala (Glenn, Raine, & Schug, 2009; Veit *et al.*, 2010), and right fusiform gyrus (Deeley *et al.*, 2006, along with Müller *et al.*, 2003). One other result in common between two of the latter four studies, which included conditions entailing receipt of physical punishment (Birbaumer *et al.*, 2005; Veit *et al.*, 2010), is decreased activation of the insula – a region implicated in pain perception. However, some salient opposing findings are evident across some of these emotion-processing studies, including (1) *decreased* activation of frontal/prefrontal cortex in some studies (i.e., ventromedial orbitofrontal cortex in Birbaumer *et al.*, 2005; postcentral gyrus in Deeley *et al.*, 2006; right medial and left inferior frontal gyri in Müller, 2008; and medial frontal cortex, selectively in relation to higher PCL-R Factor 1, in Glenn,

Raine, & Schug, 2009) versus *increased* frontal/prefrontal activation in others (i.e., bilateral frontal/temporal cortex in Intrator *et al.*, 1997; bilateral inferior lateral frontal cortex in Kiehl *et al.*, 2001; bilateral precentral, bilateral inferior frontal, and right medial frontal gyri in Müller *et al.*, 2003; right dorsolateral prefrontal cortex in Glenn, Raine, Schug, Young, & Hauser, 2009; and dorsal and ventral medial prefrontal cortex, selectively in relation to PCL-R Factor 2, in Veit *et al.*, 2010); and (2) *decreased* activation of the amygdala specifically in some studies (Kiehl *et al.*, 2001; Birbaumer *et al.*, 2005; Glenn, Raine, & Schug, 2009; Veit *et al.*, 2010) versus *increased* amygdala activation in others (Müller *et al.*, 2003; Schneider *et al.*, 2000).

Four other published functional imaging studies have investigated psychopathy in college or community adults using the self-report based PPI. One of these (Harenski, Kim, & Hamann, 2009) focused analyses on continuous scores for the PPI as a whole and one of its subscales (Coldheartedness). The other three focused on relations of the PPI's two distinctive factors (fearless dominance, and self-centered impulsivity) with brain reactivity during testing. All four examined reactivity in affective processing or provocation tasks of one type or another (i.e., affective picture viewing, affective face discrimination, anticipation of monetary reward, and Prisoner's Dilemma), with one study (Buckholtz *et al.*, 2010) also including a separate pharmacologic challenge procedure (administration of amphetamine to stimulate release of dopamine in the brain). Two of the three studies that examined PPI factor scores, one using an affective face discrimination task (Gordon, Baird, & End, 2004) and the other a Prisoner's Dilemma paradigm (Rilling *et al.*, 2007), found relations specifically between higher scores on PPI-1 (fearless dominance) and decreased brain activation in designated regions of interest. However, no overlap was evident between the three regions that showed effects of this type in one study (right amygdala, medial prefrontal cortex, and right inferior temporal cortex; Gordon *et al.*, 2004) and the single region that exhibited a decrease in the other (rostral anterior cingulate cortex; Rilling *et al.*, 2007). In addition, the first of these studies reported *increased* activation in two other brain regions for participants high in PPI-1 (visual cortex, right dorsolateral prefrontal cortex), along with – in direct contrast to results for PPI-1 – *increased* activation in the right amygdala for participants classified as high versus low on PPI-2 (self-centered impulsivity). The other study that presented results for PPI factor scores (Buckholtz *et al.*, 2010) focused primarily on reactivity in the nucleus accumbens and found effects exclusively for PPI-2 – with higher scorers showing increased dopamine release in the accumbens both following amphetamine administration and during anticipation of monetary reward.

The final study in this set reported results for PPI total scores and Coldheartedness scale scores (Harenski *et al.*, 2009). This study examined brain reactivity to presentations of unpleasant pictures, some depicting moral dilemmas and others not, under conditions of simple viewing and instructed emotion regulation (i.e., suppress reactivity to pictures when they occur). During simple viewing of unpleasant moral-violation scenes, participants with higher overall PPI scores showed *decreased* activation in one brain region of interest (medial prefrontal cortex) not identified

in other PPI studies, but consistent with results for some PCL-R studies (Birbaumer *et al.*, 2005; Müller, 2008; Glenn, Raine, & Schug, 2009). For simple viewing of scenes of this type, participants high specifically in PPI Coldheartedness showed decreased activation for one brain region (amygdala) that showed a decrease in one other PPI study (Gordon *et al.*, 2004) as well as in four out of eight PCL-R/emotion-processing studies (Kiehl *et al.*, 2001; Birbaumer *et al.*, 2005; Glenn, Raine, & Schug, 2009; Veit *et al.*, 2010). In the instructed regulation condition of this study, participants with higher overall PPI scores showed *increased* activation in specific subdivisions of prefrontal cortex (superior, ventrolateral) – again consistent with results from a number of PCL-R/emotion-processing studies (Intrator *et al.*, 1997; Kiehl *et al.*, 2001; Müller *et al.*, 2003; and right dorsolateral prefrontal cortex in Glenn, Raine, Schug,Young, *et al.*, 2009; Veit *et al.*, 2010).

