REWARD AND PUNISHMENT PROCESSING IN SUBGROUPS OF YOUTH WITH CONDUCT PROBLEMS: CHARACTERIZATION OF THE NEURAL RESPONSE AND IMPLICATIONS FOR INTERVENTION

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Extensive research has focused on abnormalities in reward and punishment processing as a mechanism underlying childhood-onset conduct problems (CP), particularly among CP youth with callous-unemotional (CU) traits. However, there is still debate about the neural underpinnings of this mechanism. Moreover, while researchers suggest that these youth may be resistant to social learning based interventions due to deficits in reward and punishment processing, this has not been empirically investigated. This dissertation expands on previous research by 1) examining neural abnormalities in reward and punishment processing among CP youth with and without CU traits relative to healthy controls (HC); and 2) assessing whether individual differences in reward and punishment processing are associated with CP following intervention. Prior to treatment, neural responsivity to reward and punishment was assessed in key regions of interest among a sample of boys (ages 8-11; n=64) using an event-related fMRI task. CP youth were then randomly assigned to an empirically supported treatment (Stop-Now-And-Plan (SNAP) or treatment as usual, and were re-evaluated following intervention. Baseline differences in brain function were examined as a predictor of post-intervention CP. Results demonstrated differences in neural reactivity to be most reliable and robust with regard to amygdala responsivity to punishment. Specifically, boys with CP demonstrated reduced amygdala reactivity to punishment relative to HC; however, there was no difference in responsivity between subgroups of children with CP, suggesting that reduced punishment

sensitivity may be characteristic of boys with early-onset CP regardless of CU traits. Regarding reward, CP youth with low levels of CU exhibited reduced reactivity to reward across several key regions of interest (e.g., caudate, amygdala) while CP youth with CU were characterized by significant activation to reward that did not differ from HC; notably, this was reduced to non-significance after controlling for co-occurring internalizing problems. Finally, although random assignment to SNAP resulted in significant reductions in CP at post-treatment follow-up, responsivity to reward and punishment was unrelated to post-treatment levels of CP. Findings highlight the importance continuing to investigate the role of reward and punishment processing in the development of early-onset CP and point to potential implications for intervention.

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PREFACE

I will be forever indebted to the many that have helped to make the completion of this journey possible. Thank you to my committee members for all of their feedback and guidance throughout my dissertation and the many milestones that preceded it. A special thank you to Steve Manuck, who has gone above and beyond to facilitate and support my growth. To my advisor, Dustin Pardini, thank you for taking a chance on me as your first graduate student. You have continually challenged me to be a better thinker, a better writer and a better researcher. This would not have been possible without you.

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1.0 INTRODUCTION

Longitudinal research has consistently shown the presence of childhood-onset conduct problems (CP) to be an important risk factor for the development of severe and protracted trajectories of antisocial behavior and delinquency. Improving our understanding of the mechanisms that underlie the manifestation and persistence of early CP has significant implications for prevention and intervention efforts. Extensive research has focused on abnormalities in reward and punishment processing as one potential mechanism contributing to the development of CP in youth, particularly in CP youth with callous-unemotional (CU) traits or psychopathic features. Historically, reward and punishment processing has been conceptualized in terms of two neurobiological systems and considerable behavioral work has focused on potential associations between CP and deficits in one or both of these systems. While behavioral work documents fairly consistent performance deficits on tasks targeting reward/punishment responsivity, these studies are limited in their ability to completely disentangle the neural mechanisms underlying aberrant reward and punishment processing. Recent advances in neuroscience have the ability to address these limitations by examining the implicated neural circuitry; however, a dearth of research remains. Moreover, there are no known investigations that examine whether potential abnormalities may be specific to or most pronounced within subgroups of CP youth, particularly among those characterized by high levels of CU traits or psychopathic features. Lastly, preliminary research in this area has focused on these mechanisms in adolescence, a

developmental time period characterized by substantial changes in the neural circuitry underlying reward and punishment processing. As such, it may be particularly important to evaluate potential abnormalities in this circuitry during pre-adolescence, prior to a period of heightened neural maturation. *Therefore, a primary aim of this dissertation is to characterize the neural response to the receipt of reward and punishment among subgroups of CP youth (age 8-11) relative to healthy controls (HC).*

2.0 BACKGROUND AND SIGNIFICANCE

Decades of research have identified multiple causal factors that underlie the development and persistence of chronic trajectories of CP in youth. Theories on the etiology of CP have emphasized a wide variety of biological and environmental factors, recognizing that the development of these behaviors is likely the result of a complex interplay between child, family, and broader social factors. Given the active role individuals play in shaping their social environments (Patterson, Reid, & Dishion, 1992; Plomin, DeFries, & Loehlin, 1977), one prominent area of research has focused on further elucidating child-specific mechanisms. As described above, research has emphasized further exploring abnormalities in reward and punishment processing, as deficits within this realm have been conceptualized as one potential causal mechanism underlying chronic and severe CP (e.g., Fowles, 1980; Newman & Wallace, 1993; Quay, 1993). Along these lines, the current dissertation attempts to take a more nuanced approach in testing this theory and in doing so, also seeks to expand on the literature by exploring how aberrant reward/punishment processing may impact responsiveness to intervention.

The current chapter begins by presenting a detailed description of CP in youth and subtyping schemes that have attempted to delineate a more homogenous, etiologically unique group of at-risk youth. Next, an overview of the theoretical and behavioral evidence for abnormalities in reward/punishment processing among youth with CP as well as subgroups of

CP youth with CU traits and psychopathic features will be presented. In addition, important developmental considerations relevant to the current dissertation are highlighted. This dissertation will then offer a rationale for the utility of examining the basic neural circuitry associated with reward and punishment processing and review emerging neuroimaging work that demonstrates abnormalities in youth with CP. Finally, research on treatment of CP in youth will be presented, highlighting the proposed contribution of reward and punishment processing and how abnormalities within this domain may impact the effectiveness of intervention. Following the presentation of background information, Chapter 3 provides the details of study design, methods, and analytic strategy utilized to examine the proposed hypotheses. Chapter 4 provides the aim specific results and a brief summary of the findings. Finally, a general discussion, implications and future directions are presented in Chapter 5.

2.1 CONDUCT PROBLEMS IN YOUTH AND SUBTYPES

CP refers to a set of problematic behaviors encompassed within the diagnostic categories of oppositional-defiant disorder (ODD) and conduct disorder (CD) set forth in the *Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition* (DSM-5; American Psychiatric Association, 2013). Symptoms associated with ODD reflect a recurrent pattern of behaviors that tend to be irritable and defiant in nature while CD is associated with a more severe cluster of behaviors such as aggression towards people and animals, destruction of property, deceitfulness or theft, and status offenses. Prevalence estimates for CP peak higher than 10% across childhood and adolescence (Hinshaw & Lee, 2003; Maughan, Rowe, Messer, Goodman, & Meltzer, 2004), with CP representing one of the most common reasons youth are referred for mental health

treatment (Reid, 1993). Longitudinal research links the early manifestation of these problem behaviors to increased risk of persistent CP throughout childhood and adolescence as well as serious antisocial and delinquent behavior in adulthood (Broidy, et al., 2003; Byrd, Loeber, & Pardini, 2012; Loeber, Farrington, Stouthamer-Loeber, Moffitt, & Caspi, 1998). While many youth desist from these behaviors over time, there is consistent evidence to suggest that a small proportion of those children demonstrating early CP will show persistent levels throughout development (Broidy, et al., 2003; Loeber, et al., 1998).

Given the noted heterogeneity that exists among youth exhibiting CP (Frick & White, 2008) researchers have proposed various subtyping schemes in hopes of demarcating a more homogenous subgroup of youth at risk for exhibiting severe and chronic CP. One of the most prominent subtyping distinctions is based on research suggesting that early (i.e., childhood) versus late (i.e., adolescent) onset of CP is associated with a prolonged, stable course of problem behaviors (Moffitt, 1993). More recently, considerable focus has been directed toward the presence of psychopathic features in youth, particularly CU traits, as research has consistently shown these characteristics to be associated with severe and protracted CP (Byrd, et al., 2012; Frick & White, 2008; Lynam, Caspi, Moffitt, Loeber, & Stouthamer-Loeber, 2007; Pardini & Loeber, 2008). While psychopathic features are defined as a constellation of interpersonal (e.g., manipulative or deceitful), emotional (e.g., callous, lacking guilt) and behavioral (e.g., impulsive) deficits, CU traits are circumscribed to the emotional dimension and include a lack of empathy, deficient guilt and remorse, and shallow affect. CU traits are of particular relevance because, until recently, they were not adequately represented among definitions of CP. In response to extensive research in this area, the DSM-5 added a 4-item specifier (i.e., ‘with limited prosocial emotions’; American Psychiatric Association, 2013) based on the presence of

CU traits, which has resulted in a continually growing interest in this area. These features are thought to be indicative of distinct causal processes characterized by a unique neurobiology that lead to a heightened proclivity for persistent CP (Dadds, Fraser, Frost, & Hawes, 2005; Frick, Bodin, & Barry, 2000; Pardini, 2006). Theoretical and empirical work suggests that one potential etiological pathway may be related to a reward dominant response style and deficient punishment processing that increases risk for early and protracted CP (Frick, et al., 2003; Frick & Marsee, 2006; Pardini, 2006). Therefore, examining whether abnormalities in the neural response to reward/punishment are most pronounced in a subgroup of youth with childhood-onset CP and CU traits may be particularly informative.

However, it should be noted that, to date, there has been substantial variability in the measurement of these characteristics across studies, with many researchers assessing total psychopathic features, defined broadly as a constellation of interpersonal, affective and behavioral characteristics, and few focusing specifically on the presence of CU traits. Moreover, there have been no studies in this area to examine these features using criteria set forth in the DSM-5 'limited prosocial emotions' specifier (American Psychiatric Association, 2013). Given this lack of a 'gold standard' with regard to measurement, distinctions between assessments of CU traits versus total psychopathic features are highlighted throughout the review of the literature. Thus, despite theoretical conjecture, it remains unclear whether the presence of CU traits, in particular, or psychopathic features, broadly defined, are associated with abnormalities in reward/punishment processing. This limitation is addressed directly in the current dissertation.

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2.2 THEORETICAL MODELS OF LEARNING AND CONDUCT PROBLEMS

The processing of reward and punishment has profound implications for associative and contingency learning, which serves as the foundation for many aspects of behavioral, social and emotional development (Akers 1998; Kochanska 1994). From a behavioral perspective, rewards can be considered any stimulus that acts as a reinforcer and increases the likelihood of that behavior recurring in the future; conversely, punishment is conceptualized as any stimulus that decreases the likelihood of that behavior recurring in the future (Skinner, 1969). Classical and operant conditioning are two fundamental models of learning that provide a framework for understanding how aberrant reward/punishment processing may give rise to the development and persistence of CP in youth.

Classical conditioning involves learned associations between reflexive responses and antecedent stimuli or events (Pavlov, 1927). Many researchers have applied models of classical conditioning to the engagement in and persistence of CP (e.g., Damasio, 1994; Kochanska, 1994). Overall, these theoretical models emphasize the importance of reflexive emotional responses to punishment and suggest that individual differences in sensitivity to these cues may have cascading effects that ultimately increase the likelihood of engaging in CP. For example, Kochanska (1994) emphasized the role of classical conditioning in conscience development, suggesting that the internalization of social norms is facilitated by the negative emotional arousal a child experiences when being disciplined or punished for wrongdoing. Eventually this emotional arousal becomes paired with the act of wrongdoing and through repeated disciplinary interactions, youth likely become conditioned to experience increases in negative arousal when contemplating or engaging in misconduct. Importantly, this occurs even in the absence of an authority figure and is a key feature of guilt and remorse. Youth who are particularly insensitive

to punishment, as evidenced by low anxiety and low temperamental fearfulness, experience relatively little negative emotion when punished for rule breaking behavior and thus fail to establish conditioned associations between disciplinary interactions and emotional arousal. These youth may be less likely to encode parental messages about the acceptability of behaviors, which could hinder the internalization of moral beliefs that guide prosocial behavior. Research suggests that punishment insensitivity is linked to reduced concern for the suffering of others (Young, Fox, & Zahn-Waxler, 1999) and less guilt following transgressions (Rothbart, Ahadi, & Hershey, 1994), characteristics that increase the likelihood that one will engage in CP. Along these lines, Blair (2004; 2005) proposed that CP youth, particularly those with psychopathic features, fail to encode the emotional components of reward and punishment and are thus, unable to acquire conditioned associations. For example, distress cues in others, such as sad or fearful expressions that occur following an act of their own wrongdoing, fail to elicit negative emotional arousal and in turn impede the acquisition of important affective associations. This is believed to have downstream consequences and hinders the development of empathy and remorse, resulting in a heightened risk for engagement and persistence of CP.

Operant conditioning refers to the learning and modification of non-reflexive, voluntary behaviors through contingent stimuli or feedback (i.e., reward/reinforcement or punishment). It is founded on the principle that behaviors that are reinforced or rewarded are strengthened and perpetuated while punished behaviors are weakened and diminished (Skinner, 1969). Social learning theories of CP rely heavily on operant principles, suggesting that parents may unintentionally reinforce CP while simultaneously failing to reinforce prosocial behaviors (Patterson, et al., 1992). Patterson and colleagues (1992) focused on a coercive cycle that exists in parent-child interactions, whereby parents respond to CP with inconsistent and harsh

punishment techniques that serve to escalate the severity and frequency of problem behaviors over time. Accordingly, a central component of parenting interventions is to break this coercive cycle by shifting behavioral contingencies and teaching parents to positively reinforce prosocial behaviors, while setting clear and consistent consequences for disruptive behaviors (Kazdin, 2003; Serketich & Dumas, 1996). It is possible that these negative parenting behaviors, such as harsh and inconsistent discipline, may be particularly detrimental for youth with deficits in reward/punishment processing and could serve to exacerbate CP (see Dadds & Salmon, 2003; Matthys, Vanderschuren, Schutter, & Lochman, 2012b). Moreover, social learning theorists have also explored ways in which peers function to reinforce and perpetuate CP (i.e., deviancy training; Dishion, Spracklen, Andrews, & Patterson, 1996; Patterson, Dishion, & Yoerger, 2000). Specifically, association with deviant peers has been consistently linked to higher levels of risk taking and CP over time (Rusby, Forrester, Biglan, & Metzler, 2005). The presence of deviant social influences may be particularly prominent for those youth with a reward dominant response-style and decreased sensitivity to punishment and these deficits may make youth more vulnerable to negative social influences.

2.3 REWARD AND PUNISHMENT PROCESSING IN YOUTH WITH CP: THEORETCIAL BACKGROUND

Gray's (1975, 1981, 1987) Reinforcement Sensitivity Theory provides one of the most cited frameworks for the study of reward and punishment processing. Historically, reward and punishment processing has been conceptualized in terms of the Behavioral Approach System (BAS) and the Behavioral Inhibition System (BIS1981, 1987). These systems serve to enhance

cortical arousal, facilitate the redirection of attention to relevant environmental stimuli, and initiate subsequent behavioral responses. Drawing almost exclusively on basic animal learning models, Gray proposed that BAS activity reflected activation in the mesocorticolimbic circuit, while BIS functioning was linked to the septohippocampal system (Gray, 1982). Specifically, the BAS serves to increase activity and initiate goal-directed behavior in response to conditioned signals of reward, while the BIS functions to inhibit goal-directed action and avoid negative, painful, or threatening outcomes in the presence of conditioned aversive stimuli or punishment. Gray (1981, 1987) viewed variations in the functioning of the BAS as an index of reward sensitivity, with heightened levels of BAS activation resulting in increased propensity to engage in reward-directed behavior. BIS responsivity was conceptualized as an index of punishment sensitivity, with heightened activation manifesting behaviorally as increased avoidance and a greater propensity to anxiety. Conversely, lower BIS activation is thought to be associated with insensitivity to punishment and/or threat, leading to increased reward seeking behaviors.

Extensions and modifications of this theory have focused on associations between CP and primary deficits in one or both of these systems. Quay (1988, 1993) was the first to extend Gray's (1981, 1987) theory to manifestations of CP in youth, suggesting that these behaviors stem from a hyperactive reward system (BAS). Specifically, Quay (1988, 1993) proposed that the excessive BAS activity in antisocial youth results in a reward dominant response style that predominates the BIS and leads to persistent approach or reward-seeking behaviors. Others proposed that CP instead reflects an inherently hypoactive reward system that necessitates excessive sensation seeking (Cloninger, 1987; Zuckerman, 1996). This theory suggests that a chronically underactive reward system represents an aversive physiological state, requiring

individuals to seek stimulation (e.g., antisocial behavior) in order to increase activation and alleviate an unpleasant internal condition.

In contrast to a central focus on reward, researchers have also posited a primary deficit in punishment processing, where CP is reflective of a hypoactive inhibition system and reduced sensitivity to cues of punishment (Eysenck, 1977; Fowles, 1980; Lykken, 1995; Patrick, 1994). This theory suggests that individuals with reduced BIS functioning fail to experience negative arousal in response to punishment and/or fail to pair this response with behaviors or cues that result in punishment. As a result, they demonstrate difficulties inhibiting reward-seeking behaviors, due primarily to a notable reduction in conditioned fear/anxiety to punishment. Incorporating aspects of both reward and punishment systems, Newman and colleagues (Newman, 1998; Patterson & Newman, 1993; Wallace & Newman, 2008) proposed that CP can be attributed to deficits in the modulation of *both* systems, specifically when the avoidance of punishment requires overriding a dominant reward response. Drawing upon these theories, considerable behavioral work has evaluated the extent to which CP youth manifest abnormalities in reward and/or punishment processing. In addition, researchers have attempted to examine the degree to which potential abnormalities may be specific to a subset of youth, characterized by high levels of CU traits or psychopathic features. This works is review below, following a review of important developmental considerations.

2.3.1 Developmental Considerations

Research in this area has focused primarily on adolescents with CP and it is important to highlight several relevant development considerations prior to a review of the literature. First, there may be substantial developmental change in the manifestation of CP over time, specifically

with regard to frequency and severity (Farrington, 1986; Hinshaw & Lee, 2003; Loeber, et al., 1998). Adolescence marks a transition period noted for drastic physical, psychological, and social development. Most pertinent to our interpretation of the current literature are marked behavioral increases in risk-taking and reward seeking behaviors that are thought to reflect still developing neurobiological systems (Steinberg & Morris, 2001). Along these lines, it is important to note the substantial change in the neural circuitry subserving reward and punishment processing in youth, seen most prominently during adolescence. Specifically, there is a significant increase in axonal myelination coupled with decreases in both cortical and subcortical gray matter as well as with functional changes in reward/punishment neural circuitries (e.g., Giedd, 2004). Some studies have documented a heightened sensitivity to reward in the striatum when comparing adolescents to adults (Ernst, et al., 2005; Galvan, et al., 2006) and this, coupled with underdeveloped regulatory frontal regions, has been hypothesized to lead to increases in problem behaviors during adolescence (Fareri, Martin, & Delgado, 2008; Luna, et al., 2001). Indeed, the prevalence of delinquent behaviors tends to rise and peak in adolescence, followed by dissipation for most individuals into adulthood (Farrington, 1986). As such, attempts to characterize reward/punishment mechanisms that give rise to early-onset, chronic CP may be most effective during pre-adolescence, prior to heightened neural maturation and associated increases in CP related behaviors. Thus, the following review of the literature seeks to highlight gaps in the current literature related to this issue, emphasizing the importance of developmental timing with regard to interpretation.

2.4 REWARD AND PUNISHMENT PROCESSING IN YOUTH WITH CP: BEHAVIORAL EVIDENCE

Extensive behavioral work has attempted to disentangle the contributions of reward and punishment processing in CP youth using a variety of behavioral paradigms. Results from past empirical research are summarized below within the context of each of the proposed mechanisms underlying severe and persistent CP: 1) primary abnormality in reward processing; 2) primary abnormality in punishment processing; or 3) abnormalities in both reward and punishment processing. In addition, efforts to evaluate the extent to which these abnormalities may be most pronounced in a subgroup of CP youth with 1) CU traits or 2) psychopathic features are highlighted. Lastly, distinctions between samples of youth in late childhood versus adolescence are noted as this is particularly important with regard to interpretation and design of the current dissertation.

2.4.1 Primary Abnormality in Reward Processing

Research attempting to examine whether aberrant reward processing characterizes CP youth has utilized a variety of paradigms, the majority of which assess 'risk taking' or responsivity to immediate rewards despite potential punishment. These tasks included the Iowa Gambling Task (IGT; Bechara, Damasio, Damasio, & Anderson, 1994), the Risky Choice Task (RCT; Rogers, et al., 2003) and the Balloon Analogue Risk Task (BART; Lejuez, et al., 2002). Studies utilizing these tasks have fairly consistently shown youth with CP to exhibit a greater affinity for large, immediate rewards despite a high probability of punishment relative to controls (Fairchild, et al., 2009; Miura, 2009; Schutter, van Bokhoven, Vanderschuren, Lochman, & Matthys, 2011) and

this has been interpreted as evidence for a primary deficit in reward processing. Interestingly, no differences in risk taking behavior were seen within groups of CP when subtypes were based on the severity of CP (e.g., violent vs. non-violent; Miura, 2009) or age of onset (Fairchild, et al., 2009). However, research assessing samples of CP youth with increased psychopathic features, were linked to higher levels of risk taking (Blair, Colledge, & Mitchell, 2001; Fairchild, et al., 2009), suggesting these abnormalities may be most pronounced in this subgroup of youth. Interestingly, those studies examining CU traits specifically found no significant differences in overall risk taking (Centifanti & Modecki, 2013; Marini & Stickle, 2010), suggesting that reward sensitivity and heightened risk taking may be less associated with the core affective features of psychopathy.

Taken together, findings may seem to provide initial evidence for abnormalities in reward processing among youth with CP, particularly those with psychopathic features. However, it is important to consider these findings within the context of several limitations. First, while these tasks aim to assess reward processing, the incorporation of both reward and punishment preclude firm notions about the mechanism underlying the reward dominant response style as abnormalities in reward and/or punishment processing may be responsible for these effects. It is also noteworthy that null findings in this area are specific to tasks that more successfully isolated responsivity to reward by reinforcing the majority of responses and in some instances excluding punishment (Castellanos-Ryan, Rubia, & Conrod, 2011; MacPherson, et al., 2010; Marini & Stickle, 2010; Newman & Kosson, 1986), negating theories that propose a primary dysfunction in reward processing. Second, and perhaps more importantly, all of the aforementioned studies utilized samples of adolescents, with the majority of positive studies failing to include adequate control groups. Moreover, the only study to examine reward processing in late childhood found

risk-taking to be unrelated to CP measured both concurrently and longitudinally (MacPherson, et al., 2010). Thus, given discrepancies based on developmental timing of assessment and lack of control groups, it is possible that performance deficits reflect more normative increases in risk-taking and reward-seeking behaviors during adolescence.

These findings, while notably limited, fail to provide support for a primary dysfunction in reward processing and instead suggest that deficits in behavioral performance may be most evident in the presence of competing reward and punishment cues. However, as underscored above, behavioral attempts to isolate and examine reward processing in youth with CP are limited and highlight the need for alternative empirical methods (e.g., neuroimaging) that may be more effective in evaluating abnormalities in reward processing in youth with CP. Moreover, there is a dearth of research examining reward processing as a mechanism underlying CP in childhood, necessitating the need for continued investigation within this domain.

2.4.2 Primary Abnormality in Punishment Processing

Empirical work investigating a primary deficit in punishment processing has mostly utilized psychophysiological measures to examine reflexive responses to punishment, with the majority of studies focusing on individual differences in responsivity to inherently aversive stimuli (e.g., loud tones). Research in the area demonstrates consistent results across both late childhood and adolescence, with CP youth, relative to controls, demonstrating reduced responsivity to randomly presented aversive tones (Fairchild, van Goozen, Stollery, & Goodyer, 2008; Herpertz, et al., 2001; van Goozen, Snoek, Matthys, van Rossum, & van Engeland, 2004) and to cues of impending punishment (Fairchild, et al., 2008; Loeber, Pardini, Stouthamer-Loeber, & Raine, 2007; Raine & Venables, 1981; Raine, Venables, & Williams, 1996). This suggests that youth

with CP experience relatively little physiological arousal when punished, potentially hindering their ability to form associations with cues of impending punishment. At the same time, there is some evidence to suggest that CP youth can cognitively identify cue-punishment pairing in a post-task questionnaire (Fairchild, et al., 2008), indicating that they may be aware of these contingencies but exhibit deficits in the affective component of processing.

Further, despite long standing theory that punishment insensitivity is characteristic of individuals with psychopathic features, the only study that attempted to examine this empirically found no differences in responsivity to punishment among delinquent youth with high vs. low psychopathic features (Fung, et al., 2005). Given the consistent findings described above, one may conclude that these deficits are not specific to this subgroup of CP youth and are instead associated with CP more generally. At the same time, it is important to note that research in this area is limited and Fung et al. (2005) failed to differentiate between variants of psychopathy as indexed by CU traits. Thus, further investigation is warranted.

Finally, the majority of work in this area has focused on reactivity to inherently aversive stimuli, with much less research examining abnormalities in responsivity to other forms of punishment (e.g., loss of money). Those studies that have examined the extent to which youth with CP demonstrate reduced sensitivity to loss of money have produced inconsistent results (Beauchaine, Katkin, Strassberg, & Snarr, 2001; Matthys, van Goozen, Snoek, & van Engeland, 2004). It is particularly important to better understand potential differences in processing alternative punishments as they are inherent to everyday experiences and are often used as integral components of parenting interventions.

As a whole, studies in this area provide strong evidence for reduced sensitivity to inherently aversive stimuli (e.g., loud tones), which is suggestive of a primary deficit in

punishment processing among youth with increased CP. However, there is a paucity of research examining responsivity to alternative forms of punishment, such as monetary loss, as well as research investigating whether aberrant punishment processing is specific to CP youth with heightened CU traits.

2.4.3 Abnormalities in Reward and Punishment Processing

The majority of empirical work examining reward/punishment processing in youth with CP has implemented tasks that incorporate aspects of both reward and punishment processing. Two of the most commonly used paradigms (i.e., passive-avoidance learning, response-reversal) require participants to learn by trial-and-error and vary in the predictability and probability of received reward (e.g., fixed versus variable). In both instances, youth are required to adapt their performance based on the receipt of reward and punishment. Results consistently find CP youth to show performance deficits in the face of competing reward and punishment relative to controls, suggesting difficulties inhibiting a dominant response to reward despite increasing punishment (e.g., Fonseca & Yule, 1995; Matthys, et al., 2004; O'Brien & Frick, 1996; O'Brien, Frick, & Lyman, 1994). These findings have been replicated in community, clinical, and offender samples of youth in late childhood (Daughtery & Quay, 1991; Fonseca & Yule, 1995; Matthys, et al., 2004; Matthys, van Goozen, De Vries, Cohen-Kettenis, & Van Engeland, 1998; O'Brien & Frick, 1996; O'Brien, et al., 1994) and adolescence (Budhani & Blair, 2005; Fisher & Blair, 1998; Fonseca & Yule, 1995; Frick, et al., 2003; Shapiro, Quay, Hogan, & Schwartz, 1988). In addition, CP youth with psychopathic features showed pronounced deficits on these tasks relative to CP youth without psychopathic features, with some evidence that CU traits in particular may differentiate a subgroup of CP youth with severe performance deficits (Budhani

& Blair, 2005; Fisher & Blair, 1998; Frick, et al., 2003; O'Brien & Frick, 1996). This indicates that CP youth, particularly those with CU traits/psychopathic features have difficulty inhibiting a prepotent reward response in the face of increasing punishment, specifically when the avoidance of punishment requires overriding a dominant reward response.

In light of the consistent deficits on tasks that examine punishment sensitivity, it may be that abnormalities in punishment processing are driving performance differences on these tasks. However, it is also possible that youth with CP evidence greater difficulties when cognitive demands are high and they are required to shift attention to less salient cues of punishment in the face of a dominant reward focused action. This is consistent with Newman's response modulation hypothesis (e.g., Patterson & Newman, 1993), which posits deficits in the modulation of *both* reward and punishment processing systems. However, at present the mechanism underlying these performance deficits remains unclear and the extent to which this is attributable to abnormalities in reward processing, punishment processing or a combination of the two warrants further investigation.

2.4.4 Limitations

Taken as a whole, it appears that youth with CP exhibit abnormalities in reward and punishment processing, with some suggestion that deficits may be most pronounced in CP youth with CU traits or psychopathic features. However, while the behavioral literature has increased our understanding of associations between reward/punishment processing and CP, there are several limitations. First, these studies are limited in their inability to completely disentangle the mechanisms underlying reward and punishment processing. For example, while behavioral tasks may identify a reward dominant response style, it is difficult to determine whether a hyperactive

or hypoactive reward processing system is responsible for such findings. In addition, many of the behavioral paradigms discussed above incorporate aspects of reward and punishment, making it difficult to discern potential differences in the strength of associations with CP. Moreover, behavioral studies and the theory they are founded upon often fail to acknowledge the complexities of reward and punishment processing, as each of these mechanisms are comprised of multiple phases of learning (Ernst, Pine, & Hardin, 2006; Seymour, Singer, & Dolan, 2007). As such, aberrant reward/punishment processing could result from abnormalities at one or multiple phases. For example, abnormalities may exist during 1) encoding, defined as the initial processing of a stimulus; 2) acquisition, the process of associative learning that occurs with the repeated pairing of two stimuli or stimuli and response; or 3) extinction, the removal of an expected stimulus (Balsam, Drew, & Gallistel, 2010). A failure to evaluate these mechanisms as nuanced processes drastically limits our understanding of their unique contributions to the etiology of CP. While the majority of research to date has utilized complicated tasks that incorporate multiple phases of processing, the current dissertation takes a bottom-up approach, focusing first on a single phase of processing (i.e., encoding) in an attempt to lay the foundation for a more comprehensive understanding of these complex processes.

Recent advances in neuroscience have the potential to build upon behavioral research by further elucidating these mechanisms. Specifically, researchers have identified neural circuitries associated with reward and punishment processing and have linked specific neural substrates to distinct phases of processing. An overview of these circuitries follows along with a review of emerging neuroimaging studies examining reward/punishment processing in youth with CP.

2.5 NEURAL CIRCUITRIES OF REWARD AND PUNISHMENT PROCESSING

Extensive empirical work over the past several decades has identified specific neural circuitries associated with reward and punishment processing and emerging neuroimaging work has helped to refine and enhance our understanding of reward and punishment processing systems in the human brain. While a comprehensive examination of the complex circuitry is beyond the scope of this dissertation, there are various subcortical and cortical regions that have been consistently implicated as significant components of these multifaceted networks including the ventral and dorsal striatum (VS and DS, respectively; Delgado, 2007), the amygdala (LeDoux, 2000; LeDoux, 2003), the anterior cingulate cortex (ACC; Rogers, et al., 2004), the medial prefrontal cortex (mPFC; Clark, Cool, & Robbins, 2004), and the orbital frontal cortex (OFC; Cardinal, Parkinson, Hall, & Everitt, 2002; O'Doherty, Kringelbach, Rolls, Hornak, & Andrews, 2001). A parsimonious overview of these key nodes will be discussed in terms of three neural systems, mirroring the triadic model (Ernst, et al., 2006): 1) reward/ approach; 2) punishment/avoidance; and 3) regulatory. Although these circuits are discussed here in isolation, it is important to note that there is considerable overlap between systems as well as extensive functional connections that include both direct and indirect projections (Carmichael & Price, 1995; Fuster, 2001; McDonald, 1991).

2.5.1 Reward/Approach System

Extensive research on the reward system has implicated regions of the basal ganglia, namely the striatum, in addition to higher order cortical areas included within the frontal cortex (discussed below). The striatum is comprised of two anatomically and functionally distinct regions: the

ventral and dorsal striatum (VS and DS, respectively; Delgado, 2007). The VS contains the nucleus accumbens (NAcc), and receives input from a variety of regions including the ventral tegmental area (VTA), a region implicated in the initial detection or encoding of a reward stimulus (Fields, Hjelmstad, Margolis, & Nicola, 2007) and the amygdala, an area associated with the emotional salience of reward (Cardinal, et al., 2002; Groenewegen, Wright, Beijer, & Voorn, 1999). Given these afferent connections, it is not surprising that the NAcc has been shown to play an important role in the anticipation or prediction of reward (Knutson & Cooper, 2005) and affective or hedonistic experiences of receiving reward (Cardinal, et al., 2002; Knutson & Greer, 2008). The DS contains the caudate and putamen, two areas that have been consistently linked to learning reward-response contingencies (Balleine, Delgado, & Hikosaka, 2007; Packard & Knowlton, 2002). Research has shown these regions to be involved in both the acquisition and extinction phases of learning. Specifically, the DS is engaged in reward-prediction errors or the comparison of actual versus predicted rewards as well as the coding of reward-action associations (Delgado, Stenger, & Fiez, 2004; O'Doherty, et al., 2004). For the purpose of the current dissertation, the NAcc, caudate and putamen comprise one region of interest, though distinctions between the VS and DS are noted.

2.5.2 Punishment/Avoidance System

Decades of empirical work have identified the amygdala as central to punishment processing, namely classical (aversive) conditioning (LeDoux, 2000; LeDoux, 2003). The amygdala can be divided into two anatomically and functionally distinct components, including the basolateral complex and the central nucleus (Amaral, Price, Pitkanen, & Carmichael, 1992; Swanson, 2003). In serial processing models, the basolateral complex is linked to processing sensory and

contextual stimuli and has been shown to be particularly important in the acquisition of cue-stimuli contingencies (LeDoux, 2000; 2003). This area has reciprocal projections with various regions of the prefrontal cortex, facilitating its influence on complex behaviors, as well as extensive connections with the VS and central nucleus (Everitt, Cardinal, Parkinson, & Robbins, 2003; Parkinson, Cardinal, & Everitt, 2000). Propagation of this information to the central nucleus serves to mediate a response through projections to the hypothalamus, midbrain reticular formation and brainstem, areas that are associated with behavioral and autonomic responses (Kapp, Whalen, Supple, & Pascoe, 1992). Although the amygdala is noted for its role in the processing of inherently aversive stimuli, it is also implicated in operant conditioning, particularly with stimulus-reinforcement learning (Balleine & Killcross, 2006). Specifically, the basolateral complex and the central nucleus play important roles in the emotional value of other forms of punishment (e.g., loss of money) and are thus thought to influence motivation (Balleine, et al., 2007; Cardinal, et al., 2002). As such, the current dissertation will examine the role of the amygdala in the initial encoding of punishment cues.

2.5.3 Regulatory System

The ACC, mPFC and OFC are noted for their involvement in higher order processing and are extensively enervated by direct and indirect projections from subcortical regions linked to reward (i.e., striatum) and punishment (i.e., amygdala) circuitries (Bechara, Damasio, Damasio, & Lee, 1999; Cardinal, et al., 2002; Rogers, et al., 2004). The ACC has been linked to error monitoring of both reward and punishment, with evidence suggesting that it not only detects and monitors errors but also serves to initiate action in response to error detection via connections with the motor system (Rogers, et al., 2004). The rostral-ventral portions of the ACC in particular have

been linked to reinforcement and emotional learning as well as reward preference, with strong connections to the mPFC, OFC and striatum (Carmichael & Price, 1996; Öngür & Price, 2000). The mPFC is involved in outcome evaluation, pattern detection, and decision making (Clark, et al., 2004) and given extensive connections with the amygdala, is thought to play an integral role in emotional learning (Damasio, 1994). The OFC has also been implicated in outcome evaluation and decision making and functions to shape behavior according to the estimated value of actions associated with reward and punishment contingencies (Cardinal, et al., 2002; O'Doherty, et al., 2001). Medial and lateral regions of the OFC respond to various rewards and punishments, respectively and have been implicated in the representational value or magnitude of reward/punishment (Elliott, Dolan, & Frith, 2000). Thus, OFC, mPFC and ACC play distinct roles in the processing of reward and punishment cues and represent three regions of interest in the current study.

2.5.4 Summary

It is important to note that while the aforementioned regions of interest represent a central focus of the current dissertation, activation within these regions should be considered within the context of a broader, interconnected circuitry that incorporates aspects of diverse and relevant processes such as attention, arousal and executive control. It is possible that variation in blood-oxygenation level-dependent (BOLD) response in these ROI may be influenced by input from other areas that are beyond the scope of this dissertation. While striatum, amygdala, ACC, mPFC and OFC were ROIs in the current dissertation, whole-brain analyses were also conducted to explore additional neural circuitry that may be involved in processing of reward and punishment

cues. Evidence of reward/punishment dysfunction in the stated ROIs among CP youth and CP youth with CU traits/psychopathic features is described in the following section.

2.6 REWARD AND PUNISHMENT PROCESSING IN YOUTH WITH CP: FMRI EVIDENCE

While various techniques have been used to examine the underlying neurobiology of reward and punishment processing systems, the focus of the current dissertation is functional magnetic resonance imaging (fMRI) due to its ability to spatially localize neural activation during reward and punishment processing. This technique noninvasively quantifies changes in BOLD response, an assessment of the ratio between oxygenated and deoxygenated blood in the brain that is thought to reflect neural activation. Functional MRI is based on the assumption that increases in neuronal activity in a particular area of the brain lead to increases in cerebral blood flow in the same brain areas. Thus, task-specific changes in neural activity can be identified with good temporal and spatial resolution thereby linking the components of a given task to regions of the brain in order to localize specific functions (Buxton, 2002; Toga & Mazziotta, 2002).

As was evident in the behavioral literature, emerging fMRI research among samples of CP youth use a variety of different paradigms. Taken as a whole, results find CP youth to have altered processing in the aforementioned ROIs relative to control groups. Rubia and colleagues (2009) were the first to provide evidence for OFC dysfunction in 9-16 year old youth with CP. This study utilized a rewarded continuous performance task to examine differences between responsivity to reward vs. non-reward among youth with early-onset CP, youth with ADHD, and healthy controls. Youth with CP demonstrated less activation in the lateral and medial OFC

relative to both ADHD youth and healthy controls. Given the role of the OFC in outcome evaluation and the representational value of reward/punishment (Elliott, et al., 2000) these results may be interpreted as evidence of a hyposensitivity to reward. In a second study, youth with CP and ADHD showed reduced activation in the ACC while simultaneously showing increased activation in the DS (Gatzke-Kopp, et al., 2009). In this experiment, youth completed a monetary incentive task during which they were rewarded during every other block of trials (i.e., every 10 trials). Differences in this task appeared to be specific to omission of expected reward, suggesting CP may be linked to a failure to process changes in reward contingencies. Along these lines a recent study found adolescent youth with CP to evidence greater activation in the VS to reward and perhaps somewhat contrary to early work, greater activation in the mPFC relative to healthy controls (Bjork, Chen, Smith, & Hommer, 2010). Increased activation in the VS as well as prefrontal regions to both the anticipation and receipt of reward has been interpreted as support of a hypersensitivity to reward in CP youth. Overall, while results are indicative of aberrant reward processing and in the absence of expected reward, replication of results in this area are limited and somewhat inconsistent.

Two additional studies have attempted to examine reward/punishment processing in subgroups of CP youth between the ages of 10 and 17, focusing on those with increased levels of psychopathic features. Finger and colleagues (2008) examined the BOLD response in CP youth with psychopathic features, youth with ADHD, and healthy controls during a task that requires participants to learn by trial-and-error. CP youth with psychopathic features demonstrated increased activation in the OFC as well as the DS (i.e., caudate) during punished errors, though no differences were seen in responsivity to correct rewarded responses. This increase in activation was also positively associated with a continuous measure of CU traits; CP youth with

higher levels of CU traits showed greater activation in the caudate and OFC in response to punished errors. This somewhat mirrors findings seen in undifferentiated samples of CP youth, with differences in processing most prominent during trials of absent expected reward (Gatzke-Kopp, et al., 2009) and at the same time provides some evidence for hypersensitivity to the receipt of reward in CP youth with psychopathic features relative to controls. Somewhat contrary to these findings, a later study by Finger and colleagues (2011) found CP youth with psychopathic features to demonstrate reduced responsivity in the OFC to rewarded trials relative to healthy controls, with no notable differences in response to the absence of expected reward or in response to punished errors. Such results may be interpreted as evidence of a hypo-sensitivity to reward.

2.6.1 Summary

Though an examination of the underlying neurobiology has the potential to further elucidate mechanisms subserving behavioral differences, there is a paucity of fMRI studies in youth with CP. Therefore, it is difficult to draw firm conclusions from the limited and inconsistent research in this area. While some studies provide support for a hypo-responsivity to reward in CP youth (e.g., Rubia, et al., 2009), others suggest that youth with CP are hypersensitive to reward (e.g., Bjork, et al., 2010). There is also some indication that CP in youth may be less related to abnormalities in processing reward and more associated with a failure to process contingency change, specifically when it involves a failure to receive an expected reward (e.g., Finger, et al., 2008; Gatzke-Kopp, et al., 2009). Attempts to examine the extent to which aberrant reward/punishment processing may be most pronounced or specific to a subgroup of youth characterized by psychopathic features or CU traits mirrors the inconsistency seen in

undifferentiated samples of CP youth. Moreover, these studies focused on samples of adolescents and failed to include a group of CP without CU traits/psychopathic features, limiting conclusions about the specificity of these findings among this subgroup.

In light of the aforementioned limitations, the current dissertation seeks to extend and further clarify past literature by examining potential abnormalities in reward and punishment processing among subgroups of youth with CP between the ages of 8-11 relative to HC. Importantly, the current dissertation differs from past research in three important ways. First, it utilizes a basic paradigm that isolates receipt of reward and receipt of punishment, allowing for the separate characterization of neural response following monetary cues of reward and punishment. Second, it proposes the examination of the BOLD response in pre-adolescent youth, prior to noted maturation of the neural circuits that are of primary interest. Lastly, it examines responsivity to reward and punishment among subgroups of CP youth (with and without CU; with and without psychopathic features) relative to HC and represents the first imaging study to examine reward and punishment processing among these subgroups.

The extent to which differential responsivity to reward and punishment has meaningful implications that extend beyond our understanding of etiology is explored in the next section. Specifically, research has suggested that aberrant reward/punishment processing may not only impact the development and persistence of CP but could also influence responsiveness to intervention. The following section explores this notion and provides an overview of the intervention literature among youth with CP, focusing on the effectiveness of the multi-modal empirically-validated intervention that was used in the current dissertation.

2.7 YOUTH WITH CP, INTERVENTION EFFORTS & THE POTENTIAL ROLE OF REWARD AND PUNISHMENT PROCESSING

Better characterizing potential abnormalities in the responsivity to reward and punishment may not only help us to better understand the development of CP but could also be particularly important with regard to intervention. Noteworthy, the majority of interventions targeting CP are grounded in social learning theory and place strong emphasis on behavioral strategies associated with reward and punishment contingencies. While burgeoning empirical research suggests that intensive, empirical-validated interventions function to reduce these problem behaviors over time (Eyberg, Nelson, & Boggs, 2008; Hawes & Dadds, 2007; Kolko, et al., 2009; Kolko & Pardini, 2010; McDonald, Dodson, Rosenfield, & Jouriles, 2011; Somech & Elizur, 2012; White, Frick, Lawing, & Bauer, in press), it is also well-documented that interventions for CP youth are not effective for everyone (Hawes, Price, & Dadds, 2014; Matthys, et al., 2012b; Webster-Stratton & Hammond, 1997).

Along these lines, researchers have investigated myriad moderators that may undermine the effectiveness of interventions, the majority of which have focused on demographic risk factors (e.g., poverty), parental psychopathology (e.g., depression) and other related stressors (family conflict; for review see Shelleby & Shaw, 2013). There is also some suggestion that child factors may influence the effectiveness of intervention (Matthys, et al., 2012b), with more recent focus on the presence of CU traits or psychopathic features (Hawes, et al., 2014). As described above, these features are believed to demarcate a more homogenous subgroup of youth that are most severe and seemingly resistant to traditional interventions (Frick, Ray, Thornton, & Kahn, 2013; Pardini & Frick, 2013). Despite noted clinical pessimism, research in this area remains mixed, with emerging studies suggesting that intensive, multimodal interventions may

contribute to reductions in both CP and CU over time (see Frick, et al., 2013; Waller, Gardner, & Hyde, 2013). Nonetheless, treatment resistance within this population has been linked to abnormalities in reward and punishment processing (Dadds & Salmon, 2003; Matthys, et al., 2012b). Along these lines, research suggests that youth with increased reward seeking and punishment insensitivity may respond well to the reward-based components of parent training (e.g., praise, token reinforcement) yet appear insensitive to the disciplinary components of treatment (e.g., time-out). For example, treatment studies have found CP youth with CU traits to respond significantly worse to punishment focused techniques (e.g., "time-out"; Haas, et al., 2011; Miller, et al., 2014) while reward-oriented strategies have been found to work equally well across CP youth with high and low levels of CU traits (Hawes & Dadds, 2005). While this implies that individual differences in reward and punishment processing may influence responsiveness to intervention, this notion has yet to be empirically tested.

2.7.1 Overview of Treatment Literature

Multifaceted, multimodal intervention efforts appear to be particularly effective for children exhibiting heightened levels of CP. Specifically, research has suggested that child-focused CBT and skills training coupled with parent management training (PMT) serves to reduce CP in young children over time (Eyberg, et al., 2008; Kazdin, Siegel, & Bass, 1992; Webster-Stratton, Reid, & Hammond, 2004). Child-focused components rely heavily on CBT principles and are designed to enhance problem-solving techniques. Specifically, these interventions teach strategies that aim to interrupt impulsive and perseverative, reward-focused action by encouraging youth to think about the consequences of their behaviors and develop a socially appropriate plan of action. At the same time, prominent PMT interventions, strongly founded in behaviorist principles, target a

coercive cycle that exists in parent-child interactions, whereby parents respond to CP with inconsistent and harsh punishment, which inadvertently increases the frequency of these behaviors over time while simultaneously failing to reinforce prosocial behaviors (Patterson, DeBaryshe, & Ramsey, 1989; Patterson, et al., 1992). PMT breaks this coercive cycle by shifting behavioral contingencies and teaching parents to positively reinforce prosocial behaviors, while setting clear and consistent consequences for disruptive behaviors (Serketich & Dumas, 1996).

Meta-analytic reviews examining the effectiveness of each of the aforementioned intervention modalities in quality coded, randomized control trials (RCT) have demonstrated promising effects. For example, an examination of 29 child-focused interventions aimed at increasing self-control over impulsive, reward-seeking behaviors in CP youth showed significant reductions in subsequent delinquency (Piquero, Jennings, & Farrington, 2010). This review focused on early interventions for youth aged 10 and below that utilized primarily CBT and skills training. While these studies only examined outcomes up to age 12, they reported increased self-control in CP youth across informants (i.e., teacher-report, self-report, direct observation; ES range=.28-.61) and more importantly a reduction in CP over time, though this was specific to teacher-reported behaviors (ES=.30). At the same time, meta-analytic reviews of intervention efforts focused primarily on PMT have also demonstrated significant reductions in CP over time (Farrington & Welsh, 2003; Serketich & Dumas, 1996). More recently, Lundahl and colleagues (2006) conducted an extensive meta-analysis examining 63 peer-reviewed studies and found behaviorally focused PMT interventions to show decreases in CP both immediately following the intervention (ES=.47) as well as at later follow-up (ES=.25), though these effects are notably within the small to moderate range. Taken as a whole, the literature suggests that these types of early interventions may be particularly beneficial for at risk youth.

Moreover, empirical studies have found the combination of child-focused interventions and parent behavioral training modalities to produce greater changes in CP over time relative to the implementation of a single modality in isolation (Burke, Loeber, & Birmaher, 2002; Kazdin, et al., 1992; Webster-Stratton & Hammond, 1997), with some suggestion that a multimodal approach produces more sustained treatment gains over time (Kazdin, et al., 1992; Webster-Stratton, et al., 2004). Along these lines, a variety of early intervention programs designed to include both child and parenting components have been widely disseminated (e.g., Problem Solving Skills Training/PMT; The Incredible Years; Coping Power) and demonstrate fairly consistent success, showing reductions in problem behavior over time (e.g., Eyberg, et al., 2008; Kazdin, 2010). The current dissertation focuses on a similar multimodal early intervention designed to reduce CP in at-risk youth. As is detailed below, the Stop-Now-And-Plan (SNAP) Under 12 Outreach Project is an empirically supported, manualized program that incorporates child-focused CBT and skills training as well as PMT.

2.7.2 Stop-Now-And-Plan Intervention

SNAP was created in 1985 in Toronto, Canada and targets children under the age of 12 who have had previous contact with the juvenile justice system or are at serious risk for police contact. The SNAP program takes a multimodal approach, comprised of two primary components, each of which is developed with gender-specific programming. The first is child-focused and teaches children cognitive-behavioral self-control skills and problem-solving techniques within a group setting. Youth are taught strategies (e.g., deep breathing, counting to 10) that aid in interruption of potential reward-focused actions, helping them to “STOP” and think about the positive and negative consequences of their behaviors. Next, they are taught to “PLAN” effective solutions to

their problems by focusing on ways that make their problems smaller instead of bigger and keep themselves and others safe. In addition, groups are designed to provide youth with structured 'practice experiences' during which they are able to apply their skills under a variety of different circumstances (e.g., stealing, anger management, peer pressure). The second component is focused on teaching parents effective child management strategies. Specifically, parents are taught behavioral strategies that focus on consistent reward and punishment implementation designed to improve the quality and consistency of their response to negative (e.g., defiance) and positive (e.g., compliance) child behavior. Groups include of modeling, behavioral rehearsal/role plays and parents are given home practice exercises. Parents are also informed of the cognitive and behavioral self-control techniques that their children are learning. Both of these core components are offered simultaneously within a weekly 90-minute group setting for 12 consecutive weeks. Youth and their families are also offered additional components based on need and preference. These include family therapy, individual befriending designed to connect youth with positive structured activities in their community, and academic tutoring for youth who are not performing at their grade level.

Initial studies evaluating the effectiveness of SNAP found that youth who attended the program had a significant reduction in CP from pre to post treatment that was maintained at 6- and 12-month follow-ups (Hrynkiw-Augimeri, Pepler, & Goldberg, 1993). In addition, more than half of youth enrolled in SNAP successfully refrained from future contact with the criminal justice system for up to 11 years post-treatment (Day, 1998). Bolstering early work, more rigorous examinations of the SNAP program have utilized RCT or matched control designs and allow for stronger conclusions about the overall effectiveness of the program. Augimeri and colleagues (2007) found 16 youth who were randomly assigned to SNAP to exhibit reductions

in delinquent and aggressive behaviors relative to 14 youth assigned to non-clinical, recreational activities. Significant reductions in CP were evident post-treatment and gains were maintained at 6-, 12- and 18-month follow-ups. Expanding on this study, an additional 50 SNAP participants matched on age, sex and level of CP were included in analyses and compared to the original groups examined by Augimeri and colleagues (2007). Results indicated reductions in delinquency, major aggression, and minor aggression for youth completing SNAP relative to controls (Koegl, Farrington, Augimeri, & Day, 2008). Moreover, youth participating in SNAP who attended 9 or more group sessions had significantly fewer convictions up to age 18 (36% vs. 68%) relative to those who attended fewer than 8 sessions. In a larger sample, youth enrolled in SNAP (*n*=223) demonstrated significantly greater decreases in parent-reported problem behaviors, including rule-breaking, aggression and conduct problems when assessed 6-months post-treatment (Lipman, et al., 2008).

More recently, Burke and Loeber (2014) evaluated the effectiveness of SNAP in the first RCT to date (n=252). This study is particularly relevant because participants in the current dissertation were recruited from this sample. Results indicated that children enrolled in SNAP evidenced a greater reduction in conduct problems, aggressive behavior and overall externalizing behavior when compared to youth receiving treatment as usual (TAU). Immediately following intervention, children receiving SNAP had average scores below the 'clinical' cutoff (T-score < 70 on the CBC-L) and these effects were maintained across three follow-up assessments up to 15-months from baseline. Effect sizes were small to moderate (Cohen's *d*=.25-.31) and remained even after controlling for age, race, income, IQ and prior police contact.

Taken together, these results provide support for the effectiveness of this program for children at-risk for persistent CP. However, what remains unclear is how individual differences

in reward and punishment processing may influence responsiveness to this intervention. While there has been some suggestion that aberrant reward/punishment processing underlies treatment resistance in a subgroup of youth with CP (e.g., Hawes & Dadds, 2005), it is also possible that emphasis on consistent reward/punishment contingencies could serve to modify problem behaviors for these youth who are at-risk for more chronic forms of CP. A better understanding of how abnormalities in reward/punishment processing may impact the success of treatment (in either direction) would be particularly important with regard to further elucidating additional moderating mechanisms. Moreover, this knowledge could aid in the tailoring of intervention techniques, perhaps at a more individual level, to achieve optimal effectiveness (Dadds & Salmon, 2003). As such, the current dissertation takes an exploratory approach and seeks to investigate associations between baseline reward/punishment responsivity and post-treatment levels of CP as well as the extent to which potential deficits moderate treatment effectiveness.

2.8 RATIONALE

Abnormalities in reward and punishment processing have been conceptualized as a causal mechanism underlying the development of persistent CP in boys. However, there is still some debate about the neural underpinnings of this proposed mechanism. Specifically, some researchers have hypothesized that CP stems from an overactive reward system, characterized by heightened neural reactivity to reward and in turn, hypersensitivity to reward, while others have posited that CP reflects an inherently underactive reward system that necessitates excessive reward seeking to achieve adequate stimulation. Researchers have also suggested that a primary deficit in punishment processing, characterized by a hypoactive neural response and

consequently, reduced sensitivity to punishment, underlies chronic CP. In addition, there is some indication that these abnormalities may be most pronounced in a more homogenous sub-group of boys with elevated CP and CU traits (or psychopathic features) who are thought to be at heightened risk for severe and protracted CP. Although extensive theoretical and behavioral work as well as burgeoning neuroimaging literature provides some support for abnormalities in reward/punishment processing in CP youth, several questions remain. First, past research has often utilized complex behavioral paradigms that incorporate multiple aspects of reward and punishment processing, making it difficult to clearly delineate the strength and direction of associations between abnormalities in reward and/or punishment responsivity and CP in boys. Moreover, these studies often focus on adolescents and rarely examine potential differences in these neural processing systems *within* subgroups of CP youth relative to healthy controls. Lastly, we have a limited understanding of how abnormalities in processing reward/punishment may influence response to intervention, as child-focused cognitive-behavioral therapies (CBT) and parent management training (PMT) rely heavily on behavioral strategies associated with reward and punishment. While abnormal reward and punishment processing may help to drive early and chronic engagement in CP, child-focused CBT and skills training interventions coupled with PMT have demonstrated positive effects in reducing CP in samples of youth. Specifically, these interventions, which emphasize reward/punishment contingencies, may help to modify problem behaviors in youth characterized by aberrant reward/punishment processing who are at-risk for more chronic forms of CP. However, it is also possible that these interventions are insufficient to overcome the behavioral impairments associated with deficient reward and/or punishment responsivity in youth.

As such, the primary aims of this study are twofold: 1) to examine potential abnormalities in processing reward and punishment among subgroups of youth with CP relative to HC and 2) to assess the extent to which differences in neural processing of reward and punishment are associated with levels of CP following treatment and whether these differences serve to moderate treatment effectiveness. Neural responsivity to reward and punishment was examined using an event-related fMRI task prior to treatment initiation. BOLD response was assessed as a marker of neural activation in key regions associated with reward and punishment processing in subgroups of CP youth and HC. In addition, all CP youth were re-evaluated post-treatment and baseline differences in brain function were examined as predictors of post-treatment CP following random assignment to an empirically supported multi-modal intervention (i.e., SNAP) vs. TAU.

2.9 HYPOTHESES

Based on the theory and empirical findings described above, the following aims were examined and hypotheses were tested (see Figure 1).

Aim 1: Characterize differences in the BOLD response to the receipt of reward and punishment among boys with CP and low CU traits (CPCU-), boys with CP and high CU traits (CPCU+) and matched HC.

Hypothesis 1a: Reward. It was hypothesized that both CPCU- and CPCU+ youth would be characterized by increased BOLD response in the ventral striatum (VS) to reward relative to HC. However, no differences were expected in BOLD activation to reward between CPCU+ and

CPCU- youth. Further, continuous measures of CP were expected to show a positive association with reward activation in the VS, while CU was hypothesized to show little to no relationship.

Hypothesis 1b: Punishment. It was hypothesized that relative to HC, CPCU- and CPCU+ youth would be characterized by increased BOLD activation in the dorsal striatum (DS) to the receipt of punishment. Additionally, it was predicted that both CP groups would evidence decreased BOLD activation in the amygdala, ACC, mPFC and OFC to punishment relative to HC. Moreover, these differences are expected to be most pronounced in CPCU+ youth relative to CPCU-. Finally, both CP and CU constructs were expected to show a positive association with BOLD response to punishment in the DS, while demonstrating negative associations with BOLD activation in all other regions. These associations were hypothesized to be driven by CU.

Aim 1b: Given that prior fMRI studies have subtyped CP youth based on overall psychopathy scores rather than CU traits per se, the current dissertation will examine whether the findings from Aim1a change when CP youth are subdivided based on high and low psychopathic features. Specifically, BOLD response to the receipt of reward and punishment was evaluated among boys with CP and low levels of psychopathic features (CP PSY-), boys with CP and high levels of psychopathic features (CP PSY+) and matched HC.

Hypothesis 1c: Reward. Hypotheses regarding responsivity to reward were identical to those stated above. It was predicted that both CP PSY- and CP PSY+ youth would be characterized by increased BOLD response in the VS to reward conditions relative to HC, though no differences were expected between CP PSY+ and CP PSY- youth. Continuous measures of CP were expected to show a positive association with reward activation in the VS, while PSY was hypothesized to show little to no relationship.

Hypothesis 1d: Punishment. Also identical to primary hypotheses, CP PSY- and CP PSY+ youth were expected to demonstrate increased BOLD activation in the DS to the receipt of punishment. Both CP groups were expected to show decreased BOLD activation in the amygdala, ACC, mPFC and OFC to punishment relative to HC and these differences were expected to be most pronounced in CP PSY+ youth. Finally, both CP and PSY constructs were expected to show a positive association with BOLD response to punishment in the DS, while demonstrating negative associations with BOLD activation in all other regions. These associations were hypothesized to be driven by PSY.

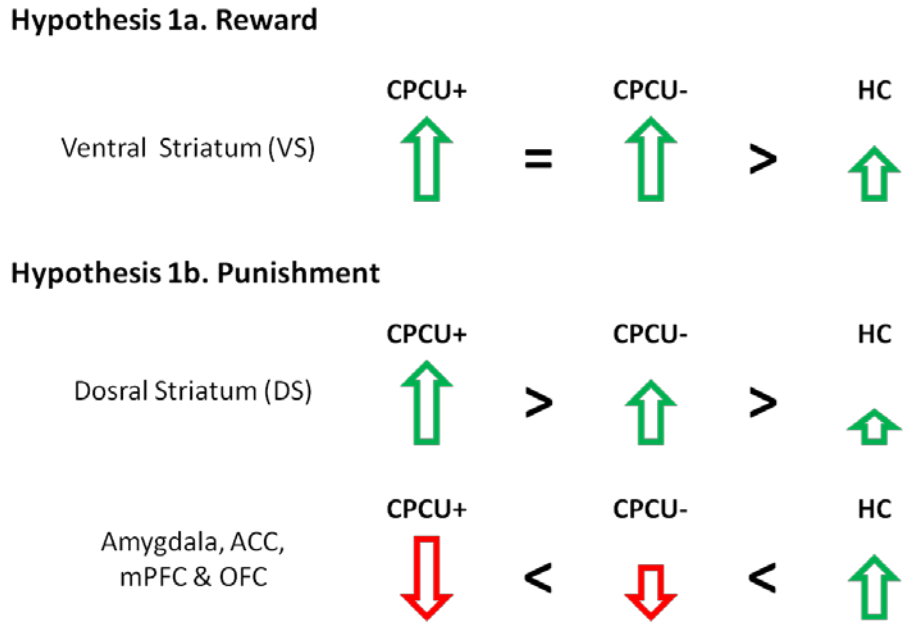
Aim 2: Evaluate the extent to which individual differences in reward and/or punishment processing are associated with responsiveness to a multi-modal intervention that emphasizes behavioral principles associated with reward and punishment contingencies. Responsivity to reward and punishment was examined as a predictor only within those regions exhibiting significant group differences.

Hypothesis 2a: Treatment Effectiveness. It was predicted that youth participating in SNAP would show greater reductions in CP at the 3-month follow-up relative to youth in TAU.

Hypothesis 2b: Main effect of brain function. Collapsed across treatment group, abnormalities in reward/punishment processing were expected to be positively associated with CP at post-treatment follow-up. With regard to reward, it was hypothesized that BOLD response in the VS would be significantly associated with increased levels of CP at post-treatment follow-up, even after controlling for pre-treatment CP severity. With regard to punishment, it was hypothesized that BOLD response in the amygdala, DS, ACC, mPFC and OFC would be associated with heightened levels of CP at post-treatment follow-up, even after controlling for pre-treatment CP severity.

Hypothesis 2c: Interaction between treatment group and brain function. While notably exploratory in nature, associations between brain function and post-treatment CP were expected to be strongest among youth participating in TAU relative to those youth assigned to SNAP.

Aim 1. CPCU Groups



Aim 1b. CP PSY Groups

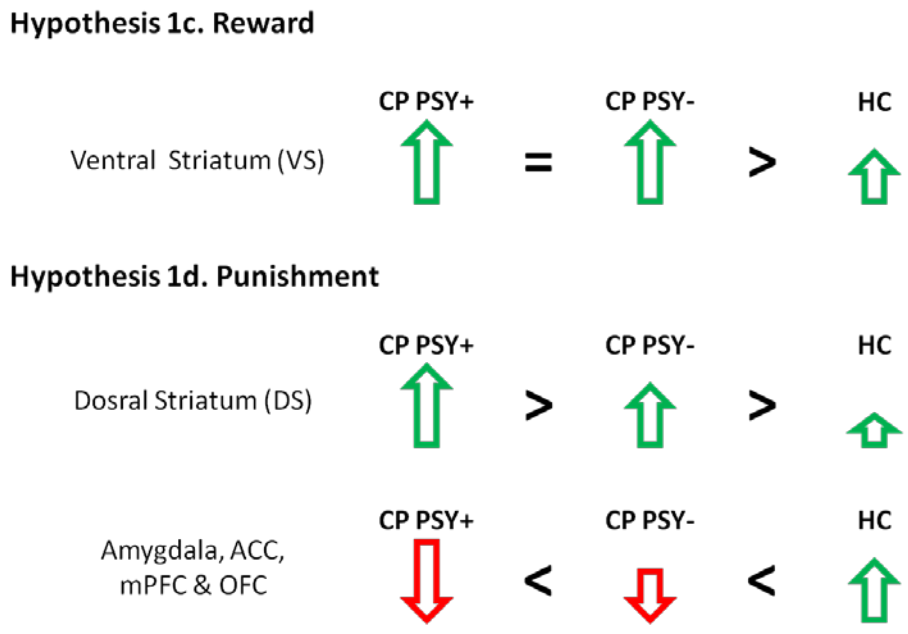


Figure 1. Diagram of hypotheses for Aim 1

Green arrows indicate positive activation while red arrows lower activation

3.0 RESEARCH DESIGN AND METHOD

The previous chapter summarizes the extant literature relevant to the current dissertation and briefly overviews the proposed hypotheses. The following section presents a more detailed description of the study design, procedures and analytic strategies. As depicted in Figures 2 and 3, following recruitment and initial screening, both CP youth (Figure 2) and matched HC (Figure 3) underwent two study phases, including a baseline assessment and a scan day assessment. Then, CP youth, as a part of a larger treatment study (Burke & Loeber, 2014), completed one of two treatment conditions for approximately 3 months and received a follow-up assessment immediately following the completion of treatment. The subsequent section provides a description of all participants, including inclusion and exclusion criteria, procedures for each phase of the study, and a detailed description of all measures used. This section also discusses the fMRI task, methods for fMRI data acquisition and processing, and the statistical model for single-subject and group level analyses.

3.1 PARTICIPANTS

Participants were recruited from a larger treatment study aimed to evaluate the effectiveness of SNAP (Burke & Loeber, 2014). The sample for the current dissertation consisted of 64 boys from 8 to 11 years old (*mean age*=10.68; *sd*=1.18) recruited from an urban city in the

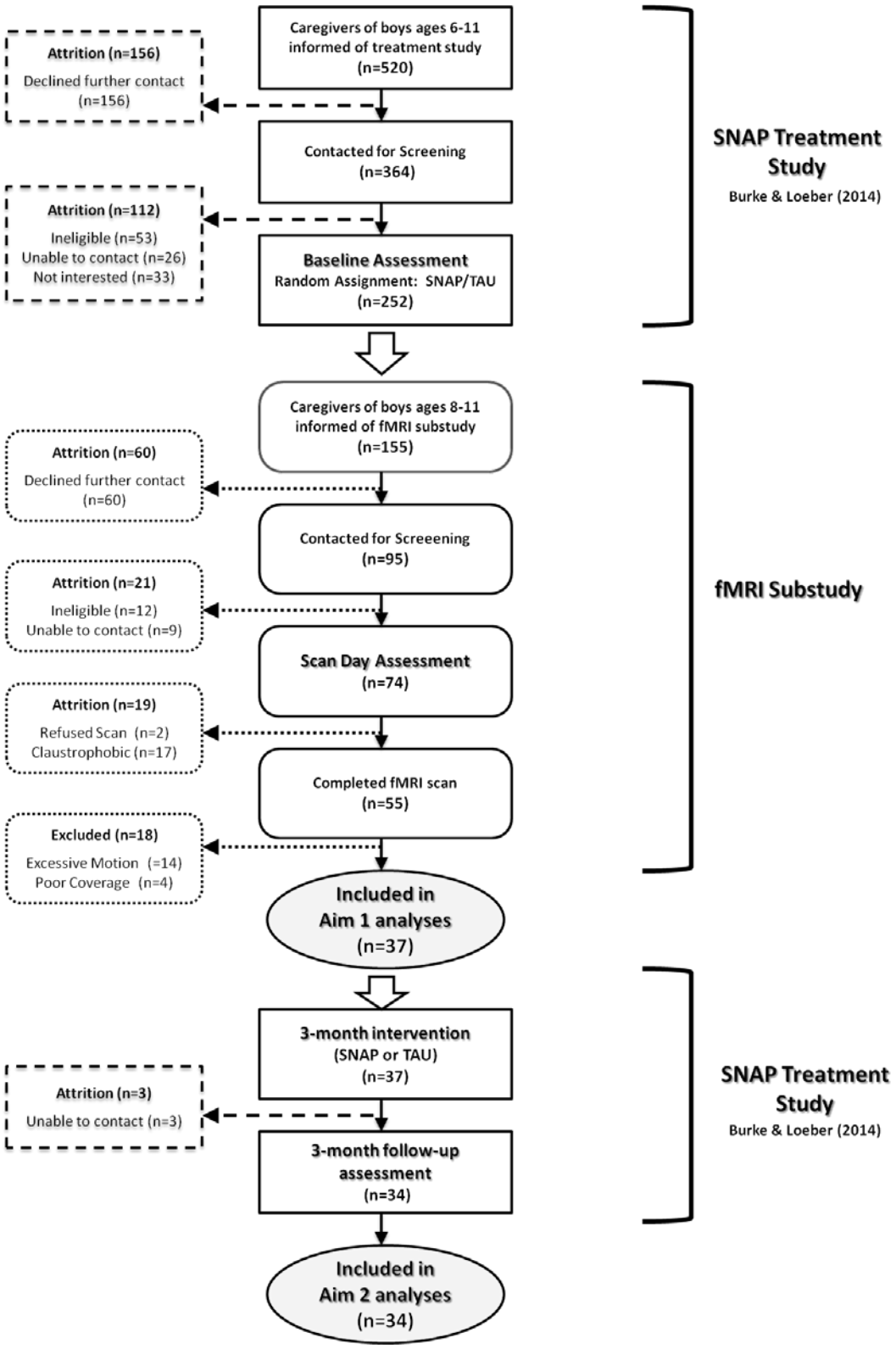


Figure 2. Flow diagram of attrition and exclusions among participants with conduct problems recruited from SNAP treatment study

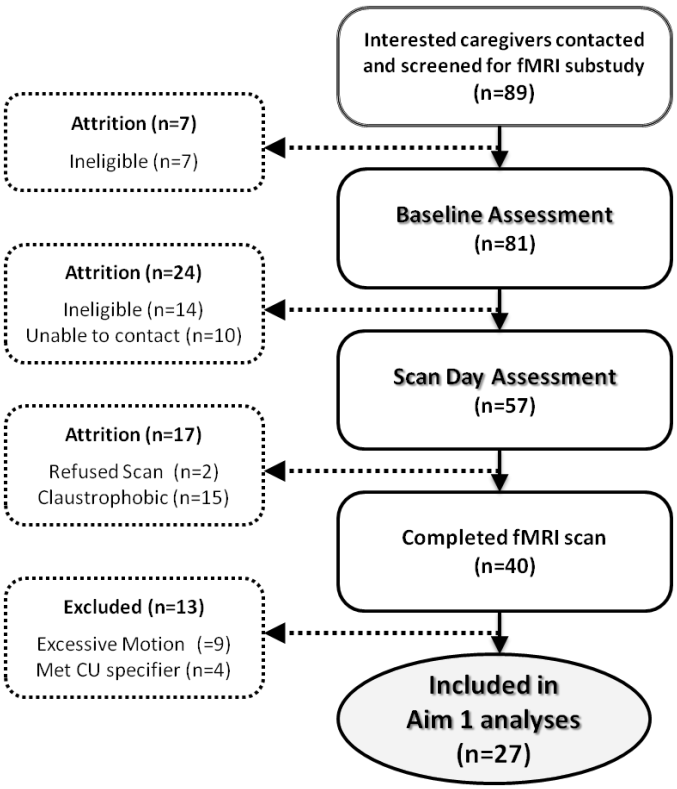


Figure 3. Flow diagram of attrition and exclusions among healthy control participants

northeastern United States, including 37 boys with CP and 27 matched HC. The majority of the participants were African-American (*n*=49, 76.6%), with the remainder being Caucasian (*n*=10, 15.6%) and mixed race (*n*=5, 7.9%). Nearly all of the boys lived with their biological mother (91%) and 28% of the boys had a biological father living in the home. Over half of the families reported receiving governmental financial assistance (63%) and the majority of families reported a total annual income of less than $20,000 per year (54%). Procedures were reviewed and approved by the Institution Review Board. Written informed consent was obtained from parents/guardians and youth provided assent prior to each assessment. Participants and youth were compensated at the completion of each assessment phase.

3.2 RECRUITMENT

Conduct Problem Youth

CP youth who participated in the current fMRI study represent a subset of youth recruited from a larger treatment study aimed to evaluate the effectiveness of SNAP (Burke & Loeber, 2014), an evidence based intervention program designed to reduce CP in children between the ages of 6 and 11 (see description below). All participants were recruited from new referrals to one of two SNAP treatment agencies in the area. Caregivers of boys between the ages of 6 and 11 calling to inquire about the SNAP program at either agency were told about the treatment study and informed that study participation would involve a random assignment to SNAP or treatment as usual (TAU) in the community. Approximately thirty percent of caregivers declined further contact regarding the study and the most common reasons for refusal was unwillingness to be randomly assigned or being involved in other services at the time. Caregivers requesting further information were contacted by research team staff and completed the screening phase of the treatment study (*n*=364). Youth from the larger treatment study were determined to be eligible if they: 1) had an estimated IQ $\geq$ 70 and 2) were rated by parents as having clinically significant behavior problems, as indexed by an age-based T-score $\geq$70 on the aggressive behavior, rule breaking, or conduct problems subscales of the Child-Behavior Checklist (CBC-L) or a T-score $\geq$ 64 on the externalizing behavior composite of the CBCL. All participants eligible for the larger treatment study were scheduled for a baseline assessment (n=252; see details below). At this time those between the ages of 8 and 11 were informed of the fMRI study (see details below).

Healthy Controls

A comparison group of HC, matched as a group to CP youth on age, race, and IQ, was recruited for the fMRI substudy predominately from local pediatricians' offices in the community. Participants were also recruited via flyers, brochures, and magazine ads placed in buses, churches and local community centers. Caregivers were informed of the study and those expressing interest completed a preliminary screener administered by local health care providers or trained research assistants (n=89). Youth were determined eligible if they had no history of services or medications for emotional/behavioral problems, no police contacts and had not received special education services for learning problems. Additionally, to provide an initial screen for CP, caregivers answered several questions from the CBCL. Eligible participants were scheduled for an in-office baseline assessment (n=81; see details below).

3.3 PROCEDURE

Baseline Assessment

All CP youth in the larger treatment study completed a baseline assessment prior to treatment initiation. This was conducted by research staff in the participant's home and both caregivers and youth completed a variety of questionnaires. At the completion of the assessment, caregivers of boys between the ages of 8-11 were informed of an additional fMRI study (*n*=155) and those that expressed interest (61%; n=95) were contacted by research staff to complete an additional screening. Any participants with a history of claustrophobia, irremovable metal (i.e., surgical implants, braces, bullets, etc.), serious medical conditions affecting brain function (i.e., meningitis) or history of concussion within the past year were excluded (*n*=12). An additional 9 participants were unable to be re-contacted or indicated that they were no longer interested

following initial screening. Eligible participants were scheduled for an fMRI scan within two weeks of their treatment start date (*n*=74) and any youth taking stimulant medications were asked not to take their medications for 24 hours prior to the study visit.

The comparison group of HC also completed a baseline assessment identical to that of CP youth. This was conducted by research staff in the office and served as a more comprehensive screening procedure. Inclusion criteria necessitated that caregivers' and youth report behavior problems below the at-risk threshold on all externalizing and internalizing scales as indexed by an age-based T-score below 60 on the CBCL. Additionally, participants with an IQ $\leq$ 70, a history of claustrophobia, irremovable metal, a history of neurological disease or structural brain injury or a concussion within the past year were excluded (*n*=24). Eligible participants were scheduled for an fMRI scan (*n*=57).

Scan Day Assessment

On the day of the scan session, CP and HC youth and their caregiver completed questionnaires (described below) prior to the fMRI scan. Once questionnaires were complete, youth underwent task training and performed a brief practice version of the reward/punishment processing task on a laptop computer to ensure task comprehension. In addition, youth were given the opportunity to complete a scan simulation in order to familiarize them with the scanning procedure. Youth then completed a one hour scan that consisted of a T2 localizer, a reward/punishment card guessing task, an implicit emotion processing task and a structural scan. For the purpose of the current dissertation, only the reward/punishment card guessing task was utilized (task and imaging details described below). Following the scan, youth completed a questionnaire about their experience in the scanner as well as their perception of the task. Of the

74 eligible CP youth, 2 refused to initiate the scan and 17 were unable to complete the scan, most often due to claustrophobia. This resulted in 52 CP youth with completed scans. Of the 57 eligible HC, 5 refused to initiate the scan and 12 were unable to complete the scan, again most often due to claustrophobia. This resulted in 40 HC with completed scans.

Treatment and Follow-up Assessment

Following the fMRI scan session, CP youth received one of two treatment conditions for approximately 3 months: 1) a comprehensive CBT/PMT intervention (i.e., SNAP) or 2) treatment as usual (TAU) in the community as a part of the larger treatment study (Burke & Loeber, 2014). Both conditions are described in more detail below. CP youth were also reassessed following treatment at 3-, 9- and 15-months from baseline, at which time measures of CP and CU were administered again. The 3-month follow-up assessment occurred directly following treatment and, due to attrition, consisted of 34 CP youth. This assessment was the focus of the current dissertation.

3.4 TREATMENT CONDITIONS

Random assignment

Upon signing consent and meeting eligibility requirements, CP youth were randomly assigned to study condition. Randomization was performed by the study investigators independently of the treatment providers using a random number generating computer program. Those enrolled in the fMRI substudy included 21 randomly assigned to SNAP and 16 to TAU; however, those assessed at follow-up included 19 youth assigned to SNAP and 15 youth assigned to TAU.

SNAP

Participants assigned to SNAP services were referred to the participating agency closest to their home. Following assignment and referral, no further efforts to influence parent or child participation in services were made by research staff to ensure the effectiveness of the trail. As described in the previous chapter, SNAP is an empirically supported, manualized program that incorporates child-focused CBT and skills training as well as PMT (Augimeri, et al., 2007). The child-focused component teaches children cognitive-behavioral self-control skills and problem-solving techniques within a group setting. The second component is focused on teaching parents effective child management strategies. Specifically, parents are taught behavioral strategies that focus on consistent reward and punishment implementation designed to improve the quality and consistency of their response to negative (e.g., defiance) and positive (e.g., compliance) child behavior. Treatment is administered in a group setting and both of these core components are offered simultaneously during weekly 90-minute group sessions for 12 consecutive weeks. The fidelity of SNAP service delivery was monitored independently by SNAP staff in Toronto through review of video recordings, and by local study team members through periodic observation of SNAP group sessions from behind one way glass. These fidelity measurements revealed an adherence to specific SNAP treatment protocols of at least 92% or greater at all measurement occasions.

Treatment as Usual (TAU)

Participants who were assigned to the TAU condition received assistance from project staff in their efforts to engage in treatment services, with a particular focus on securing evaluations to determine eligibility for wraparound services available in the local community. Wraparound services were considered to reflect the highest intensity of service in the community

since they involve multiple team members who typically provide a total of 10 or more service hours per week. Research staff assisted participants by facilitating contact between participants and a wraparound provider agency close to them. TAU participants were provided with a letter summarizing the primary indicators of the level of severity of behavioral and affective problems from their initial study measures, so that parents might give this information to potential providers. Despite the high level of behavioral problems shown by participants, clinical evaluations conducted by providers in the community did not always result in recommendations for wraparound services. In some instances, recommendations were made for less intensive service options. For those receiving recommendations, parents reported a number of barriers that impeded their ability to obtain services, including availability of appointments, issues with travel and the commitment of time, and parental motivation.

3.5 MEASURES

Child-Behavior Checklist (CBCL; Achenbach, 1991). The CBCL is 113-item parent-report questionnaire that assesses emotional and behavioral problems in children. This measure includes scales for problem behaviors as well as Diagnostic and Statistical Manual of Mental Disorders (DSM)-oriented clinical scales. Caregivers rated their children's behavior using a 3-point scale (0='*not true'* to 2='*very often true'*), with higher scores representing more severe CP. Scores on the DSM-oriented conduct problem subscale (17 items) served as the focus of the current dissertation; however, scores on the aggressive behavior subscale (18-item), rule breaking subscale (17-item) and externalizing behavior composite (35-item) are also noted given

their role in inclusionary criteria. All caregivers completed the CBCL during the baseline assessment and caregivers of CP youth completed the CBCL again during the 3-month follow-up assessment. The reliability alpha for the CP subscale at baseline (α=.93) and follow-up (α=.83) ranged from excellent to good. The reliability alpha for the aggressive behavior subscale (α=.96), rule breaking subscale (α=.87) and externalizing behavior composite (α=.96) at baseline also ranged between excellent and good.

Antisocial Process Screening Device (APSD; Frick & Hare, 2001). The APSD is a 20 item scale that has been extensively used to assess psychopathic features in children. This scale has shown evidence of construct and predictive validity in numerous previous studies with children (e.g., Frick, et al., 2003) and factor analysis has consistently indicated that the APSD assesses 3 interrelated dimensions in both clinic and community samples, including a 6-item CU dimension (e.g., "*you feel bad or guilt when you do something wrong*"), a 7-item narcissism dimension (e.g., "*you use or 'con' other people to get what you want*") and a 5-item impulsivity dimension (e.g., "*you do risky or dangerous things*") (Frick, et al., 2000). Caregivers and youth were asked to rate items on a 3-point Likert scale (0=*'not true'* to 2=*'very true'*) and positively worded items were reverse scored so that higher values represent increased levels of these features. For the purpose of the present study, items were combined across the two informants by taking the higher of the two ratings for each item and the CU subscale served as the primary focus (see below for more details). All caregivers and participants completed the APSD during the scan day assessment and CP youth and their caregivers completed the APSD again during the 3-month follow-up assessment. The reliability alpha for each of the subscales (CU, narcissism, impulsivity) and total score at baseline ranged between acceptable and good (α=.69, α=.76, α=.71 and α=.89, respectively). Similarly, the reliability alpha for each of the subscales and total

score at follow-up ranged between poor and acceptable (α=.53, α=.72, α=.38 and α=.72, respectively).

Potential Confounds

The variables outlined below were examined as potential confounds in light of research documenting their consistent association with conduct problems in previous studies (Campbell, Shaw, & Gilliom, 2000; Loeber & Keenan, 1994; Waschbusch, 2002).

Earlscourt Family Information Form (Earlscourt Child and Family Center, 2001). The Earlscourt Family Information Form is a parent-report questionnaire used to attain basic demographic information. All caregivers answered questions about their child's age and race (dichotomized as Caucasian=0, African-American=1) as well as questions regarding their family's socioeconomic status (SES). The current dissertation focused on caregivers' report of annual income and receipt of public assistance (dichotomized as no=0; yes=1). Parents rated their annual income from all sources on a Likert scale from 0 (between $0-$4999) to 13 (over $150,000).

Kaufman Brief Intelligence Test-2 (KBIT-2; Kaufman & Kaufman, 2004). The KBIT is a well-validated brief (i.e., 15-30 minutes) assessment instrument designed to index IQ (age range: 4-90 years). The KBIT is comprised of two subscales that provide indices of verbal and non-verbal intelligence. These subscales can be combined to provide a composite score indicative of overall IQ. This composite was used in the current dissertation and has been shown to correlate at .80 with the Wechsler Intelligence Scale for Children—Revised Full Scale score.

Child-Behavior Checklist (CBCL; Achenbach, 1991). Parent-report on the CBCL was used to assess co-occurring ADHD and internalizing symptoms. The ADHD subscale (7-item) and internalizing composite scale (32-item) of the CBCL exhibited high internal consistency

(α=.88 and α=.83, respectively). Participants were classified as having clinically significant or at risk versus non-significant ADHD symptoms and internalizing problems, operationalized as a T-score of ≥ 65 on the CBCL on the respective scale, and this dichotomous variable was used in the current dissertation.

3.6 GROUP CLASSIFICATION

CPCU

To examine potential differences in reward/punishment processing within subgroups of children with CP, boys were first divided into groups based on the presence of CU as measured by the APSD. This group classification is referred to as 'CP CU'. In line with the new 'with limited prosocial emotions' specifier for conduct disorder in the DSM-5 (American Psychiatric Association, 2013), 4 items from the CU subscale (i.e., lack of remorse or guilt, lack of empathy, unconcerned about performance, and shallow or deficient affect) were used to categorize CP youth with and without CU traits. To form the specifier, items scored as '*very true*' were rated as present and youth with the presence of at least two of the four items met criteria for the specifier, consistent with the existing DSM-5 symptom threshold (American Psychiatric Association, 2013) . This resulted in 24 youth with CP only (i.e., CPCU-) and 13 youth with CP and CU (i.e., CPCU+). Noteworthy, four HC were excluded from analysis due to high CU traits (i.e., met criteria for CU-subtype specifier), resulting in 27 HC.

CP PSY

Secondary analyses examined an alternative classification criterion that more closely mirrors past research in this area (e.g., Finger et al., 2008; 2011). Specifically, these analyses

examined psychopathic features more broadly defined using the APSD total score, which includes features associated with CU, narcissism and impulsivity. This group classification is referred to as 'CP PSY'. Consistent with previous studies (Budhani & Blair, 2005; Finger, et al., 2011; Finger, et al., 2008), a cutoff score of 20 or higher was used to delineate youth with high and low psychopathic features. This resulted in 11 youth with CP only (CP PSY-) and 26 youth with CP and psychopathic features (CP PSY+). One HC was excluded from these analyses due to increased psychopathic features (i.e., APSD total score=23) resulting in 26 HC. A summary of group membership and participant overlap between the two classifications is presented in Table 1.

Table 1. Crosstab of overlap between CPCU and CP PSY group classifications

		CU specifier		
		CPCU-	CPCU+	Total
Psychopathic Features (APSD Total)	CP PSY -	9	2	11
	CP PSY +	15	11	26
	Total	24	13	37

Note. CU=callous-unemotional traits; CP=conduct problems; APSD=Antisocial Process Screening Device.

3.7 FMRI CARD GUESSING TASK

During each fMRI scan, participants completed an event-related task designed to assess neural response to the receipt of uncertain reward and punishment outcomes (Delgado, Nystrom,

Fissell, Noll, & Fiez, 2000). Participants were told they would be playing a card guessing game with the goal of accumulating as much money as possible, up to a maximum of $20, which would be paid to them after completing the task. They were informed that the card had an unknown value between 1 and 9 and were instructed that they could earn money by 'guessing' whether the number was higher or lower than 5. A schematic illustrating the events of each trial is presented in Figure 4. Trials began with the presentation of a card with a centrally located question mark (2.5 seconds). Using a response glove, participants indicated whether they thought the number on the card was higher (right index finger) or lower (right middle finger) than 5. After their guess was made, the "actual" number was presented in the middle of the screen for 750ms, followed by feedback indicating whether their guess was correct or incorrect (750ms). Feedback consisted of one of 4 possible outcomes (i.e., big reward, little reward, big punishment, little punishment), specified by an arrow and monetary value. A correct guess led to the display of either a large green arrow with a monetary reward of $2.00 (big reward) or a small green arrow and a reward of $0.20 (little reward). Conversely, an incorrect guess led to the display of either a large red arrow pointing downward with a loss of a $1.00 (big punishment), or a small red downward arrow with a loss of $0.10 (little punishment). For trials in which a response was not made in time, a pound sign (#) was shown as feedback, and the trial was considered to be

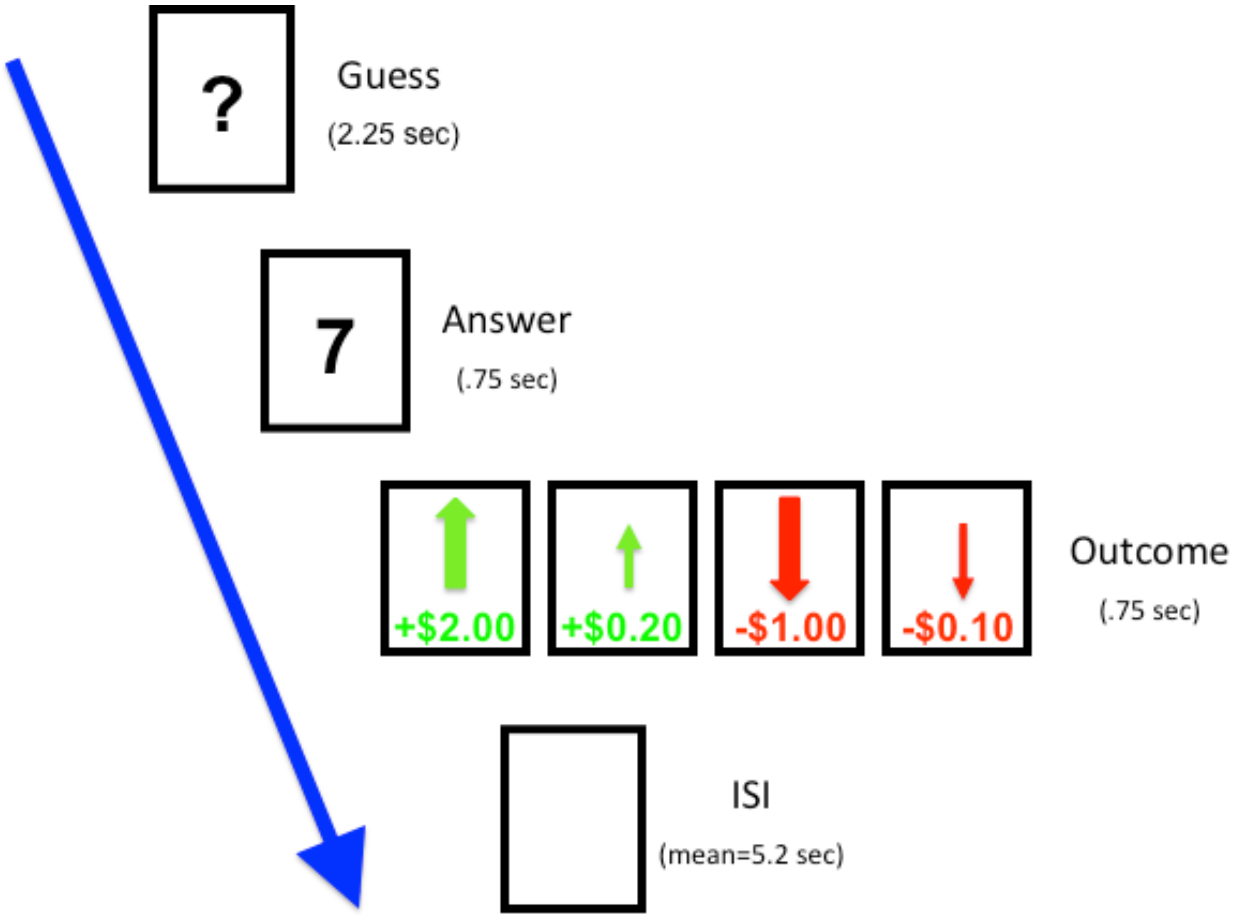


Figure 4. Schematic of events within each trial of the fMRI reward/punishment task

"missed." The outcome of each card guessing trial was predetermined and presented in a fixed, pseudorandom order across runs. The monetary gain-to-loss ratio was set to 2:1 based on research indicating that the displeasure of losing a sum of money is greater than the pleasure of winning the same amount (Kahneman & Tversky, 1979; Tversky & Kahneman, 1981). In addition, the accumulation of more monetary gains than losses was designed to promote and sustain task engagement. The feedback phase was followed by a jittered inter-stimulus-interval (ISI; mean=5.2 seconds). The task was divided into 4 runs of 40 trials each (10 trials of each condition per run), with each run lasting for 4 minutes and 10 seconds.

Following task completion, participant responses on post-scan questionnaires indicated that about half of participants believed there was a 'pattern' to the task (57%). Participants reported feeling fairly confident that they won the maximum amount of money (mean rating=7.56; SD=2.52) on a scale from definitely not (1) to definitely yes (10) and rated winning the maximum amount of money on the task as 'very important' (mean rating=7.05; SD=3.10) on a scale from not at all important (1) to 'most important' (10). All participants received $20 and were debriefed about the task.

3.8 IMAGING METHODS

Imaging Acquisition

Functional images were collected using a whole brain 3.0T Siemens MRI scanner (head-only magnet). BOLD functional images (T2-weighted) were obtained with a gradient echo planar imaging sequence covering 37 interleaved oblique slices of 3.1-mm isotropic voxels (0-mm gap)

with the following parameters: TR=2 sec; TE=28 ms; flip angle=90 degrees; 64 X 64 matrix with FOV = 20 X 20. Structural images were acquired over the course of 7 minutes and 17 seconds using a 3-dimensional MPRGAGE pulse sequence covering 176 axial slices of 1 mm thickness with the following parameters: TR=2.1 sec; TE=3.43ms; flip angle=8 degrees; 64 X 64 matrix with FOV=256 X 208.

Preprocessing

All fMRI data was preprocessed using SPM5 (http://www.fil.ion.ucl.ac.uk/spm/software/spm5/). First, all functional images were slice timing-corrected. Next, to correct for head motion that occurred during the functional scan, all images were realigned using a two-pass procedure using sinc interpolation. Specifically, images collected within a run were aligned to the first functional image collected in the run and then images across the four runs were aligned to the mean of the realigned functional image from the first run. After realignment, the structural MPRAGE image was coregistered to the corrected mean functional image. Structural images were then transformed into Montreal Neurologic Institute (MNI) stereotactic space using an automated segmentation and normalization procedure. Warping parameters from this procedure were then applied to the functional images to transform them into MNI space. Lastly, the functional images were spatially smoothed using a 6mm full-width at half-maximum (FWHM) Gaussian smoothing kernel.

Motion was estimated for each task run independently and runs with more than 6mm of motion (i.e., 2 voxels) were excluded. Exclusion due to excessive motion was a significant problem, due in part to the young age of the participants and restlessness among children with significant impulse control problems. To allow for the incorporation of the maximum number of participants, the 3 runs with the least amount of motion for each participant were used in the

analyses. There were 23 participants who were excluded from the analyses because they moved more than 6 mm during 2 or more runs (14 CP, 9 HC). Additionally, 4 CP youth were excluded due to susceptibility artifact that resulted in poor anatomical coverage of key regions of interest (e.g., ventral striatum). As a result, the final sample consisted of 37 CP and 27 HC children (see Figures 2 and 3).

3.9 DATA ANALYSIS PLAN

fMRI Single-Subject (1st Level) Analysis

For each individual, BOLD response to task events were modeled by convolving stimulus onset times with a canonical hemodynamic response function. All events were modeled separately for each run and separate regressors were specified for each of the four conditions (big reward, little reward, big punishment, little punishment), and the # sign that occurred when participants failed to make a guess in the allotted time. In addition, 6 motion parameters generated from the realignment pre-processing procedure were included to control for the influence of head movement within runs. Separate intercept values were also estimated for each run. Beta coefficients representing the average height of the hemodynamic response to the each of the four conditions across all three runs were created for each individual (i.e., big reward, little reward, big punishment, little punishment). The average BOLD response to each of these outcomes is relative to an implicit baseline representing the mean fMRI signal during unmodeled time periods (e.g., fixation). All single subject images were visually examined prior to conducting group analyses to ensure there was adequate coverage of all ROIs and there were no

significant distortions of the functional images due to signal artifact or problems with the normalization process.

fMRI Group (2nd Level) Analysis

Analyses were conducted in several steps. First, to ensure that the task successfully engaged the neural circuitry associated with reward and punishment processing, initial analyses examined the BOLD response to each condition across all subjects. These analyses were performed across the whole-brain using a voxel-level family wise error (FWE) corrected threshold of $p < 0.05$, with a minimum cluster threshold of 20 contiguous voxels. Separate one sample t-tests were used to determine where in the brain the BOLD response was significantly different from zero for events involving: 1) the receipt of any reward and 2) the receipt of any punishment. These analyses provide a depiction of the neural network responsive to the receipt of reward and punishment using data from the entire sample.

Next, group differences in the BOLD response to the receipt of reward and punishment were examined using a 3x4 ANOVA, with group (HC, CPCU-, CPCU+) entered as a between-subject factor and condition (big reward, little reward, big punishment, little punishment) entered as a within-subject factor. Main effects of group and condition as well as their interaction were assessed. In addition, supplemental multiple regression analyses were conducted to examine associations between using continuous CP and CU scores and BOLD response to reward and punishment conditions. Secondary analyses employed an identical strategy to examine potential differences in reward and punishment processing based on the presence of psychopathic features (PSY) broadly defined. Associations between continuous CP, CU and PSY scores and BOLD response to reward and punishment were also examined.

For all ANOVA analyses outlined above, the nature of significant group differences was probed by calculating the mean BOLD response (i.e., beta values) within identified clusters of contiguous voxels and importing the values into SPSS to conduct between group contrasts. These group contrasts were conducted before and after accounting for any potential confounds that significantly differed between groups (e.g., IQ, income, clinically significant ADHD symptoms or internalizing problems).

Multiple Comparison Correction

All voxel-based analyses were initially tested within *a priori* anatomically-defined regions of interest, which included the amygdala, striatum (VS and DS), ACC, mPFC (i.e., BA10) and OFC (i.e., BA11/47). ROIs were generated using automated anatomical labeling (AAL) masks from the Wake Forest University (WFU) Pic-Atlas Tool (v3.0.3), with the exception of the striatum. To ensure comprehensive coverage of the dorsal and ventral striatum, a single mask was created using a $20mm^3$ sphere centered on Montreal Neurological Institute (MNI) coordinates x=0, y=14, z=-15, encompassing the ventral striatum and the head of the caudate, and this was combined with the caudate body/tail and putamen specified using AAL masks in the WFU Pic-Atlas Tool (v3.0.3). Masks encompassed the following voxels and volumes: amygdala (115 voxels, 1035 mm^3), striatum (1442 voxels, 12,978 mm^3), ACC (889 voxels, 8001 mm^3), mPFC (636 voxels, 5724 mm^3), and OFC (584 voxels, 5256 mm^3). Correction for multiple comparisons within each ROI was achieved by determining combined voxel-level and cluster extent thresholds using Monte Carlo simulations implemented in 3DclusterSim. Using 1000 randomly generated datasets, 3DClusterSim was used to calculate the cluster size needed (i.e., # of contiguous voxels) at a specified voxel-level threshold to achieve an overall corrected false positive detection rate of $p < 0.05$. Voxel-level thresholds were set at p

< .005 for each ROI except the amygdala, which was set at $p < .05$ due to significant signal loss and distortion that often occurs in this region. This procedure resulted in the following contiguous voxel thresholds required to reach statistical significance: amygdala (18 voxels, 162 mm^3), striatum (14 voxels, 126 mm^3), ACC (12 voxels, 108 mm^3), mPFC (8 voxels, 72 mm^3), and OFC (8 voxels, 72 mm^3).

Lastly, whole-brain exploratory analysis was conducted to detect potential group differences outside the targeted ROIs. This analysis used a liberal threshold of $p<.001$ with 20 contiguous voxels, uncorrected for multiple comparisons (Buhler et al., 2010). Although lack of correction for multiple comparisons increases the risk of false positives, this final pass was used to examine possible patterns of regional activation which may be of interest for future work.

Predictive Analyses

Several analyses were conducted to examine potential associations between abnormalities in reward and/or punishment processing and response to treatment. These analyses focused on the 34 CP youth who completed the 3-month follow-up. For each analysis, the following was assessed: 1) overall effectiveness of treatment group (SNAP versus TAU); 2) overall influence of brain function (defined as those clusters reaching significance in group level analyses); and 3) the interaction between treatment group and brain function. Post-treatment levels of CP were examined both continuously and categorically and baseline levels of CP were accounted for in all analyses.

First, a series of repeated-measures ANOVAs with 1 within-subject factor (time: CP at baseline, CP at 3-month follow-up) and 2 between-subject factors (treatment group, brain function) were conducted. Next, CP youth were classified as treatment responders versus non-responders, operationalized as a drop in CBCL score of at least 0.5 standard deviation (T score

change ≥ 5), in line with criteria set forth in prior imaging studies (Lewis, et al., 2008). Binary logistic regressions were used to examine main effect treatment, main effect of brain function and the interaction between treatment and brain function. For all analyses, significant interactions were probed and plotted.

4.0 RESULTS

4.1 PRELIMINARY ANALYSES

Selective Attrition

As described above, a total of 37 CP youth and 30 HC were excluded from analyses in the current dissertation. Excluded participants were compared to those participants included in the primary analyses in terms of all study variables. Analyses were conducted separately for CP youth and HC groups. In both groups, excluded participants were equivalent to study participants with one exception; excluded participants were more likely to be younger (CP: $t(70)$=4.72, p<.01; HC: $t(56)$=2.81, p<.01).

Additional analyses were conducted to ensure that the subsample of CP youth was representative of the larger treatment sample. The current CP subsample was equivalent to the larger treatment study sample in terms of all study variables with one exception. Due to the fMRI substudy inclusion criteria, youth in the larger treatment sample were more likely to be younger than those CP youth in the current dissertation ($t(255)$=9.48, p<.01).

Bivariate Correlations

Correlations between all study variables are presented separately for CP youth and HC in Table 2. With regard to demographic variables, race demonstrated negative associations with family income and IQ, but was unrelated to all other variables. Family income demonstrated

negative associations with all study variables, with one exception; it was unrelated to impulsivity as measured by the APSD subscale. IQ evidenced a negative association with CP and narcissism as measured by the APSD subscale as well as ADHD problems and internalizing symptoms. As expected, CP and CU showed robust positive associations with ADHD and internalizing symptoms and were strongly correlated with all other subscales of the APSD.

Group Comparisons: CPCU

Prior to primary analyses, CPCU groups and HC were compared on all study variables using a 3x1 ANOVA and group differences were probed using independent sample t-tests. Table 3 presents the means and standard deviations for all study variables by group. Boys classified as HC represented 42% of the sample (n=27). Boys with CP and low levels of CU (CPCU-) were approximately 38% of the sample (n=24) and boys with CP and CU (CPCU+) constituted 20% of the sample (n=13). Groups were equivalent with regard to age, race and receipt of public assistance; however, groups differed slightly with regard to family income and IQ. Specifically, HC were more likely to have a higher family income than CPCU- youth ($t(38)=2.42$, $p<.05$) and CPCU+ youth ($t(35)=1.99$, $p=.05$). Additionally, HC had higher IQ scores than CPCU- youth ($t(38)=2.74$, $p<.01$), though there were no differences between CPCU+ and either of the other groups with regard to IQ. As expected, CPCU- and CPCU+ youth had significantly higher levels of CP, CU, ADHD and internalizing symptoms relative to HC. However, CPCU- and CPCU+ youth only differed on levels of CU traits ($t(35)=7.72$, $p<.01$) and total APSD scores ($t(35)=2.82$, $p<.01$) and demonstrated equivalent levels of CP, ADHD and internalizing symptoms.

Task performance differed slightly between groups. Specifically, CPCU+ youth evidenced significantly slower reaction times (mean RT=1035ms) relative to CPCU- (mean RT=853ms; $t(35)=-3.32$, $p<.01$) and HC (mean RT=909ms; $t(38)=-2.14$, $p<.05$). Additionally,

CPCU+ groups had significantly more 'non-responses' relative to CPCU- ($t(35)=-2.17$, $p<.05$) and HC ($t(38)=-2.84$, $p<.05$). However, all groups responded to more than 85% of trials on average (n > 105 *trials* out of 120 trials), with each participant responding to at least 80% of trials in each condition (n >24 trials out of 30 trials).

Group Comparisons: CP PSY

CP PSY groups and HC were compared on all study variables using several 3x1 ANOVAs and group differences were probed using independent sample t-tests. Table 4 presents the means and standard deviations for all study variables by group. Boys classified as HC represented 41% of the sample (n=26). Boys with CP and low levels of PSY were approximately 18% of the sample (n=11) and boys with CP and PSY constituted 41% of the sample (n=26). Groups were equivalent with regard to age, race, IQ and receipt of public assistance; however, groups differed slightly with regard to family income. Specifically, HC were more likely to have a higher family income than CP PSY- youth ($t(35)=2.08$, $p<.05$) and CP PSY+ youth ($t(50)=2.30$, $p<.05$). As expected, both CP groups had significantly higher levels of CP, CU, ADHD and internalizing symptoms relative to HC. However, CP PSY- and CP PSY+ youth only differed on levels of psychopathic features (CU: $t(35)=-3.59$, $p<.005$; narcissism: $t(35)=-5.80$, $p<.001$; impulsivity: $t(35)=-3.40$, $p<.005$; APSD total score: $t(35)=8.24$, $p<.001$) and demonstrated equivalent levels of CP, ADHD and internalizing problems. Task performance was also examined and there were no group differences with regard to mean reaction time or number of non-responses.

General Task Activation to Reward and Punishment

Prior to examining potential group differences, preliminary analyses were conducted to examine task-specific, whole-brain activation to the receipt of 1) reward and 2) punishment to

ensure the task successfully engaged the hypothesized neural circuitry The average BOLD response to reward (i.e., big and small combined) across all participants indicated that the task produced robust activation throughout expected reward-related circuitry (Figure 5, Table 5). Clusters of significant positive BOLD response were observed in the bilateral striatum (including VS and DS), extending laterally to inferior frontal gyrus and OFC (BA47), caudally to the ventral portion of the posterior cingulate gyrus and rostrally to the insula; bilateral middle and inferior frontal gyri, extending to the mPFC (BA10) and OFC (BA11); bilateral dorsal ACC, extending to superior frontal gyrus; superior and inferior parietal lobe; and bilateral occipital lobe.

The average BOLD response to punishment (i.e., big and small combined) across all participants indicated that the task produced BOLD response patterns throughout the expected punishment-related circuitry (Figure 6, Table 6). While overlap with reward-related circuitry was considerable, BOLD response to punishment was notably less robust. Clusters of significant positive BOLD response were found in the bilateral ACC, extending to superior frontal gyrus; bilateral thalamus, extending to parts of the caudate body and tail; bilateral inferior frontal gyrus, extending to insula and OFC (BA47); bilateral middle frontal gyrus extending to the mPFC (BA10); superior and inferior parietal lobule; and bilateral occipital lobe.

Table 2. Correlations between all study variables

	1	2	3	4	5	6	7	8	9	10	11
1. Age											
2. Race	.037										
3. Family Income	.036	.075									
4. Public Assistance	-.078	-.407**	-.310*								
5. IQ	-.105	-.284*	-.204	.309*							
6. ADHD problems	.161	.128	.061	-.276*	-.330**						
7. Internalizing sx	.122	-.078	-.013	-.367**	-.287*	.566**					
8. Conduct Problems	.092	.229	.047	-.356**	-.396**	.783**	.609**				
9. APSD CU	.083	.016	.059	-.262*	-.062	.579**	.537**	.581**			
10. APSD Narcissism	.091	-.007	.118	-.253*	-.259*	.580**	.492**	.649**	.598**		
11. APSD Impulsivity	.109	.034	.039	-.207	-.201	.624**	.487**	.645**	.638**	.758**	
12. APSD Total	.119	.011	.075	-.279*	-.226	.690**	.584**	.728**	.826**	.906**	.896**

Note. Sx=symptoms; ADHD=attention deficit hyperactivity disorder; CU=callous-unemotional traits; APSD=Antisocial Process Screening Device; * Correlation significant at p<.05; ** Correlation significant at *p*<.01.

Table 3. Means and standard deviations for all study variables by CPCU group

	HC n=27		CPCU- n=24		CPCU+ n=13	
	M/ %	SD	M/ %	SD	M/ %	SD
Age	10.46	*1.24*	10.82	*1.22*	10.83	*0.89*
Race (African-American)	78%	---	88%	---	85%	---
Family Income	Between [a] $25,000 - $29,999		Between [b] $15,000 - $19,999		Between [b] $15,000 - $19,999	
Public Assistance (yes/no)	63%	---	54%	---	77%	---
IQ	100.63[a]	*15.52*	90.29[b]	*11.30*	96.23[a,b]	*10.69*
ADHD symptoms	50.56[a]	*1.31*	67.29[b]	*8.80*	68.15[b]	*7.57*
% Clinical Significant	0%[a]	---	71%[b]	---	62%[b]	---
Internalizing symptoms	51.37[a]	*3.19*	63.96[b]	*6.97*	62.08[b]	*11.72*
% Clinical Significant	0%[a]	---	71%[b]	---	46%[b]	---
Conduct Problems†	51.00[a]	*2.04*	76.67[b]	*7.70*	77.00[b]	*8.62*
APSD CU	3.96[a]	*1.58*	5.96[b]	*1.27*	9.38[c]	*1.33*
APSD Narcissism	3.18[a]	*2.35*	6.96[b]	*2.27*	7.62[b]	*2.26*
APSD Impulsivity	3.48[a]	*1.76*	6.79[b]	*1.32*	7.08[b]	*2.29*
APSD Total Score	10.85[a]	*4.79*	21.33[b]	*4.38*	25.85[c]	*5.11*

Note. ADHD=Attention Deficit Hyperactivity Disorder; APSD=Antisocial Process Screening Device; CU=Callous-Unemotional Traits; HC=Healthy Controls. Means designated with different subscript letters are significantly different from each other (p<.05) based on post-hoc independent sample t-tests.

†Group differences on the aggressive behaviors subscale, rule breaking subscale and externalizing composite were also examined. CPCU- and CPCU+ were equivalent on each (p>.50) and both groups evidenced significantly greater scores than HC (p<.05).

Table 4. Means and standard deviations for all study variables by CP PSY group

	HC n=26		CP PSY- n=11		CP PSY+ n=26	
	M/ %	SD	M/ %	SD	M/ %	SD
Age	10.48	*1.26*	10.47	*1.30*	10.97	*1.00*
Race (African-American)	77%	---	100%	---	81%	---
Family Income	Between [a] $25,000 - $29,999		Between [b] $10,000 - $14,999		Between [b] $15,000 - $19,999	
Public Assistance (yes/no)	62%	---	64%	---	62%	---
IQ Composite	99.92	*15.37*	95.73	*11.34*	90.96	*11.22*
ADHD symptoms	50.57[a]	*1.33*	66.91[b]	*7.44*	67.88[b]	*8.75*
% Clinical Significant	0%[a]	---	73%[b]	---	65%[b]	---
Internalizing symptoms	51.96[a]	*3.63*	59.36[b]	*8.58*	65.04[b]	*9.16*
% Clinical Significant	0%[a]	---	73%[b]	---	58%[b]	---
Conduct Problems †	51.00[a]	*2.08*	77.36[b]	*7.68*	76.54[b]	*8.15*
APSD CU	3.81[a]	*1.39*	5.55[b]	*1.76*	7.85[c]	*1.85*
APSD Narcissism	3.00[a]	*2.19*	5.00[b]	*1.26*	8.12[c]	*1.93*
APSD Impulsivity	3.38[a]	*1.72*	5.55[b]	*1.63*	7.46[c]	*1.39*
APSD Total Score	10.38[a]	*4.21*	16.91[b]	*2.63*	25.46[c]	*3.42*

Note. ADHD=Attention Deficit Hyperactivity Disorder; APSD=Antisocial Process Screening Device; CU=Callous-Unemotional Traits; HC=Healthy Controls. Means designated with different subscript letters are significantly different from each other (p<.05) based on post-hoc independent sample t-tests.

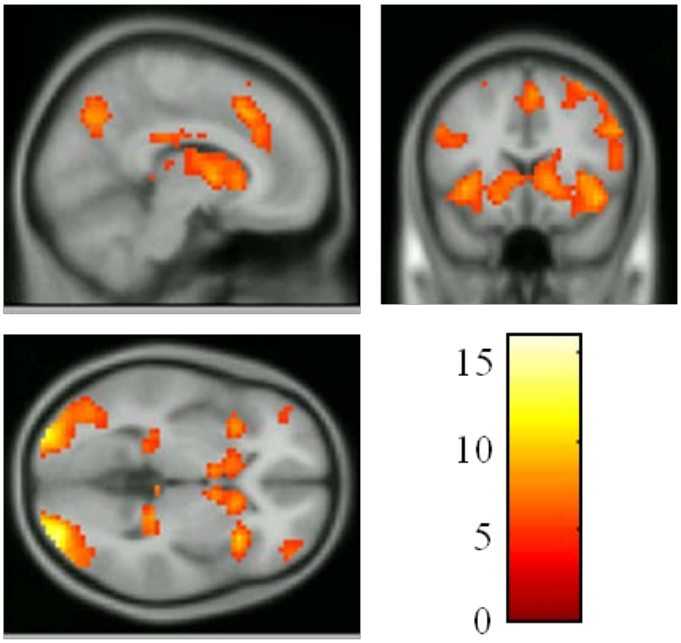
† Group differences on the aggressive behaviors subscale, rule breaking subscale and externalizing composite were also examined. CP PSY- and CP PSY+ were equivalent on each (p>.50) and both groups evidenced significantly greater scores than HC (p<.05).

Table 5. Suprathreshold clusters associated with combined effects of large and small reward relative to baseline

			Peak Coordinates (MNI)			
Region	R/L	Voxels	X	Y	Z	t
Posterior Cingulate Gyrus, Insula, Thalamus, Striatum	R/L	1129	3	-28	28	10.86
Middle Frontal Gyrus	R	829	50	9	34	9.99
Inferior Parietal Lobule	R	781	47	-47	56	14.73
Middle Occipital Gyrus, Fusiform Gyrus	R	606	34	-90	-6	16.34
Middle Occipital Gyrus	L	501	-28	-94	-3	12.62
Superior Parietal Lobule, Precuneus, Inferior Parietal Lobule	L	483	-25	-66	43	9.26
Inferior Frontal Gyrus	L	384	-44	6	25	10.25
Anterior Cingulate Gyrus (BA32)	R/L	338	3	22	43	10.32
Middle Frontal Gyrus	L	54	-28	6	59	6.39
Parahippocampal Gyrus	L	47	-22	-31	-3	6.82
Cerebellum, Occipital Lobe	L	43	-16	-72	9	6.72
Posterior Cingulate Gyrus, Insula, Thalamus, Striatum	R/L	1129	3	-28	28	10.86
Middle Frontal Gyrus	R	829	50	9	34	9.99
Inferior Parietal Lobule	R	781	47	-47	56	14.73
Middle Occipital Gyrus, Fusiform Gyrus	R	606	34	-90	-6	16.34

Note. R=right; L=left; BA=Brodmann's area.

a.



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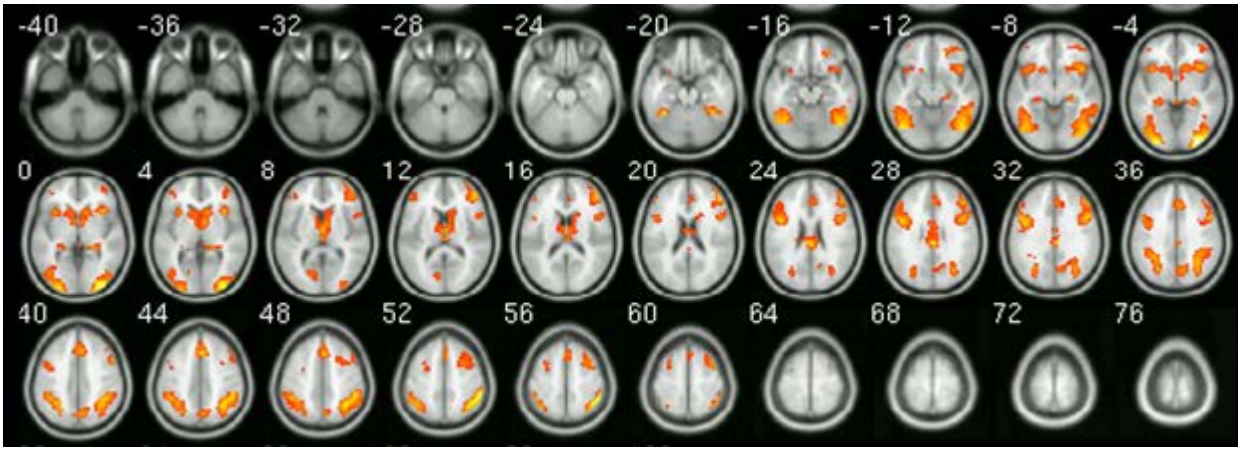


Figure 5. Combined effects of large and small reward reveal robust task-related activation throughout reward-related circuitry

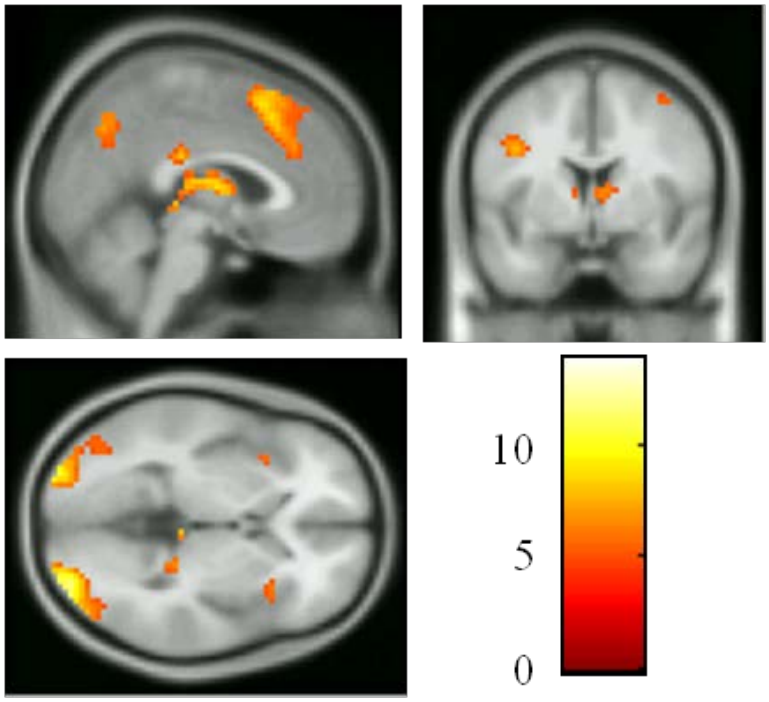
Overall task-related activation associated with large and small reward compared with implicit baseline, collapsed across group, with whole-brain family-wise error (FWE) correction of $p < 0.05$, 20 voxel extent threshold. a) Slices shown at x = 8, y = 16, z = -1; b) Transverse slices shown every 4 units on the y-axis.

Table 6. Suprathreshold clusters associated with combined effects of large and small punishment relative to baseline

			Peak Coordinates (MNI)			
Region	R/L	Voxels	X	Y	Z	t
Posterior Cingulate Gyrus, Insula, Thalamus, Striatum	R/L	1129	3	-28	28	10.86
Middle Frontal Gyrus	R	829	50	9	34	9.99
Inferior Parietal Lobule	R	781	47	-47	56	14.73
Middle Occipital Gyrus, Fusiform Gyrus	R	606	34	-90	-6	16.34
Middle Occipital Gyrus	L	501	-28	-94	-3	12.62
Superior Parietal Lobule, Precuneus, Inferior Parietal Lobule	L	483	-25	-66	43	9.26
Inferior Frontal Gyrus	L	384	-44	6	25	10.25
Anterior Cingulate Gyrus (BA32)	R/L	338	3	22	43	10.32
Middle Frontal Gyrus	L	54	-28	6	59	6.39
Parahippocampal Gyrus	L	47	-22	-31	-3	6.82
Cerebellum, Occipital Lobe	L	43	-16	-72	9	6.72
Posterior Cingulate Gyrus, Insula, Thalamus, Striatum	R/L	1129	3	-28	28	10.86
Middle Frontal Gyrus	R	829	50	9	34	9.99
Inferior Parietal Lobule	R	781	47	-47	56	14.73
Middle Occipital Gyrus, Fusiform Gyrus	R	606	34	-90	-6	16.34

Note. R=right; L=left; BA=Brodmann's area

a.



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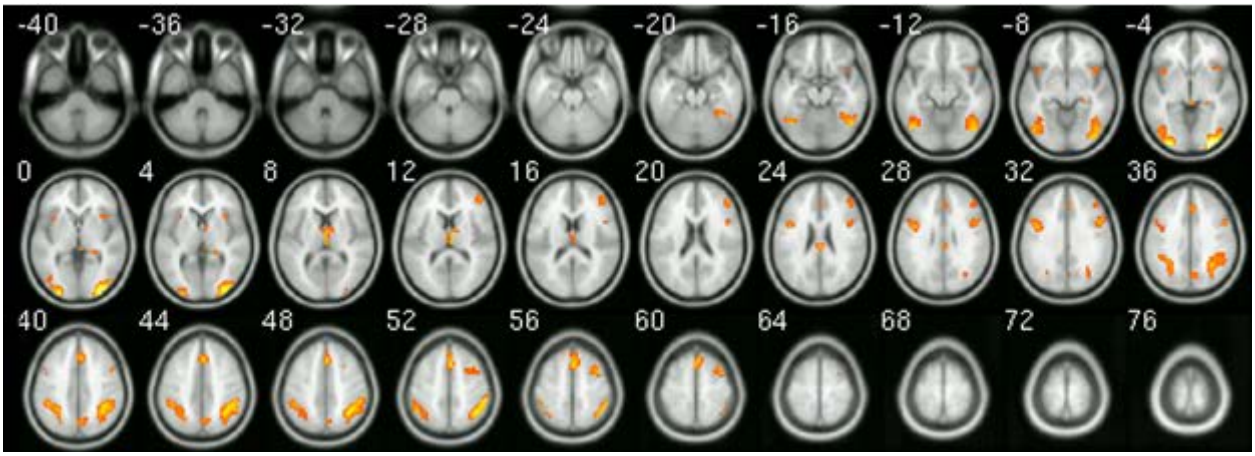


Figure 6. Combined effects of large and small punishment reveal task-related activation throughout punishment-related circuitry

Overall task-related activation associated with large and small punishment compared with implicit baseline, collapsed across groups, with whole-brain family-wise error (FWE) correction of $p < 0.05$, 20 voxel extent threshold. a) Slices shown at x = 3 y =1, z = -1; b) Transverse slices shown every 4 units on the y-axis.

4.2 AIM 1: ARE THERE DIFFERENCES IN THE NEURAL RESPONSE TO THE RECEIPT OF REWARD AND PUNISHMENT AMONG BOYS WITH CP AND CU?

The first primary analysis of interest examined potential group differences in reward and punishment processing using a 3x4 ANOVA. While the focus was on the main effect of group and the interaction between group and condition, the main effect of condition was also examined and significant results are presented. All significant group differences were re-examined accounting for potential confounds (i.e., family income, IQ, clinically significant ADHD and internalizing symptoms). Lastly, CP and CU constructs were examined continuously as predictors of BOLD response to reward and punishment within a regression framework.

Main effect of condition within a priori ROIs

A significant main effect of condition was found for each of the ROIs examined indicating differential BOLD response to reward and punishment conditions across all participants (Table 7). In line with the whole-brain analyses described above, there was greater activation to reward relative to punishment within the bilateral amygdala, striatum, ACC, bilateral mPFC and bilateral OFC. Pairwise t-tests corrected for multiple comparisons indicated that within each of these regions BOLD response to big and little reward was significantly greater than BOLD response to big punishment (*ps*<.005, *ps*<.05, respectively); additionally responsivity to big reward was greater relative to little punishment (*ps*<.001).

Main effect of group within a priori ROIs

Significant between-group differences for BOLD response collapsed across all reward and punishment conditions were only evident in the mPFC (BA10; Table 7). Figure 7 presents the mean BOLD response for the cluster that significantly differed between groups. Results indicated that across all conditions both groups of CP youth exhibited lower BOLD response;

however, significant differences emerged only between boys in the CPCU- group and HC. However, this finding was reduced to trend level significance after controlling for potential confounds (p=.09).

Group X condition interaction with a priori ROIs

Brain regions exhibiting a significant group by condition interaction are displayed in Table 7. A significant interaction emerged for a cluster of voxels in the left amygdala and probing revealed significant differences in response to big reward and big punishment (Figure 8). Follow-up group comparisons with extracted mean BOLD values from this cluster indicated that both CP groups exhibited significantly lower activation following the receipt of punishment relative to HC, who evidenced significant activation within this cluster. Importantly, these differences remained significant after accounting for potential confounds; however, there was no significant difference between CPCU- and CPCU+ youth in terms of their BOLD response to big punishment within this region. Additionally, CPCU- also exhibited a significantly lower BOLD response to big reward in the amygdala relative to HC. However, this was reduced to non-significance after accounting for potential confounds and clinically significant internalizing problems emerged as a significant predictor (p=.02).

Another significant group by condition interaction emerged within the left striatum, specifically within the caudate body (Table 7). Further probing of the interaction revealed significant group differences in BOLD response to big reward and big punishment (Figure 9). While CPCU+ youth demonstrated the increased reactivity to big reward, BOLD activation was equivalent to that of HC. Significant differences emerged only for CPCU- youth who exhibited a significantly lower BOLD response to the receipt of a big reward relative to HC and CPCU+ youth. Within this region, the CPCU- group also exhibited a significantly lower BOLD response

to big punishment relative to HC youth; however, no differences were seen between CPCU+ youth and HC. All group differences were reduced to non-significance after accounting for potential confounds, though none of the control variables emerged as significant predictors.

Whole Brain Analyses: Exploratory

Exploratory whole brain analyses failed to identify any areas of activation associated with the overall main effect of group. However, two clusters of activation emerged related to the group X condition interaction and they included the bilateral cingulate gyrus (BA24/BA32) and the left postcentral gyrus (Figure 10). Consistent with analyses described above, post-hoc analyses revealed that groups differed in their responsivity to big reward and big punishment. In the cingulate gyrus, CPCU+ youth demonstrated a significantly greater BOLD response to reward relative to CPCU- youth, though neither group differed from HC. Within this same cluster, both CP groups had lower activation following punishment relative to HC, however, only CPCU- youth significantly differed from HC. In the postcentral gyrus, CPCU+ youth evidenced a significantly greater BOLD response to the receipt of reward relative to CPCU- youth and HC.

Continuous Analyses within a priori ROIs: Associations with CP and CU

To augment the group based findings, analyses were re-run using continuous CP and CU scores for all participants to predict BOLD responding to each of the reward and punishment conditions within the targeted ROIs. First, the bivariate associations between CP and CU and individual differences in BOLD response to reward and punishment were examined. Next, multivariate analyses examined the unique association between CP and CU and the BOLD response to reward and punishment after controlling for their co-occurrence. All bivariate and multivariate results are presented in Table 8.

Bivariate Associations

BOLD response to the receipt of big reward was only significantly associated with CP and this was specific to the amygdala. Specifically, higher CP was associated with reduced activation in the left amygdala following reward. With regard to punishment, the BOLD response was negatively associated with CP in all of the ROIs examined. Higher levels of CP were correlated with lower BOLD response in the bilateral amygdala, bilateral striatum, bilateral ACC, left mPFC and bilateral OFC. Additionally, CU demonstrated a negative association with BOLD response to punishment in the bilateral amygdala, left dorsal striatum (i.e., caudate and putamen) and left OFC; however, these associations were notably less robust than those with CP.

Unique Associations

When CP and CU were entered simultaneously to examine unique associations with BOLD response after accounting for their overlapping variance, significant results emerged only within the bilateral amygdala and only to the receipt of punishment (Table 8). Increased CP was negatively associated with BOLD response to punishment in the amygdala, after accounting for CU (Figure 11); however, CU failed to contribute any unique variance. All other bivariate associations were reduced to non-significance, though one association that approached significance is worth noting. CU demonstrated a positive association with BOLD response in the left caudate after controlling for CP, though this association failed to reach the cluster threshold (voxels=13; *z*-score: 3.45; $p<.001$; MNI peak coordinate: z=3.45, x=19, y=25).

Summary

Several differences emerged between HC and CP groups in terms of BOLD responsivity to reward and punishment. Notably, these differences were specific to receipt of big reward and big punishment. Regarding responsivity to reward, differences within the left caudate, left amygdala and left mPFC were found. In contrast to expectation, CPCU- youth exhibited lower

BOLD responding in the caudate, amygdala, and mPFC to reward relative to HC while CPCU+ youth did not significantly differ from HC in reactivity to big reward in any region. Taken together, CP youth without CU traits appear to exhibit a pattern of hypoactive neural responding to reward across several key brain regions, whereas CPCU+ youth exhibit a more normative neural response to the receipt of reward. Noteworthy, these findings were reduced to trend level significance after accounting for potential confounds, with some suggestion that reduced BOLD response to reward in the amygdala was uniquely associated with clinically significant internalizing problems.

With regard to reactivity to punishment, differential responsiveness was consistently shown within the amygdala and in the predicted direction. As hypothesized, both the CPCU- and CPCU+ youth exhibited reduced neural responsivity in the left amygdala following the receipt of big punishment and this was in direct contrast to HC who demonstrated increased BOLD response to big punishment in this same region. These findings remained significant after controlling for potential confounds and were consistent with regression analyses demonstrating unique associations between reduced reactivity to punishment within the amygdala and CP severity. Additionally, both groups of CP youth demonstrated similar levels of (reduced) responsivity to punishment within the caudate and mPFC. However, when compared to HC, who were characterized by increased BOLD response to punishment in both of these regions, only CPCU- youth demonstrated significantly lower activation.

Overall, while there were several significant differences between groups of children with CP and HC regarding responsivity to both reward and punishment, there was little difference in responsivity *within* subgroups of children with CP. In fact, the only difference that did emerge was specific to responsivity to big reward within the caudate and this was contradictory to

hypotheses. While this may provide some initial evidence for differential reward processing among subgroups of CP youth with and without CU traits, results more consistently point to reduced amygdala responsivity to punishment among youth with CP, regardless of the their levels of CU traits, relative to HC.

Table 7. Suprathreshold clusters for CPCU group differences: 3x4 ANOVA

			Peak Coordinates (MNI)				
Brain region	R/L	Voxels	X	Y	Z	F	*p*-value
Main Effect of Condition							
Amygdala	L	47	-16	0	-15	17.25	0.000
	R	38	19	0	-12	14.97	0.000
Striatum	R/L	1000	16	9	-6	36.75	0.000
ACC	R/L	503	-3	41	6	14.01	0.000
mPFC (BA10)	R/L	104	-3	53	-3	15.30	0.000
OFC (BA 11/47)	R/L	245	28	41	-12	13.55	0.000
Main Effect of Group							
mPFC (BA10)	L	8	8	-6	50	7.63	0.001
Group X Condition Interaction							
Amygdala	L	22	-22	-6	-19	9.41	0.000
Caudate	L	14	-12	3	15	4.37	0.000

Note. R=right; L=left; ACC=anterior cingulated; mPFC=medial prefrontal cortex; OFC=orbital frontal cortex; BA=Brodmann's area.

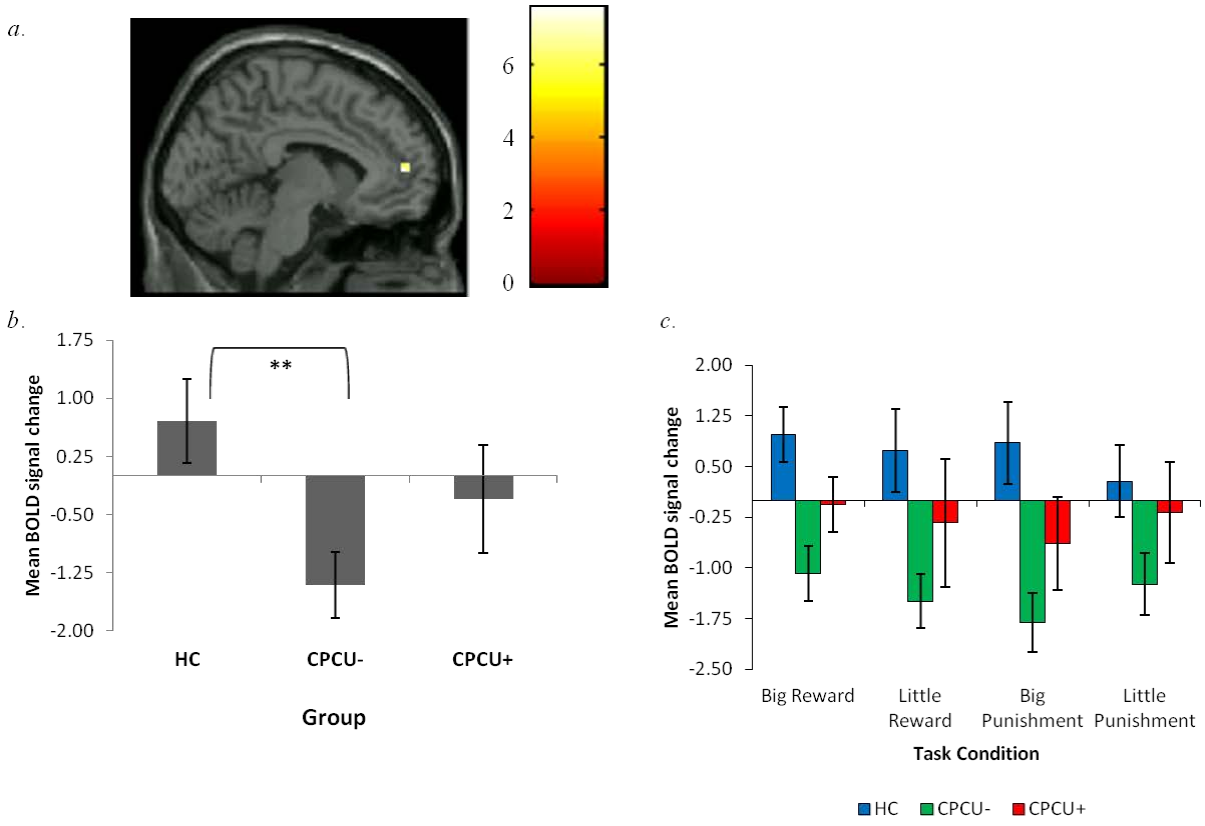


Figure 7. Activation in left BA10 is associated with main effect of CPCU group

a) Region in BA10 significant at $p < 0.005$, corrected using 3DclusterSim threshold for contiguous voxels ($F(2, 244)=7.63$, 8 voxels). Slices shown at x= -5, y=50, z =9 (MNI peak voxel); *b*) Bar graph depicts extracted mean blood oxygen level-dependent (BOLD) response for each group across all conditions within the cluster along with standard errors; *c*) For descriptive purposes, mean level activation, along with standard errors, within the significant cluster by group and condition are also presented.
** = $p < 0.01$. The *p*-values are based on Games-Howell pairwise comparisons for extracted mean BOLD response.

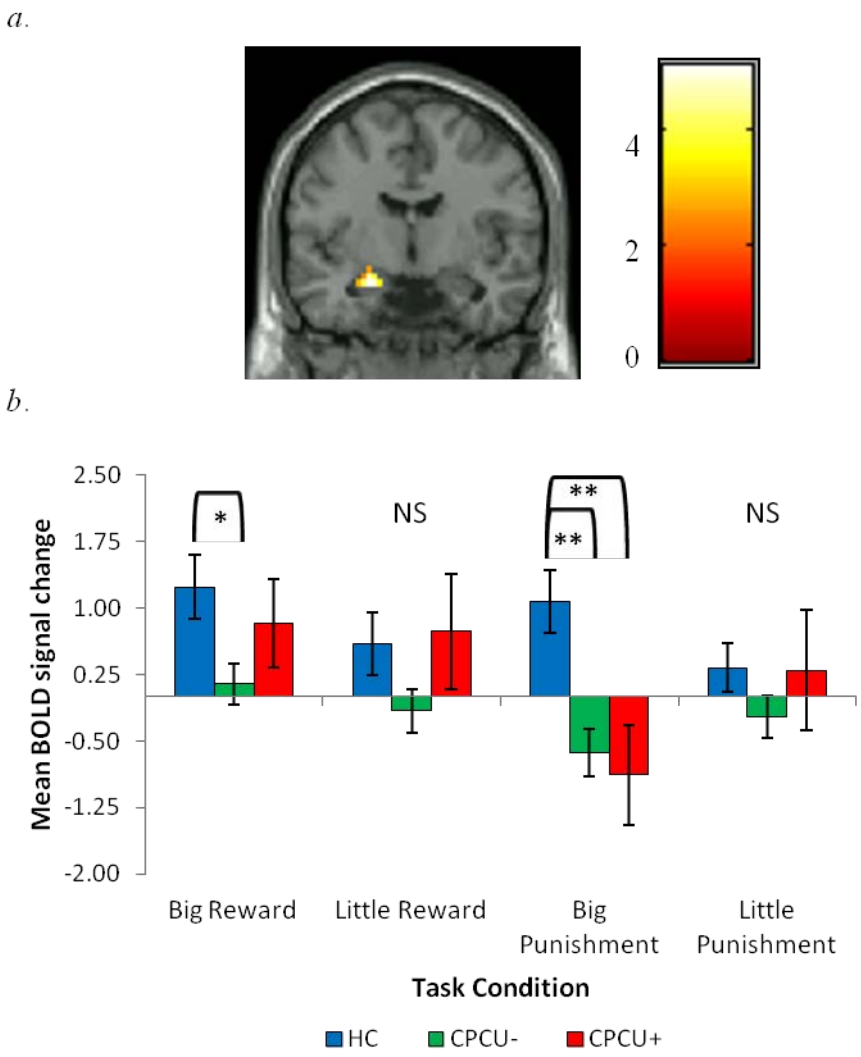


Figure 8. Activation in the left amygdala is association with CPCU group X task condition interaction

a) Region in the amygdala significant at $p < 0.05$, corrected using 3DclusterSim threshold for contiguous voxels ($F(6,244) = 9.41$, 22 voxels). Slices shown at x = -22, y = -6, z = -19 (MNI peak voxel); *b*) Bar graphs depict extracted mean blood oxygen level-dependent (BOLD) response across all voxels within the cluster along with standard errors.
* = $p < 0.05$; ** = $p < 0.01$. The *p*-values are based on Games-Howell pairwise comparisons for extracted mean BOLD response. NS=non-significant.

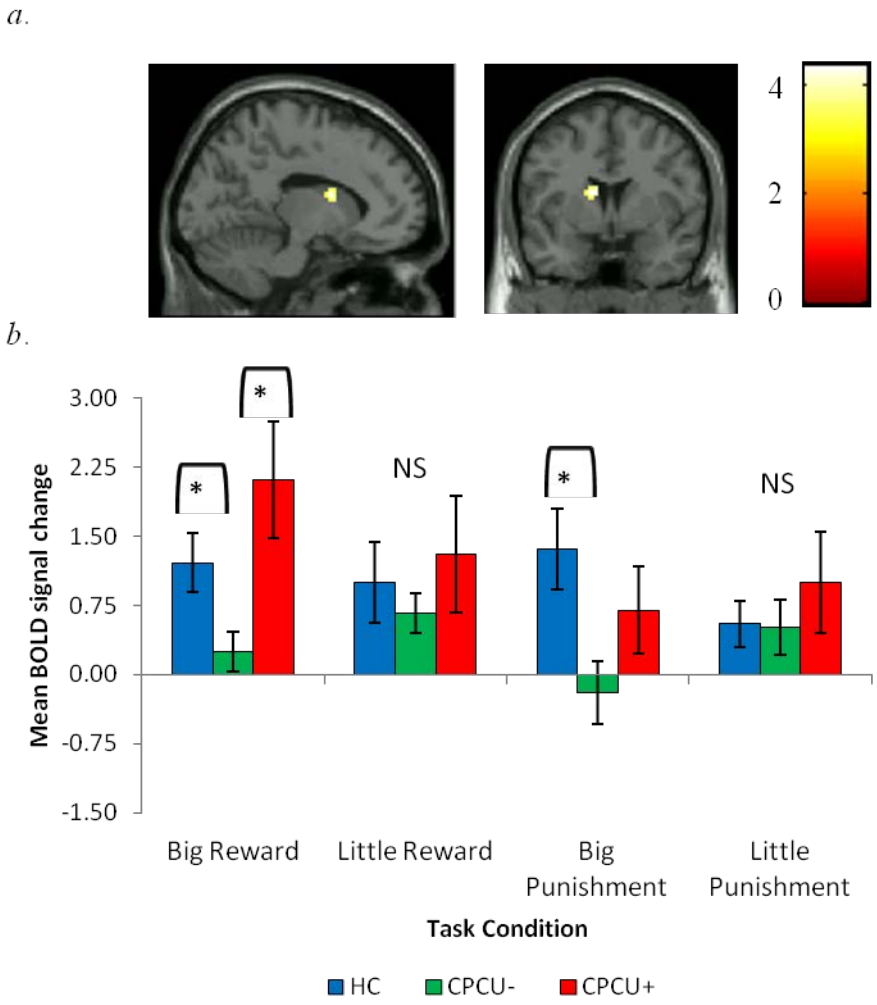


Figure 9. Activation in the left caudate is associated with CPCU group X task condition interaction

a) Region in the caudate significant at $p < 0.005$, corrected using 3DclusterSim threshold for contiguous voxels ($F(6,244) = 4.37$, 14 voxels). Slices shown at x = -12, y =3, z =15 (MNI peak voxel); *b*) Bar graphs depict extracted mean blood oxygen level-dependent (BOLD) response across all voxels within the cluster along with standard errors.
* = $p < 0.05$. The *p*-values are based on Games-Howell pairwise comparisons for extracted mean BOLD response. NS=non-significant.

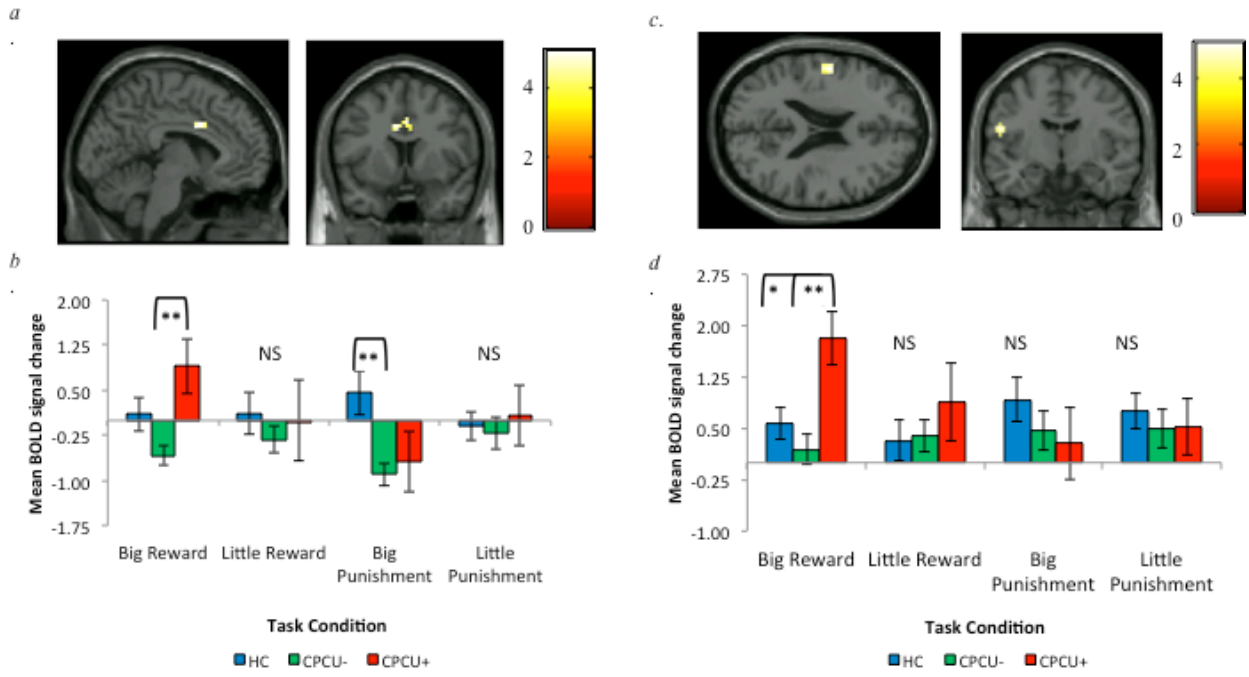


Figure 10. Exploratory whole brain analyses revealed CPCU group X task condition interaction within the bilateral cingulate gyrus and left postcentral gyrus

a) Region in the bilateral cingulated gyrus significant at a threshold of $p<.001$ with 20 contiguous voxels, uncorrected for multiple comparisons ($F(6,244)= 4.37$, 25 voxels). Slices shown at x =5, y =9, z =31; *b*) Bar graphs depict extracted mean blood oxygen level-dependent (BOLD) response across all voxels within the cingulate gyrus cluster along with standard errors; *c*) Region in the left postcentral gyrus significant at a threshold of $p<.001$ with 20 contiguous voxels, uncorrected for multiple comparisons ($F(6,244)= 4.37$, 27 voxels). Slices shown at x=-53 y=-9, z=21; *d*) Bar graphs depict extracted mean blood oxygen level-dependent (BOLD) response across all voxels within the postcentral gyrus cluster along with standard errors. * = $p < 0.05$; **= $p < 0.01$. The *p*-values are based on Games-Howell pairwise comparisons for extracted mean BOLD response. NS=non-significant.

Table 8. Suprathreshold clusters for CP and CU severity: Univariate and multivariate regressions

				Peak Coordinates (MNI)				
	Brain Region	R/L	Voxels	X	Y	Z	*z*-score	*p*-value
Bivariate Associations								
Big Reward								
CP (- association)	Amygdala	L	20	-22	-3	-19	2.61	0.005
Big Punishment								
CP (- association)	Amygdala	R	46	34	3	-22	4.22	0.000
	Amygdala	L	40	-28	0	-22	3.88	0.000
	Striatum	R/L	279	3	-3	-12	3.99	0.000
	ACC	R/L	178	0	31	-6	3.73	0.000
	mPFC	L	23	-3	53	-6	3.28	0.001
	OFC	R	51	25	12	-19	3.41	0.000
	OFC	L	31	-25	34	-6	3.29	0.001
CU (- association)	Amygdala	L	26	-28	0	-25	3.75	0.000
	Amygdala	R	25	34	3	-22	3.00	0.001
	Caudate/Putamen	L	16	-19	19	9	2.99	0.001
	OFC	L	28	-25	34	-6	3.29	0.000
Unique Associations								
Big Punishment								
CP controlling for CU (- association)	Amygdala	R	33	34	3	-22	3.06	0.001
	Amygdala	L	29	-22	-6	-15	2.77	0.003

Note. R=right; L=left; CP=conduct problems; CU=callous-unemotional traits; + = positive; - = negative; mPFC=medial prefrontal cortex

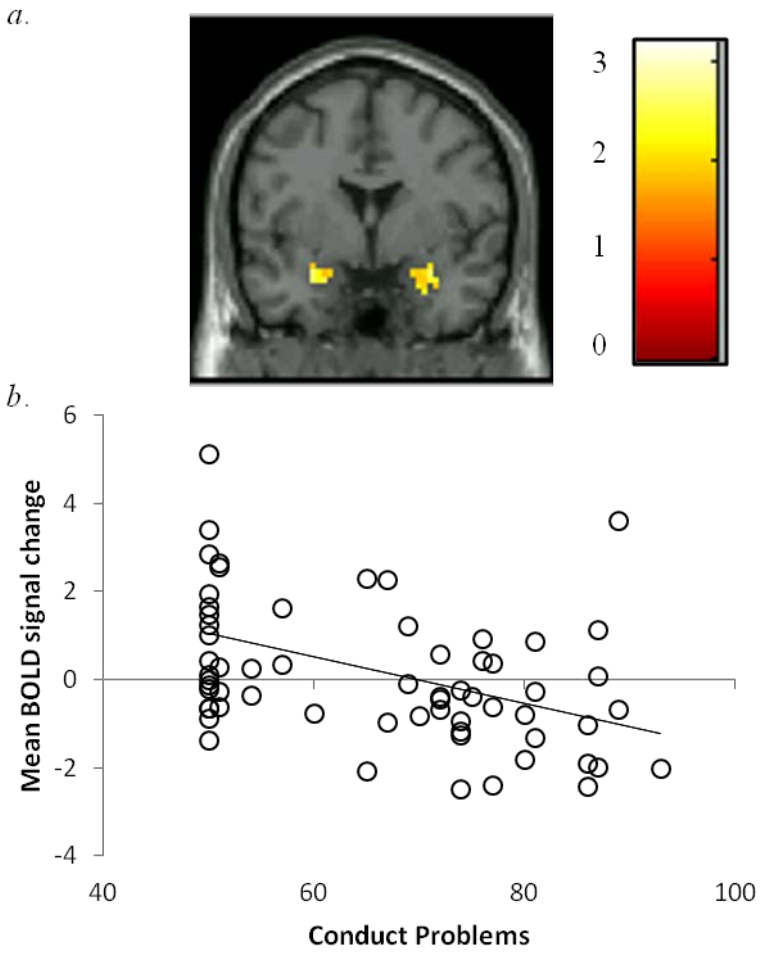


Figure 11. Activation in the bilateral amygdala is negatively associated with conduct problems, even after controlling for variance associated with CU traits

a) Region in the bilateral amygdala significant at $p < 0.05$, corrected using 3DclusterSim threshold for contiguous voxels (Right amygdala: 33 voxels, z = 3.06; Left amygdala: 29 voxels, $z = 2.77$). Slice shown at x = 28, y =0, z =-28; *b*) Scatter plot depicts association between baseline levels of conduct problems (x-axis) and mean BOLD change in the amygdala (y-axis) after controlling for co-occurring CU traits (r=-.42).

4.3 AIM 1B: ARE THERE DIFFERENCES IN THE NEURAL RESPONSE TO THE RECEIPT OF REWARD AND PUNISHMENT AMONG BOYS WITH CP AND PSYCHOPATHIC FEATURES?

The following set of secondary analyses examined potential group differences in reward and punishment processing using alternative classification criteria (i.e., total level of psychopathic features) that more closely mirrors past research in this area. Analyses were conducted identically to those described above. Main effects of condition are described above and are not reiterated here (see Table 7).

Main effect of group within a priori ROIs

No significant main effects of group were detected for any of the ROIs.

Group X condition interaction with a priori ROIs

Brain regions exhibiting a significant group by condition interaction are displayed in Table 9. A significant interaction emerged in the bilateral amygdala (Figure 12) and follow-up analysis indicated that groups differed in their responsivity to big punishment. Youth with CP PSY+ demonstrated significantly lower activation following the receipt of punishment relative to HC and this finding remained significant after accounting for potential confounds. However, CP PSY- did not differ in their level of BOLD response to punishment when compared to CP PSY+ youth or HC.

Another significant group by condition interaction emerged within the left striatum and this was specific to the putamen (Table 9). Further probing of the interaction revealed significant groups differences in BOLD response to big punishment (Figure 13). Similar to activation patterns seen within the amygdala, CP PSY+ evidenced significantly lower activation to punishment relative to HC, while youth in the CP PSY- group did not differ significantly from

either group in their responsivity to punishment. Findings remained significant after accounting for potential confounds.

Whole Brain Analyses: Exploratory

Exploratory whole brain analyses failed to identify any areas of activation associated with the overall main effect of group or the group X condition interaction.

Continuous Analyses within a priori ROIs: Associations with CP and PSY

As described above, analyses were re-run using continuous CP and PSY scores to BOLD response to each of the reward and punishment outcomes within the targeted ROIs using all participants (Table 10). First, the bivariate associations between PSY and individual differences in BOLD responding were examined (see Table for bivariate associations with CP). Next, multivariate analyses examined the unique association between CP and PSY and the BOLD response after controlling for their co-occurrence.

Bivariate Associations

Consistent with group-based analyses, PSY was unrelated to responsivity to reward in all of the ROIs examined. