



PHYSIOLOGICAL MARKERS OF EMOTION AND BEHAVIOR DYSREGULATION IN EXTERNALIZING PSYCHOPATHOLOGY

Theodore P. Beauchaine

Much of the research conducted in our lab over the past decade has focused on identifying peripheral and central nervous system (CNS) markers of both trait impulsivity and emotion dysregulation in preschoolers (e.g., Crowell et al., 2006), middle schoolers (e.g., Shannon, Beauchaine, Brenner, Neuhaus & Gatzke-Kopp 2007), and adolescents (e.g., Crowell et al., 2005). This body of work includes studies of boys with attention-deficit/hyperactivity disorder (ADHD), boys with conduct disorder (CD; e.g., Beauchaine, Katkin, Strassberg, & Snarr, 2001), and girls with borderline personality traits (e.g., Crowell, Beauchaine et al., 2008). One key assumption of this work is that inherited impulsivity interacts across development with socialized deficiencies in emotion regulation (ER) to promote the development of conduct problems among boys and borderline traits among girls. Although space constraints preclude a full description of the theoretical bases of this assumption, in writing this chapter, I summarize how the use of autonomic nervous system (ANS) markers, neuroimaging, and genetic data have led my research group to our current thinking about the roles of impulsivity and emotion dysregulation in the development of externalizing psychopathology. I note at the outset that my discussion of environmental risk is limited given the objectives of this monograph. However, I consider such risk factors to be as important in the development of psychopathology as biological vulnerabilities (see Beauchaine, Hinshaw, & Pang, 2010). Furthermore, although not discussed in this chapter, and not difficult to identify in humans, epigenetic alterations in the DNA structure that are brought about through adverse life events are also likely to potentiate psychopathology (Mead, Beauchaine, & Shannon, 2010; Tremblay, 2005).

Corresponding author: Theodore P. Beauchaine, Department of Psychology, Washington State University, Pullman, WA 99164, email ted.beauchaine@wsu.edu

The conceptual model that informs my research on the development of externalizing behaviors and borderline personality traits has been described in several recent reviews (Beauchaine, Gatzke-Kopp, & Mead, 2007; Beauchaine, Klein, Crowell, Derbidge, Gatzke-Kopp, 2009; Beauchaine, Crowell, & Linehan, 2009). Broadly speaking, this model can be summarized as follows (Beauchaine et al., 2009, 2010): (1) trait impulsivity, derived largely from heritable compromises in central dopamine (DA) function, is a principal predisposing vulnerability to externalizing behavior disorders, including borderline pathology; (2) impulsive individuals are especially vulnerable to developing externalizing behavior disorders within high-risk family environments in which emotional lability is shaped by operant reinforcement contingencies; and (3) over time, these reinforcement contingencies result in enduring patterns of emotion dysregulation, culminating in antisocial and borderline personality development among impulsive individuals.

TRAIT IMPULSIVITY AND EXTERNALIZING BEHAVIOR DISORDERS

Although definitions of impulsivity abound, my research group defines the construct as “behavior that is socially inappropriate or maladaptive and is emitted without forethought” (Oas, 1985, p. 142). This trait is common to all disorders along the externalizing spectrum, including ADHD, oppositional defiant disorder (ODD), CD, antisocial personality disorder (ASPD), and many drug and alcohol dependencies (Beauchaine & Neuhaus, 2008; Beauchaine et al., 2010). Behavioral genetics research indicates that these disorders share a common latent vulnerability (Tuvblad, Zheng, Raine, & Baker, 2009), which is over 80% heritable (Krueger et al., 2002) and is best described as trait impulsivity. One challenge we have faced is identifying a biological marker of impulsivity that can be used across a broad age range. Though neuroimaging can be used to identify the CNS substrates of impulsivity among adolescents (Beauchaine, Sauder, Gatzke, Kopp, Shannon, & Aylward, *in press*), it is difficult to use it with externalizing preschoolers and middle schoolers. Thus, my research group has developed alternative means for assessing biological markers of impulsivity. Achieving this goal requires knowledge of structural and functional relations between the CNS and ANS (Beauchaine, 2009).

CENTRAL DOPAMINE FUNCTIONING AND TRAIT IMPULSIVITY

It has long been known that impulsive individuals, including those with ADHD, ODD, CD, ASPD, and various addictive disorders respond differently to rewards than do controls. Across a number of monetary incentive paradigms, males with these disorders persevere in reward responding for

much longer than their peers both (a) when contingencies turn against them and they begin to lose money and (b) when incentives are discontinued entirely (e.g., Giancola, Peterson, & Pihl, 2006; Matthys, van Goozen, Snoek, & van Engeland, 2004). A core CNS substrate of aberrant reward responding is underactivation in the ventral striatum, an evolutionarily old network of interconnected neural structures that subserves approach motivation in mammals, including nonhuman primates and humans. This brain region is rich in dopaminergic projections, which are less responsive to reward—including monetary incentives—among impulsive individuals than among controls (see Durston, 2003; Sagvolden, Johansen, Aase, & Russell, 2005). Consistent with theories of underarousal (e.g., Gatzke-Kopp, Raine, Loeber, Stouthamer-Loeber, & Steinhauer, 2004), my research group argued that those with impulse control disorders engage in excessive reward-seeking behaviors in part to upregulate a chronically underactive mesolimbic DA system, which is experienced psychologically as an aversive and irritable mood state (e.g., Laakso et al., 2003).

CARDIAC PRE-EJECTION PERIOD: A MARKER OF CENTRAL DA RESPONDING?

Several sources of evidence now suggest that cardiac pre-ejection period (PEP)—indexed as the time interval between left ventricular depolarization and ejection of blood into the aorta—marks striatal DA responding during approach behaviors, including those elicited by monetary incentives (Brenner, Beauchaine, & Sylvers, 2005). PEP is controlled by the sympathetic nervous system (SNS), with shorter intervals indicating a stronger sympathetic response. The argument that PEP shortening marks central DA reactivity to reward is based on several considerations. First, behavioral approach requires expenditure of energy, and an important function of the SNS is to mobilize resources to meet metabolic demands. Furthermore, increases in cardiac output required for motivated behavior are mediated by SNS-induced changes in the contractile force of the left ventricle (Sherwood, Allen, Obrist, & Langer 1986). Finally, infusions of DA agonists into striatal structures produce SNS-mediated increases in cardiac output (van den Buuse, 1998), which are similar to those observed when normal controls participate in reward tasks. Taken together, these observations suggest that reduced SNS-linked cardiac reactivity to incentives is a likely marker attenuated DA responding. This argument is supported further by research indicating that PEP shortening among controls is *specific* to conditions of reward and is not observed during extinction (Brenner et al., 2005).

My research group and others (e.g., Bubier & Drabick, 2008) have now examined PEP responses to incentives among externalizing preschoolers, middle schoolers, and adolescents, ages 4–18 (Beauchaine et al., 2001;

Beauchaine, Hong, & Marsh, 2008; Brenner & Beauchaine, 2011; Crowell et al., 2006; Mead et al., 2004). These samples have included individuals with ADHD, ODD, CD, and antisocial personality traits. In each of our studies, male externalizers exhibited less PEP reactivity to rewards than controls. In fact, in most of our studies, *no* PEP reactivity to incentives has been observed among the externalizing groups. These findings suggest that the neural substrates of impulsivity may be established by age 4. This would be expected if (a) disorders across the externalizing spectrum, including ADHD, share a heritable etiological substrate (see above) and (b) PEP reactivity to incentives marks the biobehavioral expression of this trait.

EMOTION REGULATION AS A MODERATOR OF EXTERNALIZING VULNERABILITY

Recall from the model presented earlier that impulsivity develops into more severe behavior problems only when coupled with deficient ER. Emotion regulation comprises the processes through which emotional experience and expression are shaped—whether volitionally or automatically—in the service of adaptive behavior (Thompson, 1990). Following from this definition, emotion *dysregulation* might best be described as a pattern of emotional experience or expression that interferes with appropriate goal directed behavior. In most forms of psychopathology, one or more negative emotions (sadness, panic, rage) is experienced either too intensely or for too long to be adaptive (Beauchaine et al., 2007). Thus, emotion dysregulation is a broad risk factor for psychopathology (Beauchaine, 2001).

Much has been learned about the CNS substrates of ER in the past decade. Key neural structures that subservise ER include the amygdala and the ventromedial prefrontal cortex (VMPFC; see Goldsmith, Pollak, & Davidson, 2008). The VMPFC inhibits amygdala activation when individuals purposefully regulate negative emotions. Furthermore, lesions to the VMPFC impair ANS responses to emotional stimuli (Verbane & Owens, 1998). Much has also been written about the modulatory effects of certain brainstem nuclei—particularly the nucleus ambiguus—on emotional expression (see Porges, 2007). These nuclei serve as final common pathways—via the vagus nerve—from the central nervous system to the cardiovascular system.

RESPIRATORY SINUS ARRHYTHMIA AND EMOTION REGULATION

At the parasympathetic nervous system (PNS) level, the ability to regulate emotions is often marked by respiratory sinus arrhythmia (RSA), a quantification of cyclic increases and decreases in heart rate across the respiratory cycle (see Beauchaine, 2001; Obradović & Boyce, this volume; Porges, 2007).

Under appropriate stimulus conditions, RSA indexes neural traffic through the vagus nerve (Porges, 1995). Since publication of Porges's polyvagal theory describing relations between PNS responding and emotional expression, a consistent body of research has emerged linking deficiencies in RSA to emotion dysregulation and psychopathology (see Beauchaine et al., 2007; Hastings et al., 2008; Porges, 2007). As we have reviewed elsewhere, low baseline RSA and excessive RSA withdrawal in response to emotionally evocative stimuli have been linked to conduct problems, trait hostility, eating disorders, anxiety disorders, depression, and panic—among other adverse outcomes (see Beauchaine, 2001).

Although some researchers have suggested that impulsivity is a direct manifestation of emotion dysregulation, the two traits derive from very different etiological and neural substrates, as described previously. Accordingly, in the model presented above, I view impulsivity and ER as distinct behavioral constructs. Indeed, in contrast to impulsivity, which is almost entirely heritable, emotion dysregulation is largely socialized within families (Beauchaine et al., 2007; Beauchaine et al., 2009; Snyder, Schrepferman, & St. Peter, 1997). Consistent with this assertion, behavioral genetics studies indicate that individual differences in RSA are in large part determined by environmental factors (Kupper et al., 2005).

My research group typically measures RSA both at baseline and in response to emotionally evocative (e.g., sadness-inducing) stimuli. In fact, in each of the studies cited earlier in which PEP responding to reward was assessed, RSA data were also collected during negative emotion induction. Interestingly, among externalizers, attenuated baseline RSA and excessive RSA reactivity to emotion evocation were observed only in the conduct-disordered middle school and adolescent samples (Beauchaine et al., 2001; Beauchaine, Hong, & Marsh, 2008; Mead et al., 2004). In contrast, neither RSA nor RSA reactivity discriminated externalizing preschoolers with ADHD and ODD from controls (Crowell et al., 2006). At first, we found this perplexing because these preschoolers are at very high risk for later conduct problems and delinquency (Campbell, Shaw, & Gilliom, 2000). However, others have demonstrated that ADHD progresses to more serious conduct problems only for children in families where emotional lability is negatively reinforced (e.g., Patterson, DeGarmo, & Knutson, 2000). Accordingly, our current thinking is that impulsivity may be “regulated”—expressed as pure ADHD—or “dysregulated”—expressed as more serious externalizing outcomes—depending on ER strategies that are socialized through recurring parent–child interactions. In the case of externalizing preschoolers, it may be too soon for familial negative reinforcement processes to have fully shaped emotional lability, with consequential deficiencies in RSA (see Beauchaine et al., 2007).

As noted earlier, our model specifies that trait impulsivity confers risk for serious externalizing conduct only when *coupled with* familial socialization of

emotion dysregulation. According to this perspective, one would expect that adolescents with pure ADHD would exhibit less emotional lability, as indexed by RSA reactivity to emotion evocation, than adolescents with ADHD and CD. In one of our studies contrasting adolescents with pure ADHD versus those with ADHD and CD, this is exactly what we found (Beauchaine et al., 2001).

RSA AS A MODERATOR OF EXTERNALIZING VULNERABILITY

Given that emotion dysregulation and associated RSA deficiencies confer risk for psychopathology—especially among impulsive children and adolescents—well socialized ER skills, reflected both behaviorally and in high RSA, should *buffer* children from some of the adverse effects of trait impulsivity. In our own research, we have demonstrated buffering effects of RSA on relations between paternal ASPD and adolescent conduct problems (Shannon et al., 2007). Children with low baseline RSA tended toward conduct problems regardless of the level of paternal ASPD symptoms, whereas children high in RSA were partially protected from their father’s antisociality. Moreover, an accumulating body of literature links high RSA to children’s positive adjustment in the face of diverse familial risk factors for psychopathology, including interparental conflict, parental drinking, and parental divorce (El-Sheikh, 2005; El-Sheikh, Harger, & Whitson, 2001; Katz & Gottman, 1995).

THE IMPORTANCE OF STIMULUS CONDITIONS

It is not unusual for social scientists to mistakenly equate behavioral constructs and traits such as impulsivity with psychophysiological markers such as cardiac PEP. When this mistake is made, authors often expect the psychophysiological marker—in this case PEP—to discriminate between impulsive and nonimpulsive children—regardless of stimulus conditions (Beauchaine, 2009). However, our data show quite clearly that PEP reactivity is not observed during extinction or emotion evocation in impulsive individuals *or* controls. Rather, it is only during reward tasks that group differences emerge. Accordingly, our choice to use stimulus conditions of reward to assess PEP responding as a marker of impulsivity is based on strong theoretical considerations regarding the function of SNS-linked cardiac reactivity during approach behaviors, as outlined above (Beauchaine, 2001; Beauchaine et al., 2001, 2007). A similar argument can be advanced for RSA reactivity as a marker of emotional lability (see also Hastings et al., 2008). Here, one would expect better differentiation between labile individuals and controls during conditions of emotion evocation than during conditions of reward. Again, our data support this assertion. Unfortunately, researchers often

expect to find group differences in psychophysiological markers across all of their stimulus conditions. When they do not, results are often interpreted as null findings. This illustrates how atheoretical choices of stimulus conditions can lead to considerable confusion in the literature (Beauchaine, 2009). Researchers should therefore select their stimuli carefully, based on the specific physiological process that they seek to mark (Cole, Martin, & Dennis, 2004; Fox, Kirwan, & Reeb-Sutherland, this volume; Goldsmith & Davidson, 2004).

FUTURE DIRECTIONS: BIOLOGY × ENVIRONMENT INTERACTIONS

Following from my discussion thus far, it has become increasingly clear that certain biological vulnerabilities interact with contextual risk to potentiate psychopathology (see also Bubier, Breiner, & Drabick, 2009). In addition to psychophysiological markers of vulnerability, a number of Gene × Environment interactions have been reported in the etiology of externalizing disorders. Perhaps the most famous of these was reported by Caspi et al. (2002), who found that the combination of child maltreatment and a polymorphism in the monoamine oxidase-A (MAOA) gene predicted antisocial behavior. Those who experienced maltreatment *and* inherited the low MAOA activity gene were at much higher risk for antisocial behavior than those who experienced maltreatment but did not inherit the low MAOA activity gene.

Importantly, biological vulnerabilities and environmental risk factors are often synergistic rather than additive (Crowell, Beauchaine, & Lenzenweger, 2008; Raine, 2002). Furthermore, significant Biology × Environment interactions are sometimes observed in the absence of main effects (Beauchaine, Neuhaus, Brenner, & Gatzke-Kopp, 2008). Thus, it is critical that the joint effects of vulnerabilities and risk factors be explored—even when each in isolation is only weakly associated with adverse outcomes. For example, in a recent study of biological and behavioral correlates of self-injury among adolescent females, we reported that peripheral serotonin was reduced among self-injuring teens (Crowell et al., 2005). Independently, however, peripheral serotonin was only a weak predictor of lifetime self-injurious events. Moreover, observational ratings of negativity within mother–daughter dyads failed to predict self-injury. Nevertheless, the Serotonin × Negativity interaction accounted for a remarkable 64% of the variance in self-injurious behaviors, including suicide attempts (Crowell et al., 2008).

In addition to such moderating effects, mediational models linking genes, neural responses, and behavior are now emerging. For example, Buckholtz et al. (2008) recently reported that stronger neural coupling between the amygdala and VMPFC mediated links between MAOA alleles and personality. This finding is particularly exciting because the mediational model spanned genes → brain → behavior. It has often been noted that genes do not affect behavior

directly (see, e.g., Beauchaine, Gatzke-Kopp, & Hinshaw, 2008). Mediational models specifying neural processes through which genes influence behavior are therefore an extremely important development. These models take us one step closer to understanding the complexities of behavioral dysfunction. In our view, these studies mark a new generation in behavioral research. It is our hope that the specification of causal pathways from genes to behavior will answer important questions that behavioral scientists have been pondering for generations.

In this brief chapter, I have summarized my thinking about how heritable trait impulsivity can be amplified across development through socialization mechanisms that occur within families. I have also explained how psychophysiological variables, and to a lesser extent genetics and neuroimaging, have informed research. Though my focus has been on adverse effects of interactions between impulsivity and emotion dysregulation, our model also implies that interventions that focus on teaching strong ER skills to impulsive children and their parents may prevent the development of conduct problems as children mature. Thankfully, such interventions already appear to be effective (see, e.g., Beauchaine, Reid, & Webster-Stratton, 2005). Through careful use of ANS and CNS markers, we are learning more about the brain bases of behavior and behavioral change.