A final set of four very recent studies has focused on psychopathy in children or adolescents as indexed by the APSD (Frick & Hare, 2001). Two of these used affective-face processing procedures, and two examined brain reactivity in reward/punishment-learning paradigms. The first of the two face-processing studies (Marsh *et al.*, 2008) used a dual diagnostic criterion for identifying participants as psychopathic (i.e., to be classified as psychopathic, participants had to exceed designated cut-offs on both the APSD and the Youth Version of the PCL-R [PCL:YV; Forth, Kosson, & Hare, 2003]). Controls in this study included a group of young participants who met criteria for a diagnosis of attention deficit hyperactivity disorder (ADHD) but were rated low on APSD callous-unemotional symptoms, and a nondisorder ("healthy comparison") group. Participants high in psychopathy (i.e., those exhibiting APSD callous-emotional features along with conduct disorder symptoms) showed decreased right amygdala activation for fearful versus neutral faces, along with decreased covariation of activity between the right amygdala and interconnected structures including the ventromedial prefrontal cortex, anterior and posterior cingulate gyrus, insula, and inferior temporal/fusiform gyrus. Using a very similar task procedure, but younger participants, a somewhat different selection criteria for psychopathy (i.e., ASPD ratings in conjunction with ratings on the Strengths and Difficulties Questionnaire, a measure of conduct problems), and a single normative control group, Jones, Laurens, Herba, Barker, and Viding (2009) replicated the finding of decreased amygdala activation during processing of fearful versus neutral faces and also reported a concomitant reduction in activity of the anterior cingulate cortex. The latter of these findings coincides with results from a number of PCL-R/imaging studies (Kiehl *et al.*, 2001; Müller *et al.*, 2003; Birbaumer *et al.*, 2005; Veit *et al.*, 2010) and one of four PPI/imaging studies (Rilling *et al.*, 2007).

The other two studies that focused on psychopathy in young participants used the same dual diagnostic criterion (ASPD + PCL:YV) employed by Marsh *et al.* (2008), but examined brain reactivity in reward/punishment learning tasks. The first (Finger *et al.*, 2008) used a probabilistic reversal-learning task and reported increased activation in relation to punished reversal errors in bilateral medial frontal gyrus and right caudate regions in high-psychopathy participants as compared to ADHD and healthy comparison groups. Within the high-psychopathy group, scores

on the callous-unemotional factor of the APSD selectively predicted degree of enhanced activation for punished errors. More recently, Finger *et al.* (2011) compared brain reactivity during a passive avoidance learning task in psychopathic (APSD + PCL:YV) youth and health controls (no ADHD comparison group was included). Relative to controls, psychopathic youth showed decreased reactivity in right orbitofrontal cortex and caudate regions to earlier (as compared to later) occurrences of reinforced outcomes in the task, along with decreased reactivity in orbitofrontal cortex for correct rewarded response trials overall. A main effect of group was also evident for particular brain regions across the task as a whole, reflecting generally decreased activation for the psychopathic group in s including the amygdala, caudate, and insula, and regions characterized by the authors as components of an "attention network" (i.e., prefrontal and parietal cortex).

Summary and Critique of Existing Structural and Functional Imaging Findings

Some points of intersection are evident in findings from the above-reviewed structural and functional neuroimaging studies. Studies of both types point to psychopathy-related effects in some distinct brain regions, in particular, regions of frontal/prefrontal and temporal cortex and temporal-subcortical structures (amygdala, hippocampus). However, even in these instances, salient discrepancies are also evident. For example, whereas volume *reductions* in frontal/prefrontal regions of cortex are typically reported for high-psychopathy individuals, functional imaging studies reporting activation differences in these regions have more typically reported *increases* in activity within these regions rather than decreases. Although post hoc explanations can be formulated to account for this pattern of results (e.g., brain structures that appear abnormal in size or morphology need to "work harder" in relevant functional contexts), such explanations are completely speculative at this point. Moreover, for certain brain regions that have been identified as structurally anomalous in psychopathy (e.g., amygdala and hippocampus), increased activations have been reported in some functional imaging studies whereas decreased activations have been reported in others. In addition, some brain regions identified as abnormal in structural imaging studies (e.g., corpus collosum) have not emerged as hypo- or hyper-reactive in structural imaging studies, and other regions not identified as abnormal in structural studies (e.g., anterior cingulate) have exhibited consistent psychopathy-related differences within functional studies.

With regard to comparing findings across studies of either type (structural or functional), a number of significant difficulties exist. One is that sample sizes in these studies are generally very small – typically, below 20 – owing to the costliness of neuroimaging methodology and complexities of implementation, with clinically psychopathic samples in particular. This poses difficulties for replicability of findings. In a recent critique of the published literature on brain abnormalities in mental disorder conditions more broadly, Ioannidis (2011) argued that various factors

contribute to inflated reports of significant findings in small *n* structural imaging studies – including editorial bias against publication of null findings, investigator bias toward reporting of positive findings and omission of nonsignificant findings, and bias toward use of analytic approaches or criteria that yield positive findings in particular datasets over others than do not. In a similar vein, Vul, Harris, Winkielman, and Pashler (2009) have questioned the replicability of correlational findings for individual difference measures with brain activation variables in small *n* functional imaging studies.

