

*Cognitive and Affective Neuroscience in Disinhibitory Psychopathology:*

*Summary and Integration*

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The chapters in this section address a large group of behaviors including psychopathological syndromes, trait dimensions, and a variety of specific deficits. Examples include psychopathy, antisocial personality disorder, substance abuse, impulsivity, externalizing, instrumental and reactive aggression, high-risk sexual behavior, gambling, suicidal behavior, and deficits in empathy, decision making, moral reasoning, planning, insight, set shifting, and perspective taking.

Historically, disinhibitory behavior has been ascribed to willful misbehavior and debate continues with respect to the legitimacy of regarding disinhibitory syndromes as psychopathology (Blackburn, 1988, 1995; Harris, Skilling, & Rice, 2002). For many, establishing a link between biologically-based dysfunction and maladaptive behavior is the *sine qua non* of psychopathology (Wakefield, 1992). Progress in cognitive and affective neuroscience has made it increasingly compelling to posit psychobiological mechanisms for disinhibitory psychopathology. Such research may eventually clarify the reasons why some individuals chronically engage in behavior that has negative consequences for themselves and others. It may also clarify the processes associated with disinhibited behavior that reflect primarily situational influences as opposed to trait characteristics. The present chapters advance an assortment of potential psychobiological mechanisms and provide a foundation for such progress.

From this perspective, the field of disinhibitory psychopathology appears poised for rapid progress. Rather than a lack of plausible psychobiological models, the challenge presented by the present chapters concerns differentiating the various psychobiological mechanisms, clarifying their relation to specific forms of disinhibitory psychopathology, and identifying methods for evaluating the putative associations. In order to organize the rapidly growing evidence, contrast

the proposed mechanisms, and generate alternative hypotheses regarding their significance for diverse forms of disinhibitory psychopathology, it is useful to adopt a common conceptual framework for the various syndromes and explanatory mechanisms. Toward this end, we describe a general model of self-regulation that is, at once, broad enough to accommodate diverse symptoms and mechanisms and specific enough to distinguish among them. After outlining the conceptual framework, we review the psychobiological mechanisms presented in this section and discuss their implications for disinhibitory psychopathology. Moreover, we discuss the implications of this integration for addressing past problems and advancing future research.

### ***Integrative framework***

In this segment, we present a broad framework for conceptualizing the core features of disinhibitory psychopathology. This framework was recently set out by MacCoon, Wallace, and Newman in the Handbook of Self-Regulation (Baumeister & Vohs, 2004). The organizing and integrating construct of the framework involves *self-regulation* which the authors define as the context-appropriate balance of attention to dominant and non-dominant cues (CABA). Though often categorized as a cognitive variable, we view attention as a “top-down” self-regulatory mechanism capable of enhancing appropriate cognitions, emotions, or behaviors and suppressing inappropriate cognitions, emotions, or behaviors. While recognizing that there are important differences between the regulation of emotion, cognition, and behavior, our view is that selective attention represents a common regulatory mechanism for each of these domains. Such a mechanism is consistent with recent neural network models and neuroscientific approaches that emphasize selective attention and cognitive control (e.g., Botvinick, Braver, Barch, Carter, & Cohen, 2001; Cohen et al., 1990; Desimone & Duncan, 1995) as well as with previous writings about the response modulation deficits that characterize diverse forms of disinhibitory psychopathology (Gorenstein & Newman, 1980; Patterson & Newman, 1993; Newman & Lorenz, 2003).

In neural network models, particular cognitions, emotions, and behaviors can be represented as networks of co-activated neurons. These networks are activated automatically in a "bottom up" way as responses to particular stimuli. According to this perspective, the most activated network of neurons represents the most dominant or pre-potent cognition, emotion, or behavior. These are the most likely responses in a given situation. However, alternative responses also are available in the form of less activated neural networks. These responses can become dominant if their activation levels are enhanced by top-down, selective attention. Thus, according to this perspective, the regulation of a dominant response requires the use of limited-capacity, selective attention to enhance the activation level of more adaptive, non-dominant responses. A breakdown in self-regulation occurs when an individual fails to shift attention to non-dominant cues that might otherwise serve to activate more adaptive behaviors (i.e., modify one's dominant response set).

According to this perspective, dysregulation is likely to occur when attention is allocated in a manner that is inappropriate for a given context. However, the appropriate balance of attention to dominant and non-dominant cues depends on the particular context. In some cases, non-dominant cues may distract a person from achieving an important goal and thus lead to dysregulated behavior (e.g., when we take offense at a person's comments despite our best efforts to make a positive impression and establish a pleasant relationship). In other cases, non-dominant cues may fail to distract a person from a pre-potent goal and thus lead to dysregulation (e.g., committing a break-in despite the presence of surveillance cameras). In either case, maintaining a context-appropriate balance of attention to dominant and non-dominant cues is crucial for effective self-regulation.

Characterizing the factors that determine how attention is allocated in a context-appropriate manner in a non-homuncular way (i.e., without invoking someone or some aspect of a person that decides) is a daunting task. Nevertheless, this problem becomes tractable using the logic of neural networks (see Botvinick, Nystrom, Fissell et al., 1999; Botvinick, Braver, Barch et

al., 2001). According to this perspective (see MacCoon et al., 2004), selective attention is attracted to the currently most activated network and will activate non-dominant networks as capacity allows. Thus, less activated networks will be processed only if capacity is available after processing more activated networks. In other words, the greater the cognitive load or allocation of capacity to dominant cues, the less capacity is allocated to non-dominant cues.

Thus far, we have proposed that an individual's dominant set will largely determine what non-dominant cues receive attention. Furthermore, the more capacity that is dedicated to dominant cues, the less capacity is available to attend to non-dominant cues. This may be true even when non-dominant cues are well-learned and apparently extend to emotional cues as well (e.g., Pessoa et al, 2002). Thus, when substantial capacity is required for the processing of a dominant set, an individual may lack the capacity to attend to non-dominant cues. However, the flip side of this coin is that attention can be hijacked by a non-dominant cue if capacity is available. Given the importance of dominance within this framework, it is worth noting that MacCoon et al. (2004) characterize dominance as a continuum. That is, a cue's relevance to a dominant response set is continuous rather than dichotomous. This is consistent with feature-based models of attention (e.g., Most et al., 2001) in which a dominant response set consists of attended dimensions or features (e.g., spatial location, luminance, shape, etc.). A cue is related to a dominant set if it shares all relevant dimensions and is dissimilar to the degree that its characteristics do not overlap all the relevant attributes specified by the dominant set (see Most et al., 2001).

Another way attention can be allocated to a non-dominant network involves registration of conflict between dominant and non-dominant networks. If two (or more) networks suggesting incompatible responses achieve about the same level of activation, this conflict must be resolved by top-down attention. Otherwise, no clear response is available. In other words, when a non-dominant cue is activated to the point that it competes with the current dominant response set for control of behavior, this conflict emits a "call for processing." This call must be answered by

top-down attention in order for effective self-regulation to occur. A classic example of such conflict involves incongruent trials in a Stroop task (Stroop, 1935), for instance, when the word “red” appears in blue ink. On such trials, one response network indicates “red” as an answer while the other indicates “blue” (see Cohen & Huston, 1992) and individuals must choose between a word-related response and a color-related response. Top-down attention can resolve this conflict by activating the appropriate response. Another type of conflict is triggered by a discrepancy between expected or goal-consistent cues and unexpected cues (i.e., between expectations and reality). A classic example involves an extinction contingency in which a response that has been rewarded results in omission of an expected reward (Gray, 1987). As with a response conflict, this type of conflict emits a call for processing which may be answered by top-down attention. In this case, attention is necessary to process the incongruent cue, evaluate its implications for ongoing behavior (i.e., the working model is still valid or circumstances have changed) and, if necessary, modify the dominant goal-directed behavior.

### ***Translating the psychobiological proposals into a common framework***

From the perspective offered by the *context-appropriate balanced attention* (CABA) framework described above, the psychobiological mechanisms discussed in the present chapters reflect alternative conceptualizations of the difficulty that some people have integrating dominant and non-dominant information. That is, virtually all of the explanatory constructs invoked may be understood as a deficit in modulating the top-down focus of selective attention in response to non-dominant information.

First, we consider self-regulation deficits reflecting problems of executive function or working memory that have been linked to dorsolateral prefrontal cortex (DLPFC). Several chapters in this section focus on the importance of DLPFC for maintaining activation of non-dominant responses which, in turn, enables a person to inhibit prepotent responses that are inappropriately aggressive, antisocial, or impulsive. When top-down control is implemented in this way, the implication is that an individual has recognized, at some level, the importance of

inhibiting a prepotent response or the advantages associated with implementing a non-dominant response. According to Miller and Cohen (2001), the function of DLPFC is nicely illustrated by performance on the color-word Stroop task in which participants must use attention to name the color of words and inhibit the prepotent tendency to read the word.

Linking this problem to clinically significant behavior, Ishikawa and Raine (this volume) propose that a hypo-functioning DLPFC would interfere with a person's ability to maintain an alternative interpretation for another person's behavior that has triggered a prepotent hostile attribution and, thus, indirectly predisposed a person to behave aggressively. In reviewing the literature relating DLPFC and executive functioning, Ishikawa and Raine emphasize the importance of impulsivity as a mediating variable. Indeed, as described in their chapter, a DLPFC-related deficiency in attending to non-dominant cues would make it difficult for a person to inhibit a variety of impulsive urges ranging from inappropriate verbal statements to murder.