In neuroimaging research on psychopathy in particular, additional methodological factors create difficulties for replicating (or even comparing) findings across studies. One is that structural and functional studies have relied on many alternative approaches to diagnosing psychopathy – in some cases different inventories, and in others differing scores within inventory (e.g., total scores versus factor or subscale scores), differing cutoffs on whatever score variable is used, or continuous score correlations versus full-sample (e.g., median split) groupings versus extreme-score groupings. Another issue is that the nature of populations from which psychopathic participants or individuals varying in levels of psychopathy are recruited differs greatly from study to study. Some studies focus on incarcerated offenders or forensic psychiatric patients, others on general psychiatric patients or individuals enrolled in substance abuse treatment programs, others on college students or adults from the community, and others on children or adolescents referred for conduct problems or sampled from the general population. Given differences in procedures for diagnosing psychopathy and populations recruited from, it is clear that the severity of psychopathic tendencies in individuals included in analyses differs greatly across studies. For example, offenders from a prison or psychiatric facility who score in the upper part of the effective range for the PCL-R are likely to differ dramatically from individuals identified as scoring in the upper range of PPI scores within a small, unselected college sample. Individuals identified as psychopathic within prison or other clinical populations are also likely to possess many more confounding characteristics (e.g., problems with severe alcohol or drug abuse, other comorbid psychopathology, exposure to early abuse or trauma, and/or history of significant head injury) than individuals identified as psychopathic from a college population or from the community. In addition, studies involving group comparisons have used differing types of control samples (i.e., low-psychopathy offender or clinical samples in some cases, or nonoffender/nonclinical ["healthy"] samples in others) that are not always matched on variables of potential relevance to brain reactivity.

Some additional complexities need to be considered in interpreting findings from functional neuroimaging studies. One is that the nature and psychological interpretation of brain activations are critically dependent on the nature of the processing task used and methodological factors including the characteristics of stimuli and the circumstances (including instructions) under which they are presented, the number and timing of stimulus trials, the effectiveness of comparison conditions used to evaluate the impact of experimental manipulations, and so on. In view of this, one would expect incremental designs and systematic replication to be the rule rather

than the exception in research of this kind. Instead, most studies to date have used largely dissimilar task procedures, and even studies that have employed somewhat similar procedures have differed in important respects that may have contributed to contrasting patterns of results (see, e.g., Schneider *et al.*, 2000; Birbaumer *et al.*, 2005). The one example of systematic, constructive replication (cf. Lykken, 1968) that exists in the functional neuroimaging literature on psychopathy to date is work by Jones *et al.* (2009) that partially replicated results reported previously by Marsh *et al.* (2008). Recruitment populations for the two studies differed, and procedures for identifying high-psychopathic ("callous-unemotional") participants overlapped only somewhat, but a very similar task procedure (i.e., discriminating fearful and neutral faces for gender) was used. One would hope that additional follow-up studies might be performed using this same face discrimination task to examine reactivity of individuals from differing populations assessed using alternative psychopathy inventories – in order to understand better the impact of recruitment population and psychopathy assessment method on observed results. Alongside this, one would hope that additional studies will be performed using parametric variants of this task procedure in order to clarify the psychological and behavioral significance of brain activation differences observed in relation to psychopathy.

Electrocortical Studies of Psychopathy

As noted in the introductory section on electrocortical measures under the "Brain Measurement Techniques" section of this chapter, we focus here in particular on newer studies that have examined ERP response components in relation to psychopathy. The two ERP components that have been the focus of most research to date in this area are the P3 and the error-related negativity (ERN).

Psychopathy and P3 Brain Potential Amplitude

Several studies have investigated relations between psychopathy and amplitude of the P3 (P300) event-related potential (ERP) response.[4] The P3 is the predominant positive deflection of an ERP waveform time-locked to an attended stimulus, and tends to have maximal amplitude over parietal scalp recording sites. The best-known variant of the P3 is the oddball target P3, evoked by infrequent, task-relevant events in a stimulus sequence. The term *P3b* is sometimes used for this frequency-sensitive variant, which is theorized to reflect later attentional and memory processing, as opposed to earlier sensory-perceptual processing (Polich, 2007). This variant of the

[4] The term *P3* as used here refers to a family of ERP components including the P3 response to attended target stimuli in an "oddball" task (aka "P300," or "P3b"), and the P3 response to unexpected novel events (aka "novelty P3," or "P3a").

P3 has a posterior scalp distribution; its likely neural generators include temporal and parietal cortices (Dien, Spencer, & Donchin, 2003; Polich, 2007).

Another variant of the P3 is the "novelty P3" (Courchesne, Hillyard, & Galambos, 1975) or "P3a" (Squires, Squires, & Hillyard, 1975), which occurs in response to unexpected rare nontarget stimuli in a sequence within three-stimulus or "novelty" oddball tasks. This variant has been conceptualized as a neural indicator of attentional orienting (Courchesne *et al.*, 1975; Polich 2007; Squires *et al.*, 1975). The scalp topography of the novelty P3 shifts from being maximal at posterior scalp sites to central and anterior sites as the target/novel discrimination becomes more difficult, presumably owing to increased attentional demands (Polich, 2007). Consistent with this, investigations of patients with focal lesions in frontal brain regions (Knight, 1984, 1997), data from dense-array ERP source localization studies (Dien *et al.*, 2003), and functional magnetic resonance imaging studies (Yamaski, LaBar, & McCarthy, 2002; Fichtenholtz *et al.*, 2004) point to an important direct role of anterior brain regions (i.e., prefrontal and anterior cingulate cortices) in the allocation of attention to novel stimuli (Polich, 2007).

A number of published studies have compared target P3 amplitude between groups of offenders classified as psychopathic and nonpsychopathic using conventional total score cut-offs on established measures of psychopathy to define groups. A series of studies by Kiehl and colleagues (Kiehl, Harem, Liddle, & McDonald, 1999; Kiehl, Smith, Hare, & Liddle, 2000; Kiehl, Bates, Laurens, Hare, & Liddle, 2006) investigated the relationship between total PCL-R psychopathy scores and P3 amplitude. Kiehl *et al.* (1999) reported that offenders high in PCL-R psychopathy exhibited smaller target P3 amplitude than nonpsychopaths over central and parietal recording sites during a visual oddball task. Subsequently, Kiehl and colleagues (2000) investigated psychopathy–P3 associations by utilizing a visual Go/No-Go task, and reported that psychopathic offenders showed smaller P3 amplitude to "Go" as compared to "No-Go" stimuli over anterior scalp recording sites, whereas nonpsychopathic offenders displayed the inverse pattern. More recently, Kiehl *et al.* (2006) compared target and novelty P3 in psychopathic and nonpsychopathic individuals who completed an auditory novelty oddball paradigm that consisted of infrequent target, frequent nontarget, and infrequent novel tones as stimuli. Kiehl *et al.* (2006) presented data from two separate samples, and found evidence in one sample for psychopaths exhibiting reductions in both target and novelty P3 over midline recording sites in comparison with a nonpsychopathic group. Reducted novelty P3 for psychopathic offenders was evident over lateral scalp recording sites along with midline sites.

However, other studies investigating P3 amplitude in relation to psychopathy have reported findings different from these. For example, Jutai *et al.* (1987) did not find reliable differences in P3 amplitude between psychopaths and nonpsychopaths who completed a single- and dual-task speech identification oddball paradigm. Raine & Venables (1988) compared P3 amplitude in psychopathic and nonpsychopathic offenders (defined by median split on overall psychopathy scores) who completed a continuous performance task. In contrast to later findings by Kiehl and colleagues

(1999, 2000, 2006), Raine and Venables (1988) found evidence that the psychopathic group exhibited *enhanced* P3 over parietal recording sites (only two parietal and two temporal scalp recording sites were included in the study).

Whereas associations between psychopathy and P3 amplitude in offender samples have been mixed, research on community samples has demonstrated consistent reductions in P3 amplitude in individuals exhibiting disinhibitory traits and behaviors more broadly. In one key study, Iacono, Malone, and McGue (2003) reported findings suggesting that a biologically based vulnerability factor (externalizing) might account for observed comorbidity amongst antisocial-aggressive behavior and substance use disorders. Iacono *et al.* (2003) hypothesized that P3 amplitude reduction indexes the genetically transmitted vulnerability toward a spectrum of disinhibitory traits and behaviors that includes impulsivity, aggression, antisociality, and substance use. Subsequent support for this hypothesis has been provided by studies documenting P3 amplitude reductions in relation to impulse-related problems of various types – including child and adult antisocial deviance, along with problems involving alcohol and other drugs (Justus, Finn, & Steinmetz, 2001; Patrick, Bernat, Malone, Iacono, Krueger, & McGue, 2006). Moreover, additional follow-up work has demonstrated a heritable basis to the relationship between diminished P3 amplitude and externalizing propensity operationalized as the factor in common symptoms of various disorders (Hicks, Bernat, Malone, Iacono, Patrick, Krueger, & McGue, 2007).

A number of potential moderating variables have been described to account for the discrepant findings regarding psychopathy and P3 amplitude (Kiehl *et al.*, 2006; Gao & Raine, 2009). Differences in the experimental paradigms used and task demand characteristics may in part explain the inconsistencies in these findings. In a recent meta-analysis of the literature on P3 as related to psychopathy and antisocial behavior more broaely, Gao and Raine (2009) identified a moderating effect of experimental task procedure on the association between P3 amplitude and antisocial-psychopathic tendencies defined more broadly (i.e., the Factor 2 component of psychopathy as opposed to the core Factor 1 component). In general, findings have been more reliable for oddball task paradigms than for other task procedures (i.e., including Go/No-Go, Stroop, continuous performance, and conditioning paradigms).

In addition, the aforementioned studies of psychopathy and P3 have relied extensively on overall psychopathy scores (as opposed to factor or facet scores) in analyses. As discussed previously, there is accumulating evidence that psychopathy represents a dimensional, heterogeneous construct rather than a unitary diagnostic syndrome. In relation to this, Carlson, Thái, and McLaron (2009) noted that PCL-R factor scores in the series of studies by Kiehl *et al.* (1999, 2000, 2006) were correlated more highly ($r = .83$–$.86$) than is typical in the literature ($\sim .5$; Hare, 2003), which could have constrained the ability to detect unique contributions of psychopathy dimensions in the prediction of P3. To test the hypothesis that separable dispositional traits underlying psychopathy may relate differentially to P3 amplitude, Carlson *et al.* (2009) evaluated P3 amplitude in an undergraduate sample that was administered the PPI. These authors reported a negative association between the Self-Centered Impulsivity

(Factor 2) component of the PPI and P3 over frontal recording sites, whereas the Fearless Dominance (Factor 1) component was related to faster reaction times but not to P3 amplitude. While informative regarding the potential for separable components of psychopathy being differentially related to P3, the Carlson *et al.* (2009) study utilized a predominately female, unselected undergraduate sample that would be expected to exhibit a limited range of psychopathic tendencies. By contrast, studies that examined P3 in psychopathy prior to this relied exclusively on samples of incarcerated male prisoner samples older on average than the undergraduate sample examined by Carlson *et al.* (2009).

Psychopathy and Error-Related Negativity (ERN) Response

Although amplitude of the P3 brain potential is the most widely studied ERP correlate of psychopathy, some other electrophysiological correlates of psychopathy have been reported in the literature. The most consistent pattern of findings in this regard has been for the error-related negativity (ERN), a negative-polarity ERP deflection occurring approximately 50 ms after the commission of performance errors in speeded response tasks. The ERN is hypothesized to reflect early "endogenous" error processing reflecting the neural signaling function of the anterior cingulate cortex (ACC). Munro, Dywan, Harris, McKee, Unsal, and Segalowitz (2007) tested the hypothesis that psychopathic individuals as defined by the Self-Report Psychopathy scale version III (SRP-III; Williams, Paulhus, & Hare, 2007) would show deficient ability to internally process the commission of errors and modify subsequent behavior in terms of brain reactivity and performance on two variants of a "Flanker" task, one involving discrimination of letter strings and the other discrimination of fearful versus angry faces. Task performance and ERN amplitude in the letter discrimination version of the task was comparable between psychopathic and control groups differentiated on the basis of PCL-R total scores, but the psychopathic group was less accurate and exhibited reduced ERN amplitude in the emotional face flanker task.

In a subsequent study, Brazil and colleagues (2009) reported relatively intact amplitude of the ERN in high PCL-R psychopathy forensic patients as compared to matched healthy controls (i.e., adults without prior criminal histories or psychiatric diagnoses) in a letter discrimination flanker task. However, a reduction was evident in the psychopathic group for the amplitude of the post-error positivity (Pe), a component considered similar to P3 and thought to reflect later evaluative stages of performance monitoring. The psychopathic group also demonstrated a reduced ability to signal (through a button press) when they believed an error had been committed. In subsequent work by this research group, von Borries, Brazil, Bulten, Buitelaat, Verkes, and de Brujin (2010) examined the ERN in psychopathic forensic patients during a probabilistic learning task that included feedback (either a monetary gain or loss) regarding performance accuracy on each trial. This study reported impaired ability in the psychopathic group in learning task contingencies and increased error rates along with reduced amplitude of ERN response. In addition, these

authors examined ERP reactivity to the feedback stimuli presented within this experimental task. This ERP response, known as the feedback-related negativity (FRN), is thought to reflect activity of the ACC error detection or conflict-monitoring system in relation to "exogenous" feedback concerning task performance. The authors reported that the psychopathic group exhibited intact FRN response in relation to feedback stimuli, despite showing reduced ERN response (following performance errors, but before feedback presentation) in the same task.

Taken together, this set of findings for brain potentials assessed in performance monitoring paradigms suggests some impairment in the ability of psychopathic individuals to detect mistakes and adjust behavior their behavior accordingly. However, certain parameters of a performance task may moderate the relationship between ERN amplitude and psychopathy. For example, neither Munro *et al.* (2007) nor Brazil *et al.* (2009) found evidence of reduced ERN for high-psychopathy participants in a simple letter-discrimination Flanker task, but Munro *et al.* found a reduction for participants in the same study in a face discrimination task, and von Borries *et al.* (2010) reported reduced ERN for psychopathic participants in a probabilistic learning task. Thus, task procedures involving affective discriminations or incremental learning may be more sensitive to error monitoring deficits in psychopathic individuals than simple discrimination tasks.

Another factor that may account for inconsistencies in findings across ERN studies of psychopathy is that studies of this kind to date have relied exclusively on global psychopathy scores to group participants. As previously discussed, there is increasing evidence for heterogeneity of constructs assessed by measures of psychopathy as well as among individuals identified as high in psychopathy, and existing studies have not tested for differential roles of the distinctive affective-interpersonal and impulsive-antisocial factors of psychopathy in ERN response deficits. In this regard, findings from community samples suggest that individuals broadly characterized as behaviorally disinhibited (i.e., who consistently exhibit reductions in P3 amplitude; Iacono *et al.*, 2003; Patrick *et al.*, 2006) show reduced amplitude of the ERN (for a review see Olvet and Hajcak, 2008). For example, Dikman and Allen (2000) reported that individuals low in Socialization (a construct similar to disinhibition) exhibited reduced amplitude of the ERN. Subsequently, Hall, Bernat, and Patrick (2007) found that individuals who scored high on an inventory developed to measures impulse-related problems and traits also showed smaller ERNs. Using the same participant sample as Hall *et al.* (2007), Bernat, Nelson, Steele, Gehring, and Patrick (2011) found (consistent with von Borries *et al.*, 2010) that high disinhibited-externalizing individuals exhibited intact FRN response to feedback in a simulated gambling task, but smaller P3 amplitude (operationalized as time-frequency delta activity) to the same task stimuli. Given the strong link between the construct of externalizing and the impulsive-antisocial factor of psychopathy (e.g., Patrick *et al.*, 2005), future studies examining psychopathy/ERN-FRN associations would benefit from evaluating the contributions of distinctive factors or facets of psychopathy to reductions in brain response in performance monitoring contexts.

Summary and Critique of Existing Electrocortical Findings

The foregoing review of electrocortical findings on psychopathy suggests deficits in cognitive processing in individuals with psychopathic features in certain types of tasks. However, studies of this type have focused for the most part on total scores on differing inventories of psychopathy, and not on distinctive components of psychopathy indexed by factors or facets of these inventories. However, studies with community and nonforensic clinical samples have consistently reported reductions in amplitude of P3 and ERN reactivity in individuals exhibiting high levels of impulse-related problems and traits (i.e., tendencies most related to Factor 2 of psychopathy). This pattern of results points to possible deficits in postperceptual processing of information, including automatic online detection of behavioral errors, in high-disinhibited individuals. Future studies investigating electrocortical correlates of psychopathy in emotional as well as cognitive processing tasks would benefit greatly from efforts to examine reactivity differences in relation to distinctive subcomponents of psychopathy, as these subcomponents may reflect different underlying neural deviations.

Key Assumptions in Research on Brain Function in Psychopathy That Constrain Stability, Interpretation, and Practical Utility of Findings

While there has been enormous enthusiasm over the past several years about the potential of neuroscientific methodologies to advance our understanding of human psychological disorders, the foregoing review of findings from research of this kind on psychopathy indicates that gains along these lines to date have been modest at best. The most consistent findings to date have been for ERP measures of brain response – in particular, reductions in amplitude of P3 and ERN responses within visual-processing and performance tasks. However, these amplitude reductions occur with small (.2–.3) effect sizes in large participant samples (e.g., Patrick *et al.*, 2006; Hall *et al.*, 2007) and they appear to be associated more with general proneness to impulse control problems rather the core affective-interpersonal features that are most defining of psychopathy. In addition, the neurophysiological basis and psychological meaning of these externalizing-related ERP response reductions remains unclear (Patrick & Bernat, 2009). Findings from brain imaging studies of psychopathy have produced some mildly consistent results, but much more work – conducted in a more systematic fashion than research to date, with appreciably larger samples – will need to be done to establish the replicability of even the most consistent of these results.

Beyond the nascent state of the existing literature, it is important to consider some basic assumptions underlying neuroscientifically oriented research on psychopathy (or any form of psychopathology) that constrain interpretation of findings from such research of this kind and that place limits on the capacity of such findings

to inform applied practice and decision making. One is the basic "disease model" assumption that psychopathy represents a coherent physical entity, analogous to a discrete physical disease, whose observable symptoms can be traced to a coherent underlying biological disturbance. In contrast with this perspective, multiple lines of evidence indicate that psychopathy is not a unitary condition: rather, it encompasses distinguishable symptomatic facets with differing external correlates (e.g., Cooke & Michie, 2001; Hare, 2003; Lilienfeld & Widows, 2005; Patrick *et al.*, 2009), and even individuals who are rated high on all facets appear heterogeneous in terms of trait dispositions (e.g., Hicks *et al.*, 2004; Skeem *et al.*, 2007) and physiological or behavioral response patterns (e.g., Newman *et al.*, 1997; Sutton, Vitale, & Newman, 2002). Further, individuals who achieve high overall scores on the PCL-R or other measures of psychopathy are more likely than low-psychopathic individuals to exhibit symptoms of other disorders in conjunction with psychopathy-specific features. For example, high psychopathy scores tend to be associated with higher rates (or symptoms) of disorders such as conduct disorder, attention deficit-hyperactivity disorder, other personality disorders, and alcohol and drug abuse. As a result, psychopathy group or level differences in brain reactivity observed in experimental studies may in some cases reflect processes associated with (or common) to disorders of other types rather than processes specific to psychopathy.

Another key assumption in neuroscientific studies of psychopathy has to do with measurement fidelity. The assumption is that some direct biological counterpart exists to the constellation of behavioral features we call "psychopathy," such that measurable aspects of brain circuitry can be directly "mapped" to this behavioral entity. However, brain circuits and behavioral disorders represent *different* constructs in *separate* domains of measurement. As Campbell and Fiske (1959) noted many years ago, even indicators of the *same construct* derived from differing domains of measurement can be expected to correlate with one another only moderately, at best. This means that the level of association one would *expect* to find between a reliable behavioral measure of psychopathy (or one of its distinctive facets) and a reliable brain-based measure *of psychopathy* would be somewhere around .4 or .5. However, measures of brain reactivity (e.g., amygdala activation) in single-session experimental tasks (e.g., aversive differential conditioning) represent hypothetical indices, of unknown reliability in most cases (Vul *et al.*, 2009), of hypothetical constructs (e.g., fear) – not measures of psychopathy. From this standpoint, the level of relationship one would *expect* to see between a well-established measure of psychopathy and a brain-based index of some emotional or cognitive process is necessarily quite low, perhaps around the level one might expect to see between a sample of behavior on a single occasion and a reliable personality trait measure (i.e., probably below the level one would be able to detect reliably in samples of 10 or 20 participants; cf. Mischel, 1968).

How might this state of affairs be improved? Part of the answer may lie in repackaging mental disorders as currently conceptualized into "cleaner," finer grained units that are more amenable to neurobiological analysis (Patrick & Bernat, 2009). Traditional psychiatric categories like "psychopathy," "schizophrenia," and "bipolar

disorder" are crude targets for neuroscientific (e.g., brain-imaging and molecular genetic) studies. Spectacular failures in large-scale efforts to identify specific genes for mental disorders highlight this point. As discussed at the outset, psychopathy entails distinctive subcomponents that can be operationalized more separately and precisely to facilitate progress in understanding differing neural processes relevant to the disorder. Neuroimaging work focusing on a distinct variant of conduct disorder entailing callous-unemotional features (e.g., Marsh *et al.*, 2008; Jones *et al.*, 2009) provides an effective illustration of this, as does recent work examining neural correlates of the two distinctive factors of Lilienfeld's PPI (e.g., Gordon *et al.*, 2004; Buckholtz *et al.*, 2010). However, efforts beyond this will likely be required. Symptoms or symptom clusters may need to be reformulated in terms of constructs with more direct neurobiological referents; this is in fact the emphasis of the National Institute of Mental Health's recent Research Domain Criteria initiative (Sanislow *et al.*, 2010; see also Patrick & Bernat, 2009).

However, in pursuing efforts along these lines, it needs to be borne in mind that what we conceive of as psychological disorders will not ultimately be reducible to neural units or circuits. Brain structure and activation provide valuable points of reference for developing and refining psychological constructs, but the constructs themselves are not embodied in neural tissue or neural firing patterns – or in any other specific observable indicants (Cronbach & Meehl, 1955). The construct of psychopathy itself is a hypothetical entity that exists to organize observations of various types and their known relations in order to facilitate predictions. "Fear," "attention," and "amygdala" are also constructs. Further systematic experimentation along the lines reviewed here (and along other lines) should contribute over time to a more complete account of how neural firing patterns in particular regions of the brain differ in specific contexts for individuals exhibiting psychopathic features of one type or another, but linkages to observations and constructs at other levels of analysis will be required for an account of this type to be conceptually meaningful and practically useful (Anderson, 1998; Cacioppo & Berntson, 1992).

Implications for Legal Practice and Policy

The leading approach to measurement of psychopathy, the PCL-R and its derivatives, is often applied by psychologists in the juvenile and criminal justice systems in an effort to inform a variety of legal decisions about individual offenders. To what extent can current knowledge about brain function in psychopathy add value to, or perhaps even replace, such applications? We submit that the answer at this time – given the assumptions, limitations, and mixed findings of contemporary neuroscientific research on psychopathy – is "not much." In this section, we briefly outline the data and reasoning that underpin this belief, focusing on the legal issue that some scholars have argued is most relevant to neuroscience on psychopathy: criminal responsibility. We conclude by speculating about developments in neuroscience that could inform broader "problem-solving" policy issues, including intervention.

Criminal Responsibility and Sentencing Mitigation

Some scholars (e.g., Glenn, Raine, & Laufer, 2011; see also Kiehl & Buckholz, 2010) have used findings from neuroscientific research on psychopathy to argue, in essence, that it is wrong to punish psychopathic individuals for criminal acts. Themes of this argument involve asserting that research consistently shows that psychopathic individuals manifest clear deficits in amygdala processing of negative emotional stimuli (which ostensibly allows them to act criminally because they do not fear or care about the consequences) and clear deficits in orbitofrontal processing (which ostensibly frees them to act on criminal impulses).

Such arguments have been offered in an effort to support pleas of insanity or diminished capacity, that is, that the defendant is not blameworthy because of his or her mental state at the time of a specific criminal act. Successful pleas in judicial proceedings generally require evidence that a defendant suffered from a mental disorder that directly impaired the defendant's appreciation of the wrongfulness of the act and/or his or her ability to refrain from committing the act. Similar arguments have been offered in an effort to mitigate punishment at the sentencing phase of criminal cases. For example, Brian Dugan, a 52-year-old man already serving time for multiple murders, was newly convicted in 2009 of raping and murdering a young woman several years prior to the other murders, and was facing the death penalty. He hired Professor Kent Kiehl to assess him with the PCL-R along with fMRI methods (26 years after the murder in question) to support a mitigation argument that he "is a psychopath and could not control his killer impulses" (Hughes, 2010, p. 340). The jury, apparently unconvinced, unanimously voted to sentence Dugan to death.

We believe that attempts to apply current neuroscientific knowledge about psychopathy to legal decisions about criminal responsibility and sentencing are premature. First, this research is methodologically limited, entailing small samples, diverse designs, and an assortment of nonreplicated findings. Indeed, the findings emerging from this research are less "inconsistent" than "all over the map." Findings from structural imaging studies of psychopathy have implicated a number of brain regions, some that have been implicated in one way or another in functional imaging studies, and others not – but findings from these studies are for the most part isolated rather than systematic or replicable. In the case of functional imaging results, even for such prominently featured brain regions as the prefrontal cortex and the amygdala, studies of this type alternatively reveal reduced activation or enhanced activation, depending on the sample and the experimental processing context. Before the difficult process of validly applying group-based research findings to individual cases can be undertaken, there must be a coherent set of findings to apply. Currently, nomothetic data provide little point of reference for interpreting an individual's pattern of brain activations within an fMRI measurement procedure. An individual with a high PCL-R score could manifest reduced, amplified, or normal amygdala activity during a given emotional processing task. Neuroscientific findings on psychopathy will continue to be limited in their applicability to individual cases until

we more precisely define what psychopathy is and study more homogeneous groups of individuals that yield consistent patterns of brain correlates in psychologically meaningful contexts.

The second reason that current neuroscience on psychopathy has limited implications to policy and practice is that these data add little to what is already known about the affective, behavioral, and interpersonal features of psychopathy. For example, if imaging data consistently indicated that psychopathic individuals manifest reduced amygdala activation during exposure to fear-provoking stimuli, this would only confirm well-replicated behavioral findings that these individuals tend to be fearless; indeed, fearlessness or boldness is included in several measures of psychopathy. Although laypeople and professionals may be "wowed" by images of the brain, current neuroscience data have no special explanatory value that goes beyond behavioral data. In particular, brain correlates of psychopathy do not signify biological causation and (as explained next) cannot retrospectively explain a particular criminal act.

Even when neuroscience on psychopathy becomes better developed, there are reasons to believe that its applicability to the issue of criminal responsibility will remain limited. First, one must leap well beyond any available scientific data to argue that an individual is not responsible for a given criminal act because of psychopathic brain deficits. If a defendant manifests reduced amygdala activity while viewing aversive photographs in an fMRI scanner, this does not explain why he murdered his spouse 2 years ago. Brain data aside, it is difficult to construct a group-based chain of reasoning that would even plausibly link emotional processing deficits (which tend to be most strongly associated with interpersonal-affective features of psychopathy; Patrick & Bernat, 2009) with violent behavior (which tends to be most strongly associated with general disinhibition and antisocial behavior; Kennealy, Skeem, Walters, & Camp, 2010). Even if research could be used to construct such a chain a reasoning, it would still fail to address the key legal question of importance, that is, whether a particular individual manifested psychopathy-related brain deficits at the time of the crime *and* whether those deficits caused the criminal act of interest. Even among individuals diagnosed with psychopathy, a given criminal act may reflect a host of factors other than psychopathic personality deviation.

Second, even a mature body of research with coherent findings could not dictate the answer to fundamental moral, ethical, and legal questions. Excusing psychopathic individuals' criminal behavior because there are brain correlates that are consistent with the possibility that they do not care enough about the implications of their criminal behavior to inhibit it could well establish a slippery legal slope. Individuals with externalizing disorders like antisocial personality disorder also have brain correlates that are consistent with the possibility that they have limited resources for inhibiting criminal impulses. But most definitions of insanity exclude as an eligible "first base" disorders that are defined mainly by repeated criminal behavior (like antisocial personality disorder). If definitions of, and brain correlates for, antisocial personality and psychopathy continue to overlap, is it viable to argue that one group should be held responsible, but not the other?

Violence Risk and Treatment Amenability

Measures of psychopathy, comprised chiefly of the PCL-R and its derivatives, are most commonly used to inform legal issues that turn upon risk of violence or treatment amenability. At present, it is not clear that neuroscience findings add value to either enterprise for the reasons outlined above (i.e., methodological limitations, lack of coherent findings, and lack of additional explanatory value). In particular, there are no brain correlates that are consistently observed for, and specific to, "psychopathic violence" (if there is such a thing). At present, there are also no neuroimaging or electrocortical measures that add any incremental utility to measures of psychopathy in predicting violence or response to treatment. As noted earlier, biological correlates do not necessarily convey biologic etiology or predict treatment outcome.

Treatment and Prevention

At the outset of this chapter, we noted that the larger field's interest in applying neuroscience to psychiatric disorders is driven by the goal of understanding psychological mechanisms that underlie abnormal behavior to inform the development of optimally effective methods of treatment. To date, this goal has attracted little or no discourse in relevant neuroscience literature, perhaps because of entrenched – and exaggerated – therapeutic pessimism about psychopathy.

Recent research indicates that a variety of psychosocial treatment approaches reduce the risk of violence and other criminal behavior among psychopathic youth and adults (for a review, see Skeem, Polaschek, & Manchak, 2009). To maximize public safety, psychopathic individuals arguably should be conceptualized as high-risk cases to target with intensive and specialized treatment rather than hopeless cases to incapacitate.

Our hope is that psychopathy will be folded into the current movement to develop maximally effective treatments that target brain-linked deviations in psychological processing. Particularly relative to criminal responsibility applications, it seems that the ultimate potential for neuroscientific research on psychopathy to inform social problem solving is much greater here. Future research that isolates relevant brain-linked psychological processes (e.g., emotional under- or overreactivity), targets these processes in intervention, and evaluates their effects on behavior is sorely needed. Such research would be ideally be guided by neuroscientific understanding of key windows of development when relevant brain processes and behavior are most malleable.

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