In a related proposal, Patrick and colleagues (this volume) propose that a DLPFC-mediated deficit in working memory and other "executive functions" confers a psychobiological vulnerability to externalizing traits and disorders. While recognizing that there are important differences as well as commonalities among the externalizing disorders, Patrick et al describe externalizing as a broad latent factor that predisposes individuals to substance dependence and antisocial behavior disorders as well as conduct disorder, attention-deficit hyperactivity disorder, and the personality trait of novelty seeking. Moreover, the authors propose that acute alcohol intoxication, which is "reliably associated with impulsive, risk-taking behavior and bias toward satisfying immediate urges that would normally be inhibited" (p. 12?), represents a powerful model for addressing this common diathesis. In support of this proposal, the authors cite evidence that alcohol interferes with a person's ability to inhibit pre-potent, but inappropriate, responses on the color-word Stroop task. Moreover, there is evidence that alcohol may interfere with the inhibition of virtually any prepotent response. Related to this possibility, Patrick et al. describe a study by Casbon, Curtin, Lang & Patrick (2003) in which participants were primed

either to respond (80% target-present condition) or to withhold responses (20% target-present condition) under conditions of high- or low-cognitive load. Under conditions of high cognitive load which challenge working memory/executive functions, intoxicated participants persevere the dominant response set regardless of whether it involves responding (i.e., frequent target condition) or withholding responses (i.e., infrequent targets). Relative to the chapter by Ishikawa and Raine, the chapter by Patrick and colleagues places more emphasis on the substance abuse literature as opposed to the literature on aggression. However, both chapters cite similar evidence and develop similar arguments regarding the implications of PFC functioning for antisocial behavior and a more general problem inhibiting prepotent urges.

From the perspective of CABA, the association between DLPFC and disinhibitory psychopathology relates to attentional capacity. Maintaining CABA requires that a person have sufficient attentional capacity to maintain the activation of non-dominant networks to the point where they become dominant and control ongoing goal-directed behavior. To the extent that DLPFC deficits undermine a person's ability to maintain this type of attentional focus, they have difficulty considering alternative interpretations and response strategies in the face of prepotent interpretations and responses.

In contrast to these effects of DLPFC, the chapters focusing on orbitofrontal (OFC) and ventromedial frontal cortex (VMPC) highlight another aspect of self-regulation that is crucial for behaving in a context appropriate manner -- the process of evaluating and selecting from among diverse response options. Aside from a person's ability to implement a particular response strategy, people must be able to identify particularly adaptive and maladaptive response options so that they may pursue the former and avoid the latter. The OFC/VMPC appears to play a pivotal role in this regard and is thus critical for modulating behavior in complex situations such as those involving interpersonal interactions. In addition to being complex, interpersonal interactions typically require people to sift through the information and select responses without significant delay. For these and other reasons, social behavior places heavy demands upon a

person's ability to use "gut feelings" (i.e., somatic markers) to narrow the range of desirable responses and steer clear of context-inappropriate responses that may result in bad feelings.

With regard to CABA, such individuals possess sufficient attentional capacity to maintain a particular top-down focus of selective attention, but the process of evaluating and selecting a particular focus or goal is profoundly inefficient because of their difficulty using affective connotations to weigh the various options. Perhaps owing to this inefficiency, individuals with VMPC damage are prone to make decisions and implement pre-potent responses without processing their likely affective consequences. In other words, such individuals appear to lack the internal mechanism that normally guides a person's use of DLPFC to maintain a context appropriate balance of attention. On the Iowa gambling task, for instance, people with VMPC damage are more likely than control participants to select cards from the two decks that yield larger immediate rewards despite the fact that playing cards from these decks sometimes results in large penalties that make such choices less adaptive than playing cards from the small reward decks. Case studies involving such damage highlight the implications of VMPC for deficits in emotion processing, decision making, and impulse control (Tranel et al., this volume).

The chapter by Harmon-Jones focuses on the frontal lobes but suggests that asymmetry may represent a critical dimension for understanding vulnerability to disinhibitory psychopathology. Specifically, Harmon-Jones proposes that differential activation of the left frontal cortex predisposes a person to strong response biases that result in the rapid, inflexible implementation of approach behavior. Moreover, he presents evidence indicating that the consequences of this differential activation for anger and aggression appear to be the same regardless of whether it reflects hyper-activation of the left frontal cortex or suppression of the right frontal cortex. From the perspective of CABA, the Harmon-Jones model resembles other proposals suggesting that some individuals are prone to excessive anger and aggression because their top-down focus of selective attention is relatively impervious to non-dominant information that might otherwise alter their evaluation and behavior. However, there are also important

differences. The chapter by Harmon-Jones highlights the importance of the right hemisphere for modulating a left-hemisphere mediated, top-down focus of selective attention. In contrast to proposals involving DLPFC deficiencies, the individuals described by Harmon-Jones are not generally deficient in attentional capacity though there is often insufficient capacity to activate non-dominant networks owing to the intensity of their goal-directed behavior.

The Harmon-Jones proposal also appears to differ from proposals involving OFC/VMPC. On the one hand, differential activation of left frontal cortex appears to be associated with an unambiguous readiness for action that is strongly supported by affective associations. For example, once a comment is perceived as insulting, it is especially likely to motivate aggressive action in individuals with differential left frontal activation. Such intense reactions to a particular class of stimuli seem contrary to Tranel et al.'s (this volume) description of the affective deficiencies associated with VMPC damage. On the other hand, there is considerable evidence that OFC is important for representing and reversing approach/avoidance associations and thus moderating behavior. An intriguing possibility is that dominant (e.g., anger) and non-dominant (e.g., fear) associations of this type are differentially associated with left and right OFC respectively such that any factors that reduce right frontal activation (e.g., repetitive transcranial magnetic stimulation) will disinhibit dominant responses including approach-related aggression. Such speculation is also consistent with Tranel et al.'s conclusion that "the decision-making deficit observed both in real-life and in the laboratory is most pronounced after right, as opposed to left VMPC lesions... (and that a) "similar conclusion was reached in a case study of a patient with a right orbitofrontal lesion" (p. 17?).

Thus far, we have considered how insufficient capacity, difficulty integrating affective associations, and an exaggerated response bias will tend to favor implementation of pre-potent responses and reduce the response modulating influence of non-dominant considerations. These functions of PFC appear to be especially important for biasing attention, decision making, and inhibiting behavior. In many respects, however, these functions of PFC are a reflection of

subcortical processes. Indeed, the origin of the response modulation hypothesis for disinhibitory psychopathology (see Gorenstein & Newman, 1980) reflects a chapter by McCleary (1966) entitled: *The response modulating function of the limbic system*. More recently, investigators have documented the significant role played by the amygdala complex in mediating this response modulation function (LeDoux, 2003). Not surprisingly, then, several chapters in this section emphasize the potential importance of the amygdala complex, septo-hippocampal system, and other paralimbic structures (e.g., anterior cingulate cortex; ACC) for clarifying individual differences in the use of bottom-up information to modulate behavior.

Summarizing a variety of evidence from fMRI and evoked potential studies, Kiehl (this volume) concludes that psychopathy is associated with hypofunctioning of a temporal-limbic system that includes “the amygdala, parahippocampal regions (see also Laasko, Vaurio, Loivisto, Savolainen et al, 2001), anterior superior temporal gyrus, rostral and caudal anterior cingulate, and posterior cingulate” (p. 24). Moreover, he notes that similar abnormalities are observed during performance of affective, language, attention, and orienting tasks. With regard to the CABA framework, Kiehl’s conclusions suggest that the core processing deficits and callous antisocial behavior of psychopathic individuals reflects a problem in the neural circuitry that normally facilitates activation of non-dominant neural networks and modulates the top-down focus of selective attention. Although the end result resembles deficiencies in DLPFC and VMPC functioning (i.e., a problem using non-dominant networks to modulate goal-directed behavior), the etiology of the problem is different and is likely to have important implications for understanding and managing the psychological dysfunction. Particularly noteworthy is Kiehl’s demonstration of parallel problems affecting emotion processing, attentional orienting, and language. Though psychopathic individuals may be deficient in the processes attributed to VMPC, the evidence presented by Kiehl suggests that such deficiencies may reflect a more fundamental problem regarding, for instance, the affective associations that constitute somatic

markers. Moreover, the fundamental information processing deficit associated with psychopathy may extend to non-affective as well as to affective information.

The chapter by Newman and colleagues also emphasizes the potential importance of subcortical influences but focuses more specifically on the implications of the septo-hippocampal system (SHS) for the self-regulatory deficits associated with psychopathy. According to Newman et al., psychopathy is associated with a failure to evaluate goal-directed behavior using information that is peripheral to their dominant response set. More specifically, Newman and colleagues propose that the SHS plays an important role in maintaining the activation of non-dominant networks via recursive loops involving other neural circuitry. In turn, this process facilitates the processing of contextual information, including unanticipated events and competing goals, as well as the integration of this contextual information with a person's dominant response set. With regard to CABA, the SHS facilitates the context appropriate balance of attention via its differential response to information that is not adequately represented in the current top-down set or dominant neural network. When a person registers the occurrence of a significant stimulus that was not anticipated (i.e., incongruent with their dominant network), the SHS registers a goal-conflict which, in turn, engages other brain circuitry to evaluate and, if necessary, reconcile the apparent conflict. In other words, the SHS appears to be crucial for enhancing activation of context-relevant, but non-dominant, goals to the point that they compete with a person's top-down focus of selective attention.

According to Blair (this volume), the most salient features of psychopathy may be understood as a consequence of early amygdala dysfunction. Blair emphasizes the association between amygdala dysfunction and poor aversive conditioning, weak facilitation of startle responses while viewing unpleasant stimuli, difficulty using emotion cues to enhance word processing, and reduced responsivity to sad and fearful faces—all findings that have been linked to psychopathy. To the extent that such processes are less influential among psychopathic individuals, it would undermine their ability to withhold responses that have resulted in

punishment, use threat cues to modulate behavior, and employ sad and fearful facial (i.e., empathy) cues to modify interpersonal behavior. Similar to the proposals by Kiehl and Newman et al., the response modulation deficits of psychopathic individuals are attributed primarily to deficiencies in subcortical circuitry that would otherwise help gate information into PFC and modulate a person's top-down focus of selective attention.

Soderstrom's (this volume) approach to psychopathy involves conceptualizing the disorder as a collection of neuropsychiatric skill deficits. With regard to psychopaths' disinhibitory traits and apparent deficits in executive functioning, Soderstrom is careful to point out that psychopaths do not display the type of executive function deficits normally associated with DLPFC dysfunction and they do not differ from controls with respect to prefrontal volume (cf. Raine et al, 2000). Related to Soderstrom's proposal that DLPFC-related deficiencies may originate elsewhere in the brain, Damasio (1994) has made analogous claims with regard to the tendency of VMPC-related deficits to tax DLPFC resources. Similarly, Kiehl (this volume) discusses neuroimaging results showing that, relative to controls, psychopathic individuals exhibit less limbic system activation and correspondingly more activation of lateral frontal cortex on affect and language processing tasks. Thus, he speculates that executive function deficits associated with psychopathy may involve "impairment of the mesocortical dopamine system" which is thought to underlie arousal and cognitive processes in the prefrontal cortex" (p. ). With regard to CABA, the implication is that any cortical or sub-cortical deficiency that impairs the relatively automatic use of bottom-up information to modulate top-down selective attention will hamper the top-down / bottom-up integration of information and frequently mimic the effects of high cognitive load and executive functioning/working memory deficits.

With regard to the psychopath's deficits in empathy, social cognition, and mentalizing, Soderstrom (this volume) speculates that they involve limbic or "social brain" areas that include amygdala, hippocampi, ventral striatum, cingular gyrus, and orbitofrontal regions. Regarding a potential link among these diverse structures, he notes that they are all densely innervated by the

monoaminergic systems as well as by peptidergic systems using oxytocin, vasopressin, and endorphins as transmitters. Moreover, he reports evidence indicating that psychopathy is associated with increased HVA/5-HIAA ratios, perhaps reflecting deficient serotonergic regulation of dopaminergic activity (Soderstrom et al., 2001, 2003). Finally, Soderstrom also notes the potential relevance of deficiencies in callosal functioning for such deficits.

Although their approaches to the topic and the evidence used to develop their arguments are quite different, there is considerable overlap between Soderstrom's and Kiehl's conclusions. Both authors posit widespread hypofunctioning within limbic structures while noting normal or even hyper-activation within other regions of prefrontal cortex. With regard to CABA, the implication is that psychopathic individuals are deficient in processing bottom-up information that is crucial for modulating behaviors in interpersonal, and other relatively complex, situations. Although psychopathic individuals would be expected to perform as well as controls when implementing particular (i.e., top-down) strategies, they would be less able to integrate complex information that is not already part of their top-down set and regulate prepotent responses.

### ***Relating the psychobiological mechanisms to disinhibitory diagnoses and dimensions***

A great deal of empirical and theoretical work has focused on the development of antisocial typologies. Though theoretically meaningful and empirically robust, investigators have rarely, if ever, systematically related the types to the neurobiological mechanisms discussed in the section chapters. Toward this end, we use the CABA framework to speculate about these associations. In doing so, we hope to illustrate that the juxtaposition of these psychological and neurobiological models serves to advance both disciplines by highlighting important distinctions and generating questions for future research (discussed in the following section). First, we briefly review significant typologies.

Based on an earlier proposal by Jenkins (RL, 1942; Mental Hygiene), Quay (1987) distinguishes four delinquent or antisocial types: socialized delinquents, unsocialized psychopathic delinquents, anxious/neurotic delinquents, and attention problem/inadequate

delinquents. Although there is some variability in the precise subtypes identified, this characterization of delinquent subtypes has persisted over time and is generally supported by empirical analysis (e.g., Blackburn, 1975; Lykken, 1995; Widom, 1978). Using a time course or developmental trajectory analysis of conduct problems, Moffitt (1993) has distinguished between life-course persistent and adolescent limited types of delinquency. Whereas the adolescent-limited type resembles the socialized delinquent subtype, Moffitt's life-course persistent type appears to cut across traditional distinctions. Consistent with Moffitt's proposal, life-course persistent delinquents have been shown to display performance deficits on diverse neuropsychological tests (Donnellan, Ge, & Wenk, 2000; Piquero, 2001; cf. Raskin-White, Bates, & Buyske, 2001).

Lykken (1995) uses the terms sociopathy and psychopathy to distinguish between antisocial syndromes that are primarily social as opposed to biological (i.e., temperament related) in origin. Sociopaths, according to Lykken, are individuals "whose unsocialized character is due primarily to parental failures rather than to inherent peculiarities of temperament" (p. 7). Psychopathic personalities, on the other hand, are "distinguished by biological differences that make them difficult to socialize" (Lykken, 1995, p. 41). Another common distinction addressed by Lykken (1995) involves primary and secondary psychopathy. The inadequate socialization of primary psychopaths is presumed to reflect a fundamental deficit in the affective-inhibitory processes that normally constrain behavior (e.g., Cleckley, 1976; Hare, 1970). According to Cleckley (1976), genuine or primary psychopathy has less to do with powerful antisocial, sexual, or aggressive urges or emotionality than it does "relatively weak emotion breaking through even weaker restraints" (p. 263). In contrast to primary psychopathy, Lykken attributes secondary psychopathy to strong approach motivation and distempered psychopathy to strong situational or trait-like urges (e.g., aggressive or sexual) that overpower a person's otherwise normal capacity for inhibiting inappropriate behavior and learning socialization. Lykken's characterization of

secondary psychopaths has much in common with Quay's (1987) neurotic delinquents but the former encompasses a wider variety of motivation-related problems.

Within the field of psychopathy, a number of investigators have used factor analytic techniques (see Harpur, Hare, & Hakstein, 1989; Hare et al., 1990) to identify specific components of psychopathy such as their callous, unemotional traits (i.e., factor 1) and their impulsive, antisocial lifestyle (i.e., factor 2). More recently, investigators have proposed three- (Cooke & Michie, 2001) and four-facet (Bolt, Hare, Vitale, & Newman, 2004; Hare, 2003) models that specify separate interpersonal, affective, impulsive, and antisocial facets. In spite of their emphasis on identifying components of psychopathy, most proponents of the 2, 3, and 4 facet models maintain that the facets load on a higher-order, unifactorial construct of psychopathy. For instance, Hare (1996) wrote that the "factors appear to measure two facets of a higher-order construct, namely, psychopathy" (p. 31).

Others have turned to personality theory to assist them in parsing the heterogeneity of psychopathy and antisocial behavior. For instance, Lynam and colleagues (Lynam 2002; Miller & Lynam, 2003; Widiger & Lynam, 1998) have applied the five-factor model to psychopathy. One implication of this model is that psychopathy may be conceptualized as an unfortunate combination of personality traits each with its own psychobiological underpinnings. Alternative trait models of psychopathy have also been presented (e.g., Lilienfeld & Andrews, 1996; Levenson, Kiehl, & Fitzpatrick, 1995), though it is not always clear whether the constituent traits are being used to identify a latent variable related to the entire syndrome or whether psychopathy is being defined as a combination of etiologically distinct components.

Translating these disinhibitory diagnoses and traits into CABA terms provides an alternative means of contrasting the diagnostic distinctions and helps to link these variables to the psychobiological mechanisms presented in the chapters. By definition, socialized delinquency and sociopathy primarily reflect experience as opposed to psychobiological vulnerability. Nevertheless, it is possible to conceptualize this predisposition using the CABA framework. In

essence, the unfortunate experiences associated with these syndromes give rise to neural networks that involve antisocial values, judgments, and behaviors. Such networks increase the probability that the bottom-up influences that normally determine a person's prepotent responses will be antisocial (see MacCoon & Newman, in press). Although many individuals exposed to such developmental experiences will exhibit a chronic antisocial lifestyle, others manage to avoid the negative consequences associated with the adverse circumstances. In light of this environmental predisposition, individuals who inhibit such prepotent responses are likely to be protected by unusually effective executive functions, hypersensitivity to threat cues, or other factors that promote behavioral inhibition (see also, Krueger et al., 1994, Moffitt, 1993). In CABA terms, individuals who can exert high levels of top-down control or who are characterized by powerful bottom-up urges to avoid conflict and other arousal-inducing experiences may be resistant to the effects of an antisocial environment. Thus, despite potent environmental influences, it seems likely that psychobiological mechanisms are relevant even for socialized delinquency and sociopathy.

From this perspective, it is tempting to view Lykken's (1995) construct of secondary psychopathy in similar terms. In contrast to sociopathic individuals who are predisposed to antisocial behaviors that have been modeled and/or reinforced by experience, secondary psychopaths are predisposed to specific types of antisocial behavior by virtue of inherited temperament. That is, some individuals appear to be constitutionally predisposed to urges, such as anger, thrill seeking, and sexual misconduct that increase the likelihood of antisocial behavior. Given such urges, individuals with normal or sub-normal levels of cognitive control will be at high risk to act on these urges. Nevertheless, as with sociopathy, we presume that some individuals are protected from the negative consequences associated with such risk either because of exceptional top-down control (associated with DLPFC) or strongly activated adaptive networks (acquired via socialization). With good top-down control individuals can activate adaptive response networks even if the networks are not strongly activated bottom-up; with

strongly activated adaptive networks, less attentional capacity is required for these networks to become pre-potent. zz

These conceptualizations of sociopathy and secondary psychopathy suggest that DLPFC and working memory may play an important role in modulating the antisocial inclinations associated with maladaptive developmental experiences and difficult temperaments. An alternative view might emphasize the approach-related nature of the prepotent urges associated with sociopathy and secondary psychopathy. Sociopaths, for instance, may be motivated to attain rewards associated with gang membership, selling drugs, or dominating peers. Similarly, secondary psychopaths may be motivated by abnormal levels of thrill seeking, aggression, and sex drive. Viewed in this way, the predisposition to antisocial behavior manifested by sociopaths and secondary psychopaths may be potentiated by trait-like differences involving differential activation of the left frontal cortex which, according to Harmon-Jones (this volume), facilitates behavioral approach.

The traditional and relatively large category of neurotic psychopathy may be associated with a variety of psychobiological mechanisms described in these chapters. Though highly speculative, we suggest some potential associations for the purpose of facilitating future research. Using the Harmon-Jones model (this volume) relating differential activation of the left hemisphere to readiness for action, one could conceptualize neurotic psychopaths as individuals who are predisposed to act on their hostile urges and sense of entitlement. Alternatively, their high level of negative emotionality may interfere with top-down behavioral control. In this connection, Wallace and Newman (1997) have proposed that the intense emotion responses associated with trait neuroticism attract attention and thus reduce the attentional capacity available for regulating the prepotent responses engendered by their emotional reactivity. Krueger et al. (1994) have also noted that high levels of negative emotionality are associated with increased risk for antisocial behavior especially when coupled with low levels of constraint. A third possibility outlined by Davidson, Putnam, and Larson (2000) is that high levels of negative

emotionality and impulsive aggression may reflect, rather than engender, a deficit in top-down control. According to Davidson et al, dysfunctional serotonergic projections to prefrontal cortex may result in faulty regulation of emotion in a manner analogous to faulty regulation of other prepotent responses. The importance of serotonergic projections for regulating prepotent responses is also highlighted by Soderstrom (this volume and Lynam, 1996). A fourth possibility is the high levels of negative affect associated with neurotic psychopathy reflect the negative consequences of their chronically disinhibited behavior (see Fowles, 1987; Frick et al., 1999). According to this view, the negative affect is not an intrinsic aspect of their vulnerability but an indirect consequence of a more fundamental deficit in top-down control of the type described in the present chapters.

The chapters may also provide insight regarding the psychobiological predisposition to the attention problems/inadequate delinquent subtype. Indeed, several chapters discuss the relevance of their proposals for antisocial syndromes with co-morbid attention deficit hyperactivity disorder (ADHD). There is a substantial literature relating ADHD to disinhibitory psychopathology (Gorenstein & Newman, 1980), including conduct disorder, aggression, and adult antisocial behavior (e.g., Faraone, Biederman, Chen, Milberger et al., 1995; Lynam, 1996; Milich & Loney, 1979) as well as to substance abuse disorders and executive functioning deficits (e.g., Alterman & Tarter, 1983, Faraone & Biederman, 1998, Giancola & Moss, 1998). Thus, it appears that the attention problems / inadequate delinquent subtype described by Quay (1987) and others may relate to current conceptualizations of executive function deficits that give rise to disinhibitory psychopathology. For example, Ishikawa and Raine's (this volume) discussion of DLPFC-mediated problems in antisocial behavior disorders focuses on ADHD as a key factor mediating the association between such syndromes and executive function deficits. According to Patrick et al. (this volume) individuals with ADHD resemble other externalizing syndromes in displaying smaller P300 responses which, in turn, are related to a diminished capacity for frontally mediated neuronal inhibition (i.e., frontal dysfunction).

Overall, this characterization of the attention problems / inadequate delinquent provides a common thread that links ADHD, conduct disorder, antisocial behavior, substance abuse, and executive functioning deficits. Clearly, this grouping of syndromes and attributes overlaps with Patrick et al.'s (this volume) characterization of externalizing. In light of the neuropsychological deficits that characterize these groups, this predisposition to antisocial behavior may also overlap with the life course persistent form of conduct disorder described by Moffitt (1993). With regard to CABA, investigators appear to be quite consistent in attributing the core features of these syndromes to capacity limitations that interfere with the top-down control of pre-potent response inclinations.

In contrast to the other syndromes of disinhibition, discussions of primary psychopathy reflect a clear and consistent emphasis on weak bottom-up activation of non-dominant networks that might otherwise modulate dominant responses. For instance, Blair (this volume) describes psychopathy as an amygdala-related deficit that hampers sensitivity to bottom-up fear, empathy, and other inhibitory cues that normally command attention owing to their differential activation, at least initially, by the amygdalar complex. As already noted, Kiehl's (this volume) discussion of psychopathy cites a variety of deficiencies associated with the bottom-up activation of non-dominant networks that normally facilitate attentional orienting, affective processing, and the elaboration of linguistic stimuli (see also Hare, 1998). Similarly, Newman et al.'s (this volume) discussion of psychopathy emphasizes the potential importance of the septo-hippocampal system for activating non-dominant networks that are incongruent with the top-down focus of selective attention. Soderstrom's (this volume) conceptualization of the empathy and other social deficits associated with psychopathy closely resemble the proposals by Blair and Kiehl, though he posits different mechanisms for the disinhibited behavior of psychopathic individuals.

Mapping the VMPC model (Tranel et al., this volume) or somatic marker hypothesis (e.g., Damasio, 1994) onto the disinhibitory syndromes described in this section is complex. Although Tranel et al. use the terms sociopathy and psychopathy to describe the consequences of

VMPC damage, their definition of these terms is relatively non-specific. As noted in their chapter, the authors equate and use the terms psychopathy and sociopathy interchangeably. Moreover, the authors' definition of psychopathy appears to reflect the DSM-IV criteria for antisocial personality disorder. On the one hand, the authors describe the potential implications of their VMPC model for core symptoms of psychopathy "including failure to conform to social norms, deceitfulness, impulsivity, irritability, consistent irresponsibility, and lack of remorse." On the other hand, the laboratory evidence for the somatic marker hypothesis appears to be as much or more associated with externalizing psychopathology than it is with psychopathy more narrowly defined. As discussed below, deficiencies in the Iowa gambling task are related to substance abuse (Adinoff et al., 2003; Bechara & Damasio, 2002; Bechara & Martin, 2004), impulsive personality traits in university students (van Honk et al., 2002), and working memory capacity in both normal and clinical samples (Busemeyer & Stout, 2002; Hinson et al., 2002, 2003; Stout, Rodawalt, & Siemers, 2001). Deficiencies have also been found in psychopathic individuals (Blair, Colledge, & Mitchell, 2001; Mitchell, Colledge, & Blair, 2002), though results are inconsistent (Schmitt, Brinkley, & Newman, 1999; Lösel & Schmucker, in press) and may be depend on other cognitive variables (Lösel & Schmucker, in press). As commonly operationalized then, the VMPC model appears to apply to diverse forms of disinhibitory psychopathology. Whether this inclusiveness reflects the overlapping nature of these disorders or a lack of specificity remains to be discerned. One possibility is that a deficiency in the type of decision making associated with VMPC is characteristic of diverse disinhibitory syndromes although the etiology of the deficiency varies from syndrome to syndrome.

With regard to the PCL-R facets, Patrick et al. (this volume) relate PCL-R factor 2 to externalizing traits and presumably deficits in executive functioning whereas PCL-R factor 1 is associated with amygdala-related deficits in emotion processing. Soderstrom (this volume) offers a similar analysis of the 3-facet model, linking behavioral disinhibition with ADHD-like problems of attentional control and psychopaths' interpersonal and affective symptoms to deficits

in social brain chemistry and circuitry (i.e., the paralimbic system). Although Kiehl, Blair, and Newman et al. (this volume) also emphasize paralimbic circuitry in their discussions of psychopathy, these authors do not discuss the differential contribution of such dysfunction for the PCL-R facets. In terms of the CABA perspective, there appears to be some consensus that PCL-R factor 1 is associated with a deficiency in the bottom-up activation of neural networks that normally modulate goal-directed behavior. The conceptualization of PCL-R factor 2 is less clear, with some investigators linking it to deficits in executive functioning and top-down control while others -- presumably those who regard psychopathy as a unidimensional construct -- appear to regard the various PCL-R components as differential expressions of a common etiological process (see Harpur, Hakstien, & Hare, 1989, Cooke & Michie, 2001). Although there is solid evidence connecting factor 2 traits with behavioral impulsivity, it remains to be determined whether the psychobiological correlates of factor 2 are moderated by the presence or absence of factor 1 traits (i.e., whether or not the factor 2 traits occur within the context of the full psychopathic syndrome).

***Increasing the specificity of psychobiological mechanisms and disinhibitory syndromes: The case for bootstrapping***

As evidenced by the emphasis on antisocial subtypes described above, investigators have long been concerned about the etiological heterogeneity of antisocial syndromes and recognized the importance of distinguishing among groups with diverse psychobiological vulnerabilities, developmental trajectories, and treatment needs (see Brinkley et al., 2004). Historically, researchers have attempted to address this etiological heterogeneity using clinical signs and symptoms. The assumption is that individuals who suffer from a common psychobiological vulnerability will manifest similar symptoms and that individuals with similar symptoms suffer from a common underlying problem. However, as noted below, such assumptions may not be valid and the use of such classification strategies may not be optimal for clarifying the psychobiological correlates of disinhibitory psychopathology.

One problem relates to equifinality or, in other words, the fact that there are diverse etiological pathways to most disinhibitory syndromes (Cicchetti & Rogosch, 1996; Newman, 1997). It should be clear from our discussion of psychopathic subtypes that people may be predisposed to and meet the diagnostic criteria for antisocial personality disorder, or even psychopathy, for a variety of reasons. The problem also exists when discussing specific behavioral traits such as aggression. For example, the chapters suggest that the aggressive behavior of disinhibited individuals may be understood conversely as deficits in DLPFC, VMPC, or dysfunctions in limbic system processing. At a psychological level, the problem may be viewed as excessive activation of a dominant approach system, a problem maintaining multiple interpretations of a person's provocative behavior, a deficiency in accessing the affective consequences of inappropriate actions, or a variety of deficiencies in bottom-up processes that would otherwise modulate maladaptive goal-directed behavior. Clearly greater specificity is needed in defining such categories and dimensions if they are to be understood as manifestations of specific psychobiological processes (see Newman, 1997 for more detail).

Another concern with using clinical symptoms to parse the heterogeneity of psychopathy and other antisocial syndromes is that they may emphasize traits that distinguish syndromes rather than traits that are central to the syndromes. For instance, in setting out the construct of psychopathy, Cleckley (1976) placed considerable emphasis on the fact that genuine psychopaths do not experience high levels of neurotic anxiety. To a limited extent, this feature of psychopathy provides insight into the nature of the disorder but, primarily, it serves to distinguish psychopathic individuals from others whose antisocial behavior reflects different etiological processes. Though it is tempting to pursue the etiology of their "low anxiety" as a means to better understand the construct of psychopathy, it is unlikely that this approach will clarify the specific psychobiological processes that predispose a person to psychopathy. The low anxiety of psychopathic individuals is only one of many correlates and the truncated range (i.e., absence of high anxiety) described by Cleckley may reflect a unique feature of psychopathy that limits

neurotic anxiety rather than continuously distributed processes that underlie anxiety in nonpsychopathic individuals. For example, the consequences of VMPC damage described by Tranel et al may be relatively incompatible with high levels of anticipatory or neurotic anxiety, though VMPC is not generally regarded as a core physiological substrate of anxiety.

A related example concerns the factor structure of the PCL-R. Despite using two and three correlated factors respectively to characterize psychopathy, both Harpur et al (1989) and Cooke and Michie (2001) maintain that psychopathy may be conceptualized as a unidimensional construct. For instance, Cooke and Michie described their proposal as a 3-factor hierarchical model “in which a coherent superordinate factor, *Psychopathy*, is underpinned by 3 factors” (p. 171). In characterizing their results, Harpur et al., wrote that “although the PCL can be considered a homogeneous scale on statistical grounds, the *factors* have distinct patterns of intercorrelations with other variables.” (p. 6). The question is whether the distinct correlates of the factors are fundamental to psychopathy or, instead, provide information about independent constructs of marginal significance for the disorder. Based on their finding that PCL-R factor 1 is negatively associated with startle potentiation during unpleasant slides whereas PCL-R factor 2 is positively correlated with startle potentiation during unpleasant slides, Vanman et al (2003) recently concluded that psychopathy is best conceptualized and studied as a multifactorial construct. However, to the extent that psychopathy is defined by high scores on both factors, it is difficult to understand how any particular psychopathic individual could be both hyper- and hypo-reactive to identical stimuli. That is, the unique correlates of psychopathy’s facets may not be the ones that underlie the more integrated, latent construct that we are attempting to understand.

A third potential limitation of using symptom profiles to classify individuals is that the focus of investigators is prematurely limited to individuals who prominently display the relevant characteristics. Yet, it is possible that a less restricted sample of individuals would reveal a different understanding of the behavioral profile associated with a particular psychobiological

vulnerability. For instance, based on behavior genetic evidence indicating that the syndromes of psychopathy, antisocial personality disorder, somatization disorder, early-onset alcoholism, attention deficit hyperactivity, conduct disorder, and normal impulsivity “run in families”, Gorenstein and Newman (1980) proposed that many individuals with these disorders share a psychobiological vulnerability to disinhibitory psychopathology with diverse manifestations. They wrote: “it is the task of researchers in the areas of psychopathy, hysteria, hyperactivity, antisocial and impulsive personality, and alcoholism to coordinate efforts in discovering the common diathesis as well as the differential moderating factors that produce these separate manifestations. The search for the diathesis in particular must look beyond the phenomenon of antisocial transgression, which characterizes only some disinhibitory syndromes, and only partly at that” (p. 307). By focusing on the processes that are common to these disorders, rather than those that differentiate them, this perspective suggests a more abstract level of analysis and highlights processes such as poor inhibition of prepotent responses and lack of reflectivity (e.g., Patterson & Newman, 1993) as opposed to processes with more proximal associations with the individual syndromes (e.g., individual differences in fearlessness, somatic anxiety, or alcohol tolerance).

In light of these and other problems, there is considerable interest in using cognitive and affective neuroscience to improve psychiatric diagnosis that includes replacing traditional diagnostic categories with characterizations that conform more closely to underlying neural mechanisms. To the extent that anomalies in particular neural structures or circuits are predictive of psychopathology, it should be possible to identify individuals at risk for such psychopathology with greater reliability. In addition, to the extent that the psychological function of the circuitry has been characterized, it would be possible to characterize a person’s psychological vulnerability. Moreover, by comparing individuals with the psychobiological diathesis who do and do not manifest the psychopathology, it is possible to clarify the factors that moderate the risk associated with the psychobiological vulnerability (see Gorenstein & Newman, 1980).

It is tempting to think that the type of psychobiological mechanisms described in the present chapters could be used in place of traditional methods for diagnosing psychopathology, but such a strategy is likely to result in similar problems. This is because the type of DLPFC, VMPC, or paralimbic dysfunction described in the present chapters is likely to reflect a variety of causes (i.e., equifinality). In addition, specific investigations that focus on particular components of a psychobiological mechanism – for instance affect processing deficits associated with a hypofunctioning limbic system – risk missing the forest for the trees with regard to the consequences of limbic system dysfunction and its implications for behavior. Finally, focusing on particular structures such as the amygdala or VMPC may provide useful information about these brain regions and yet fail to inform investigators about a higher order predisposition that is correlated with the identified regions but reflects a different vulnerability. Given the widespread hypofunctioning in paralimbic structures in psychopathic individuals identified by Kiehl (this volume) for instance, there is reason to believe that dysfunction in any component of the system is a reflection of some more general process such as anomalies in the brain chemistry that modulate these paralimbic structures (e.g., Soderstrom, this volume).

Our point is that the problems of equifinality and multifinality apply to biological processes as well as to behavioral syndromes. Thus, researcher cannot assume that individuals who display similar physiological signs or anomalies suffer from a common problem or that people with a shared physiological dysfunction will display similar symptoms. However, this is not to say that the psychobiological mechanisms described in the present chapters are not useful for parsing the heterogeneity of disinhibitory psychopathology. A potential solution for the problems associated with relying exclusively on clinical or physiological signs involves “bootstrapping” (see Gorenstein, 1992).

Bootstrapping refers to the continuous process of refining a clinical syndrome (or trait dimension) in light of its association with a specific psychobiological mechanism or etiologically-relevant correlate while simultaneously refining the psychobiological mechanism to improve the

strength of its association with the clinical syndrome or trait dimension. With time, this strategy enables investigators to identify more specific (i.e., etiologically homogeneous) syndromes and dimensions as well as to develop psychobiological mechanisms with greater specificity. Importantly, such specificity provides a means of differentiating superficially similar but fundamentally distinct behavioral syndromes and psychobiological mechanisms. Bootstrapping both facilitates and requires increasing specificity with regard to psychobiological mechanisms and behavioral criteria. The bootstrapping strategy also serves to clarify the symbiotic relationship that exists between behavioral and neuroscience measures. Progress in specifying brain-behavior relations is advanced through the development of precise behavioral and biological measures and it is necessarily limited by insufficient precision at either the biological or psychological level.

To illustrate the process of bootstrapping, we will use a brief example. As described above, most investigators associate primary psychopathy with deficits in bottom-up activation or problems representing affective information in VMPC as opposed to DLPFC-related deficits of the type highlighted by Ishikawa and Raine and Patrick et al. (this volume). On the other hand, it is possible that individuals who satisfy the PCL-R criteria for psychopathy display a combination of bottom-up and top-down deficiencies as indicated by their high scores on the two major PCL-R factors (Patrick et al, this volume; Soderstrom, this volume). Using carefully defined groups of PCL-R psychopaths, non-psychopathic individuals with externalizing psychopathology (e.g., substance abuse), and controls with minimal evidence of disinhibitory psychopathology, an application of the bootstrapping technique might involve examining the association between these diagnostic groups and psychobiological dysfunction and using the results to improve the specificity of the diagnostic groups.

Although any psychobiological assessment could be used for this purpose, the utility of the results is likely to be enhanced if the assessment has theoretical and practical significance. Owing to its relevance for socialization and antisocial behavior, investigators of disinhibitory

psychopathology have frequently assessed passive avoidance using a go/no go successive discrimination task in which participants attempt to learn which stimuli indicate that they should press a button to win money and which stimuli signal that they should withhold responding to avoid losing money. Using this task, evidence of poor passive avoidance learning has been found in a variety of disinhibited groups including adult psychopathic offenders (Newman & Kosson, 1986; Newman & Schmitt, 1998; Thornquist & Zuckerman, 1995), adolescent males with high psychopathy scores on Frick and Hare's (2001) Antisocial Process Screening Devise (Blair et al., in press; Vitale et al., in press); adolescent males with conduct disorder or ADHD and adolescent girls with ADHD (Hartung et al., 2002); early-onset alcoholics with antisocial features (Finn, Mazas, Justus, & Steinmetz, 2002); university students at risk for alcohol abuse (McCarthy, Kroll, & Smith, 2001); female prisoners with borderline personality disorder (Hochhausen et al., 2002), and impulsive university students (Avila, Molto, Segarra, & Torrubia, 1995; Newman et al., 1985). In light of the diversity of groups displaying these deficits, it is unlikely that the psychobiological mechanisms associated with their passive avoidance are the same.

Given the association between poor passive avoidance and conduct disorder, antisocial behavior, ADHD, substance abuse, and impulsivity, there is reason to believe that the psychobiological processes associated with externalizing disorders contribute to the problems that many disinhibited individuals have inhibiting prepotent approach responses to avoid punishment. That is, capacity-related deficits in modulating the top-down focus of attention may undermine a person's ability to activate the non-dominant, inhibitory response in the face of reward cues. To the extent that this conceptualization has merit, it could be predicted that executive function deficits (e.g., Ishikawa & Raine, this volume), smaller P300 amplitude (e.g., Patrick et al., this volume), and anomalous DLPFC activation will mediate the poor passive avoidance of these groups.

However, there is also convincing evidence that low-anxious psychopathic offenders (i.e., primary psychopaths) commit more passive avoidance errors than controls on this task. If, as

suggested by multiple authors in this section, primary psychopathy is associated with hypoactivation of paralimbic circuits, it may be predicted that this hypoactivation and associated deficits in bottom-up modulation of top-down attention will mediate the passive avoidance deficits of this group. This prediction could be evaluated using imaging methods similar to those employed by Kiehl (this volume) in his studies of emotion and language processing in psychopathic individuals. Alternatively, researchers could use behavioral assessments of response modulation (Newman et al., this volume; see also Fisher & Blair, 1998) or other measures of bottom-up modulation to evaluate whether these deficits mediate the poor passive avoidance of primary psychopaths.

Given the apparent importance of impulsivity in the groups displaying poor passive avoidance, a third possibility is that the performance deficits of these groups reflect differential activation of the left frontal cortex and a heightened propensity to enact prepotent approach responses (e.g., Harmon-Jones, this volume; see also Newman et al., 1985). In this case, the prediction would be that the poor passive avoidance of some disinhibited individuals will be associated with differential activation of the left frontal cortex as measured using electroencephalogram or neural imaging techniques.

Using this bootstrapping approach would enable researchers to parse the etiological homogeneity associated with poor passive avoidance. In addition to testing the hypotheses described above, it would be possible to analyze the etiological specificity of the diagnostic criteria. With regard to externalizing psychopathology and deficits in top-down control, careful analysis may reveal that DLPFC-related deficits in attentional capacity may relate specifically to those externalizers who display significant levels of impulsivity or be limited to externalizers who have engaged in significant substance abuse (see Ishikawa & Raine, this volume; Patrick et al., this volume). With regard to psychopathy, it would be of substantial interest to determine whether the poor passive avoidance learning of psychopathic individuals, like that of externalizers, is associated primarily with deficiencies in top-down processing as predicted with

the two-factor conceptualization of psychopathy. Alternatively, their poor passive avoidance might be associated with deficiencies in bottom-up processing of the type emphasized by Kiehl, Blair, and Newman et al. (this volume). Of course, it is also possible that the evidence would support both models. In this case, it might be useful to augment psychopathy assessments with other descriptive characteristics such as low anxiety (see Brinkley et al., 2004) or signs of externalizing psychopathology in order to subgroup psychopathic individuals who display more homogeneous results on the psychobiological indicators. To the extent that such additional characteristics reliably identify more homogeneous subgroups, they could then be used to refine our classification of psychopathic individuals.

This example may also be used to illustrate the application of the bootstrapping technique to dimensional traits such as impulsivity. Examination of the literature on disinhibitory psychopathology reveals that the term *impulsivity* is used in a wide variety of ways. Following Gray (1981), Newman and colleagues (Wallace, Bachorowski, & Newman, 1991; Newman, 1997) equate impulsivity with heightened activation in a hypothetical approach activation system (see also Depue & Collins, 1999) and contrast neurotic extraverts (i.e., impulsive individuals) with stable introverts (non-impulsive individuals) to assess this variable. Other investigators (e.g., Krueger, McGue, & Iacono, 2001, Patrick et al, this volume) associate the latent trait underlying the externalizing dimension with the personality dimension of constraint as measured by the Multidimensional Personality Questionnaire (Tellegen, 1982). Impulsivity is also a core characteristic of psychopathy (Hare, 1991). Using the assessments described above, it should be possible to refine our definitions of impulsivity. For example, careful analysis might reveal that the type of impulsivity indexed by neurotic extraversion reflects differential activation of the left hemisphere, that the type of impulsivity associated with externalizing psychopathology relates to DLPFC-mediated deficits in executive control and reduced P300 (see Patrick et al, this volume), and that the type of impulsivity associated with psychopathy reflects hypoactivation in paralimbic circuitry (see Newman, 1997 for further discussion of these diverse pathways).

To illustrate how bootstrapping may be used to increase the specificity of psychobiological mechanisms as opposed to clinical syndromes and trait dimensions, we consider the VMPC model described by Tranel et al (this volume, see also Damasio, 1994). According to Tranel and colleagues, damage to the VMPC results in a syndrome, referred to as “acquired sociopathy”, that involves emotional detachment, poor modulation of emotional reactions, deficits in decision making, disturbances in planning and other goal-directed behavior, and poor insight. In addition, individuals with VMPC damage perform poorly on the Iowa gambling task and their performance deficits on the task appear to reflect insensitivity to future consequences as opposed to insensitivity to punishment or hypersensitivity to reward (e.g., Bechara, Tranel, & Damasio, 2000). The success of this model provides an excellent example of the potential for progress in cognitive/affective neuroscience to advance understanding of disinhibitory psychopathology.

Whereas early research on the model demonstrated that deficient use of somatic markers on the Iowa gambling task was associated with VMPC damage, there is now additional evidence indicating that it is also associated with amygdala dysfunction (e.g., Bechara, Damasio, Damasio, & Lee, 1999). In addition, Tranel, Bechara, and Denburg (2002) have demonstrated that the association between VMPC dysfunction and acquired sociopathy is specific to right-sided damage (see also, Clark et al., 2003). Furthermore, it has become apparent that poor decision making on the gambling task is associated with deficits in executive functions / working memory that are normally associated with other regions of PFC (Bechara & Martin, 2004; Busemeyer & Stout, 2002; Hinson et al., 2002). Although much of the research on the VMPC model has focused on its implications for psychopathic behavior, more recent evidence suggests that it may be equally applicable to other disinhibitory syndromes including disorders of addiction, pathological gambling, and impulsivity (Bechara, 2003, Petry, 2001). The fact that these syndromes are related to performance on the gambling task does not necessarily mean that they are related to VMPC deficiencies, though such results have led Bechara (2003) to conclude that

“VM cortex dysfunction is also evident in subgroups of individuals who are addicted to substances” (p. 23).

Overall, these recent findings raise questions about the precise implications of VMPC functioning for disinhibitory psychopathology and decision making. In light of its association with substance abuse, it is relevant to ask whether the association between VMPC is specifically associated with PCL-R factor 2 as opposed to PCL-R factor 1. Though the model’s emphasis on affective processing suggests that VMPC functioning would be associated with PCL-R factor 1 or the PCL-R total score, its associations with substance abuse, working memory deficits, and impulsivity are more consistent with externalizing psychopathology (see also, Bechara & Martin, 2004). To date, the evidence linking performance on the gambling task to psychopathy is mixed (Blair et al., 2001; Lösel & Schmucker, in press; Mitchell, Colledge, Leonard, & Blair, 2002; Schmitt, Brinkley & Newman, 1999; van Honk, Hermans, Putman, Montagne, & Schutter, 2002). One possibility is that sample-related differences in the magnitude of group differences on PCL-R factor 2 are contributing to the inconsistencies.

As noted by Kiehl (this volume), there is lack of neuroimaging data pertaining to VMPC / OFC functioning in psychopathic individuals. In addition, both Kiehl and Soderstrom (this volume) describe this brain region as operating within a broader paralimbic system circuitry. Thus, even with imaging data, it would be difficult to distinguish individual differences in VMPC functioning from bottom-up influences associated with other paralimbic structures or the diffuse influence of neuromodulators as proposed by Soderstrom. Moreover, there is reason to believe that VMPC /OFC functioning may be modulated by a person’s top-down focus of attention, especially when there are large demands on working memory. Using a secondary task to tax working memory while participants performed the gambling task, Hinson et al (2002) found that increased working memory load interfered with the use of affective reactions to guide decision making. According to the authors, such findings indicate that working memory processes play an important role in the development of somatic markers. Thus, deficiencies in the use of somatic

markers and activation in VMPC may sometimes reflect DLPFC-related deficits in working memory as well as other problems.

The literature on the somatic marker hypothesis also illustrates the bootstrapping methodology. Using traditional assessment tools to demonstrate the association of VMPC-related deficits with diverse groups is helping investigators to ask more specific questions about the nature of VMPC-mediated deficits. For instance, research demonstrating their relevance to substance abuse and other forms of externalizing psychopathology as well as psychopathy raise new questions regarding the diversity of psychobiological mechanisms that mediate and/or moderate VMPC-related deficits in decision making and self-regulation. Research on these questions may reveal that the poor decision making of psychopathic individuals is primarily a function of amygdala-related deficits that influence the formation of somatic markers (see Blair, this volume) whereas the decision making deficiencies associated with externalizing psychopathology reflects DLPFC-mediated influences in working memory. However, there are also other interesting possibilities that merit further research. As noted by Ishikawa and Raine (this volume), individuals displaying substance abuse, antisocial behavior, and impulsivity manifest reductions in PFC volume that cut across multiple regions of PFC suggesting that they may have correlated deficits in these brain regions. In this connection, it is also possible that VMPC-related deficiencies may be compensated for by application of DLPFC-mediated working memory with the results that disinhibitory psychopathology associated with VMPC deficiency will be most apparent in individuals whose working memory capacity is not sufficient to compensate for this deficit (see also, Lösel & Schmucker, in press).

### ***Summary and implications for future research***

The chapters in this section highlight four major themes of relevance to disinhibitory psychopathology: (1) the important role of mechanisms that modulate prepotent but maladaptive responses; (2) a distinction between externalizing disorders and primary psychopathy; (3) the necessity of continued refinement of specific psychobiological mechanisms associated with

disinhibitory psychopathology; and (4) the important impact of developmental processes and experiences on dysregulated behavior. We discuss each in turn.

Historically, progress in understanding and managing disinhibitory psychopathology has been hampered by a lack of compelling psychobiological explanations. As illustrated by the chapters in this section, investigators have started to address this problem. Capitalizing on rapidly developing knowledge in cognitive and affective neuroscience, the authors advance a number of psychobiological mechanisms for deficits in self-regulation and disinhibitory psychopathology. In spite of their diversity, the explanations for disinhibitory psychopathology share a common theme. In one way or another, all of the authors specify a breakdown in the psychobiological processes that modulate prepotent, maladaptive responses.

To clarify the similarities and differences among the proposed mechanisms, we translated the proposals into a common framework that conceptualizes self-regulation as maintaining a context-appropriate balance of attention between dominant and non-dominant neural networks (CABA). As noted above, this conceptualization is broad enough to encompass virtually all of the behavior problems associated with disinhibitory psychopathology. In addition, the diverse psychobiological mechanisms discussed in the chapters may be understood as alternative formulations for the difficulty that some people have integrating dominant and non-dominant information. To the extent that this abstract formulation of the core deficit applies, the task of researchers in disinhibitory psychopathology is to specify the origins, nature, and factors that moderate people's problem using non-dominant information to modulate their top-down focus of selective attention.

A second theme that emerges from this group of chapters involves the distinction between externalizing disorders and primary psychopathy. Although both forms of disinhibitory psychopathology are associated with chronic problems inhibiting maladaptive dominant responses, the explanations for these deficits are quite different. Research on individuals with externalizing disorders suggests that their failure to achieve a context-appropriate balance of

attention involves a capacity-related problem maintaining activation of non-dominant, context appropriate networks to the point where they out-compete less appropriate, but prepotent, neural networks. In other words, externalizing psychopathology appears to reflect a deficit in top-down control. By contrast, there is little evidence that deficits in executive functioning or cognitive capacity explain the deficiencies in context-appropriate attention displayed by primary psychopaths. Rather, the self-regulation problems of primary psychopaths appear to reflect deficits in bottom-up activation or related problems (e.g., restricted gating, see below) that normally modulate the top-down focus of selective attention. In light of the divergent psychobiological mechanisms associated with externalizing and psychopathy, this distinction has important implications for research on disinhibitory psychopathology as well as for the assessment and treatment of such disorders.

A third theme highlighted in this chapter involves the need for continued refinement in specifying the psychobiological processes associated with disinhibitory psychopathology. Although the distinction between psychopathy and externalizing disorders is a good starting point, it leads to other questions regarding the specific psychobiological mechanisms associated with these groups as well as the possibility of making more fine-grained distinctions within each group. The CABA framework provides a useful structure for conceptualizing and distinguishing alternative psychobiological mechanisms that undermine effective cognitive control. In addition, its links to rapidly developing areas of cognitive and affective neuroscience suggest that the framework will continue to evolve along with the science of cognitive control (MacCoon et al., 2004).

Historically, the distinction between psychopathy and other forms of disinhibitory psychopathology has emphasized emotion. Psychopathic individuals are most often characterized as antisocial by virtue of their lack of emotion whereas other antisocial groups are characterized as having cognitive, or even hyper-emotional, deficits that hamper self-regulation. The CABA framework provides a perspective on these traditional distinctions that is both broader and more

fine-grained. At the most general level, it highlights the importance of bottom-up activation, top-down control, and top-down/bottom-up interactions that modulate behavior. However, within each of these levels there are a variety of psychobiological processes that influence cognitive control. As noted, understanding of these processes is rapidly growing in sophistication along with research on cognitive control. With regard to top-down limitations in cognitive control, the chapters highlight the potential importance of DLPFC-mediated deficits in working memory that hamper inhibition. A fundamental tenet of CABA is that effective self-regulation requires sufficient cognitive capacity to activate non-dominant networks when they are more context appropriate than dominant networks. In addition to working memory capacity, however, successful self-regulation is strongly influenced by the amount of capacity needed to activate non-dominant networks to a sufficient degree. Thus, psychobiological factors that result in excessively rapid, strong, or inflexible activation of dominant networks may exceed a person's capacity for self-regulation despite normal working memory capacity (see Harmon-Jones, this volume, Wallace et al., 1991).

As this point suggests, bottom-up activation of neural networks is also a key variable influencing the demands for top-down control and the quality of self regulation. To the extent that new and potentially important information becomes activated and elaborated in a rapid and efficient manner, it requires less cognitive capacity to evaluate and, if necessary, alter the focus of top-down attention. However, any problem that hampers the registration, activation, or maintenance of bottom-up networks will have the opposite effect. It is this type of problem that the chapter authors associate with the self-regulatory deficits of psychopathic individuals. The chapters by Kiehl, Newman and colleagues, and Blair, in particular, emphasize various brain regions that might be responsible for deficient bottom-up modulation of attention in psychopathic individuals. Soderstrom highlights the potential importance of dopaminergic and serotonergic projections that mediate these response modulating functions.

Though each chapter emphasizes the bottom-up influences of limbic circuitry, the authors also acknowledge that OFC is an integral part of this system. Kiehl (this volume) makes this point explicitly in setting out his paralimbic hypothesis, Soderstrom includes OFC/VMPC in his formation of the neurobiology underlying the behavioral aspects of psychopathy (see Table 1), and Newman et al. cite Gorenstein and Newman's (1980) septo-hippocampal-orbitofrontal model as the basis for the work described in their chapter. Similarly, although he emphasizes amygdala dysfunction, Blair notes that much of the evidence is consistent with OFC dysfunction and speculates that this evidence is a consequence of developmental interactions between the amygdala and OFC. The potential importance of OFC and, especially VMPC, for disinhibitory psychopathology is also discussed by other authors in this volume (e.g., Ishikawa & Raine; Patrick et al.), though it is best elaborated in the chapter by Tranel and colleagues.

According to Tranel et al. (this volume), VMPC plays an important role in linking classes of stimuli with bottom-up somatic experiences that facilitate decision making. In addition, the authors clarify the important interactions between VMPC and DLPFC. In effect, the affective associations mediated by VMPC help to organize and determine priorities (i.e., dominance) via DLPFC and a deficit in VMPC functioning therefore increases the cognitive load on DLPFC. Conversely, experimental conditions that increase cognitive load reduce the impact of somatic markers (e.g., Hinson et al., 2003) illustrating that the use of somatic markers is dependent upon working memory capacity. Further research is needed to clarify the extent to which this limitation reflects the importance of cognitive capacity for establishing somatic markers (i.e., VMPC input) or for making use of them (i.e., VMPC output). With respect to CABA, this characterization of VMPC functioning highlights the importance of factors that mediate the interaction of top-down and bottom-up influences on attention.

As already noted, deficiencies in either top-down capacity or the strength of bottom-up activation can hamper the context appropriate balance of attention to dominant and non-dominant networks. Moreover, as illustrated by Tranel and colleagues' discussion of working memory and

VMPC, conditions that affect the efficacy of one process (e.g., top-down processing) influence the efficacy of the other (e.g., bottom-up processing) and visa-versa. However, these two variables are not the only ones influencing the quality of top-down / bottom-up integration and the context appropriate balance of attention. Identifying the range of processes that influence this integration is rapidly becoming a major focus of research on cognitive control. Recognizing the importance of top-down attention for maintaining context appropriate behavior, Cohen and colleagues (Botvinick, et al., 2001; MacDonald et al., 2000) have been investigating the brain mechanisms that modulate the focus of attention, such as the role of the anterior cingulate cortex (ACC) in conflict monitoring and engaging top-down control. The potential relevance of these ACC functions for externalizing psychopathology is discussed in the chapter by Patrick et al. and has also been a focus of Kiehl's research on psychopathy (e.g., Kiehl et al., 2001).

Another potentially important influence affecting the quality of top-down / bottom-up integration and self-regulation involves inter-hemispheric integration. As noted by Harmon-Jones, differential activation of the left frontal cortex is associated with ready expression of dominant approach responses and deficiencies in right frontal activation have been shown to have similar consequences for behavioral control. Such dynamics suggest that the context-appropriate balance of attention to dominant and non-dominant networks is affected by the balance of left and right frontal activation and may depend upon inter-hemispheric integration. Soderstrom (this volume) also notes the potential importance of inter-hemispheric integration for psychopathy. In this regard, it is noteworthy that Tranel et al. (this volume) note that it is damage to right VMPC that is associated with impaired use of somatic markers. Elsewhere (e.g., Hiatt & Newman, 2004), it has been argued that a deficit making use of right hemisphere information when the left hemisphere is differentially activated could account for most, if not all, of the processing anomalies associated with psychopathy. With regard to CABA, it may be speculated that right hemisphere resources play an important role in representing non-dominant information when left hemisphere resources are allocated elsewhere and that the use of such information to modulate

the top-down focus of selective attention relies on efficient inter-hemispheric integration (see Hiatt & Newman, 2004 for details).

Our brief consideration of ACC and inter-hemispheric integration highlights another important and understudied process that may undermine balanced attention, namely, the ease with which top-down resources may be reallocated to answer the ACC-mediated call for processing or to accommodate non-dominant information represented in the right hemisphere. Earlier, we discussed evidence demonstrating that DLPFC-mediated limitations in working memory could hamper the use of somatic markers. Indeed, there is rapidly growing evidence that diverse experimental manipulations that require top-down attention can limit capacity available for bottom-up activation, including such automatic responses as amygdala responses to fearful faces (Pessoa et al., 2002). Moreover, as illustrated by the phenomenon of “inattention blindness”, such effects may have as much to do with the focus or direction of attention as with attentional capacity per se. For example, using fMRI, Rees and his colleagues (1999) found that when attention was occupied with pictures, brain activation indicated no distinction between words and random letter strings even when these stimuli were looked at directly. The authors conclude that “visual recognition wholly depends on attention even for highly familiar and meaningful stimuli at the center of gaze” (p. 2504; see Most, et al., 2001 for a related point).

Thus, in addition to studying how DLPFC-mediated deficiencies in working memory capacity hamper self-regulation, it may be useful to consider the range of processes that modulate the top-down focus of attention and thus, indirectly limit the amount of attentional capacity available for processing non-dominant bottom-up information. That is, despite a normal “call for processing” by non-dominant networks, some people may fail to answer the call for processing if their top-down focus of attention is excessively narrow or inflexible (see Patterson & Newman, 1993). With regard to psychopathy, investigators have posited an unusual diversity of problems associated with modulation of top-down attention. As already discussed, psychopathy has been linked to hypo-functioning of the amygdala complex, the anterior and posterior cingulate cortex,

and septo-hippocampal system. In addition, psychopathy may also be associated with reduced right hemisphere influences while engaged in left-hemisphere mediated goal-directed behavior. Although it is conceivable that psychopathy is associated with dysfunction in numerous paralimbic and cortical structures, a more parsimonious explanation is that a problem gating non-dominant information into DLPFC may mediate the diverse array of information processing limitations. In this regard, Soderstrom's (this volume) evidence and speculation regarding dopaminergic anomalies in psychopathic individuals may be especially relevant. Research on the attentional gating problems associated with schizophrenia already suggests an association between particular dopaminergic projections and the gating of information into or out of PFC (e.g., Braver, Barch, & Cohen, 1999).

In contrast to proposals regarding externalizing disorders (where there is some agreement regarding deficiencies in PFC-mediated deficiencies in executive functioning), there is a greater need to specify and evaluate alternative hypotheses concerning psychobiological explanations for the information processing deficits of psychopathic individuals. The VMPC (e.g., Tranel et al), amygdala complex (e.g., Blair), septo-hippocampal system (Newman et al.), paralimbic system more generally (Kiehl), and dopaminergically-mediated gating mechanisms (Soderstrom) represent diverse proposals that should be fertile ground for generating and testing alternative hypotheses.

Although these psychobiological mechanisms are associated with overlapping behavioral problems, it is also possible to contrast their effects. For example, VMPC, amygdala, and SHS have all been associated with deficient passive avoidance learning. However, VMPC is associated with a more general failure to appreciate the affective significance of complex stimuli, the amygdala complex is associated with deficits in active as well as passive avoidance, and the SHS is associated with deficiencies in passive avoidance but normal active avoidance. Similarly, both amygdala and SHS have been associated with deficits in fear conditioning, but the SHS is associated with deficits in context conditioning and delayed conditioning whereas amygdala

damage is associated with a more general deficit in fear conditioning. To the extent that research provides support for a specific pattern of dysfunction, it may be possible to link psychopathy or specific psychopathic subtypes with a particular psychobiological mechanism.

To date, the evidence does not provide unequivocal support for any particular neural substrate. In large part, this is because the performance deficits associated with psychopathic individuals appear to depend upon circumstances that are not clearly specified by any of the psychobiological models as they are currently conceptualized. Psychopaths are deficient in passive avoidance learning but they are not deficient in active avoidance learning and even perform passive avoidance contingencies as well as controls in the absence of competing reward contingencies (Newman & Kosson, 1986). There is evidence that the fear conditioning deficits of psychopathic individuals are not specific to context or delayed conditioning (e.g., Flor et al., 2002). Whereas the first finding appears more consistent with SHS dysfunction than with amygdalar dysfunction, the latter finding is more consistent with amygdalar dysfunction. As already noted, the evidence on psychopaths' use of somatic markers in the Iowa gambling task is inconsistent. Moreover, in contrast to patients with VMPC damage, psychopathic individuals typically display normal autonomic nervous system reactivity while viewing affectively significant pictures (Levenston, et al., 2000; Patrick et al., 1993, but see Blair, Jones, Clark, & Smith, 1997). Although psychopathic individuals display less "emotion facilitation" on lexical decision tasks, this finding is moderated by which hand is used to perform the task and, thus presumably, which cerebral hemisphere is controlling response output (Lorenz & Newman, 2002).

The evidence with regard to psychopaths' performance on reversal learning and go/no-go tasks is also equivocal. To the extent that performance on these tasks is moderated by the salience of the switch or no-go stimuli as suggested by Blair (this volume), it is unclear whether psychopaths' sporadic performance deficits on such tasks relates primarily to OFC functioning or other neural circuitry that has been linked to OFC and reversal learning (e.g., SHS; Gorenstein &

Newman, 1980; Gray, 1987). Similarly, ACC is associated with error monitoring and performance on tasks involving response conflict such as Stroop and flanker tasks (Botvinick et al., 2001). However, psychopaths display comparable interference on the standard color-word task (Hiatt et al., 2004; Smith et al., 1992). Though the implications of behavioral performance for brain functioning can be misleading because people may compensate for neurological deficiencies using diverse brain regions (see Kiehl, this volume), in the case of Stroop performance compensation would involve using other resources to increase interference (response conflict) and therefore seems unlikely. Moreover, there is evidence that psychopathic individuals display significantly less interference than controls on Stroop-like tasks when the incongruent information is spatially separated from (i.e., peripheral to) the top-down focus of selective attention (Hiatt et al., 2004; Newman, Schmitt, & Voss, 1997; Vitale et al., in press). The nomological network provided by behavioral data should be valuable in pointing to further refinements of existing psychobiological mechanisms. Future behavioral data may not only clarify the psychobiological processes associated with psychopathy, but may also deepen our understanding of neurological processes mediating cognitive control more generally.

A fourth theme that emerged in the chapters concerns the effects of developmental processes and experience. With regard to the distinction between acquired and developmental sociopathy, Tranel et al. (this volume) note that individuals with acquired sociopathy late in life are less likely to exhibit violent behavior than those who sustained VMPC damage early in life or those who have been psychopathic their entire life (i.e., developmental psychopathy). Such findings indicate that at least some consequences of VMPC damage are influenced by developmental interactions. Blair (this volume) uses a developmental perspective to interpret his lab's discrepant findings on behavioral measures that have been linked to OFC. Whereas psychopathic adults appear to perform more poorly than controls on these measures, psychopathic adolescents do not. According to Blair, this pattern of results may reflect the indirect effects of early amygdalar dysfunction which, over time, weakens involvement of the OFC in reversal learning. Such

considerations highlight the fact that neurological as well as environmental factors may exert important influences on brain development. Thus, when group differences in neural activity are found using neuroimaging and related methodologies, it is difficult to discern whether such differences played a causal role in differentiating the groups or reflect an indirect manifestation of other more fundamental differences, the consequences of developmental experiences, or an interaction between a psychobiological predisposition and experience. As with performance measures then, it is crucial to interpret evidence of psychobiological dysfunction in light of theoretical considerations and systemic influences<sup>2</sup>.

### ***Conclusion***

As illustrated by the chapters in this section, there appears to be an emerging consensus that psychopathic and externalizing behavior involve problems modulating dominant or pre-potent responses. This conceptualization of disinhibitory psychopathology does not necessarily explain why people do what they do (i.e., the content of behavior) but, instead, emphasizes the processes that hamper self-regulation and predispose individuals to the disinhibited expression of maladaptive behaviors, whatever such behaviors may be.

The chapters also highlight the fact that dysregulation in psychopathic individuals is due to different psychobiological processes than other syndromes of disinhibition. Whereas psychopathy is thought to reflect deficiencies in the bottom-up processes that normally modulate attention and goal-directed behavior, the other syndromes of disinhibition are associated with deficiencies in working memory and attentional capacity which, in turn, hamper the implementation of top-down control. Although proposals highlighting the response modulating function of the limbic system are not new (e.g., Gorenstein & Newman, 1980), the importance of this function for cognitive control has only recently become a major focus of neuroscience research due to improved ability to study subcortical structures (e.g., fMRI) in humans. It seems likely that further technological advances will similarly expand the range of candidate neural mechanisms associated with deficits in cognitive-affective control. In this regard, it seems

especially important to (a) enhance understanding of cognitive - affective interactions, (b) clarify the impact of cerebral asymmetries for self-regulation, (c) coordinate behavioral and neuroimaging research, and (d) incorporate a developmental perspective on the psychobiological processes that distinguish disinhibitory psychopathology from other forms of adjustment (see Curtis & Cicchetti, 2003).

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### *Footnotes*

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<sup>2</sup> In light of such considerations, it is illustrative to consider the effects of gender on the manifestation of psychopaths' emotion processing deficits [introducing new stuff in summary?]. Whereas passive avoidance and other emotion processing deficits are considered the hallmark of psychopathy, psychopathic women do not display the passive avoidance, extinction, or emotion facilitation deficits that characterize psychopathic men (Vitale et al., 2001; Vitale, MacCoon, & Newman, 2004). However, they do display other response modulation deficits demonstrated by psychopathic men (Vitale et al., in press, Vitale et al., 2004). Although replication is needed, such evidence suggests that gender/cultural factors may influence sensitivity to threat and other emotion stimuli. It would be of substantial interest to discern the extent to which such gender-related differences in performance are also associated with differences in neural activation in the brain's emotion processing circuitry.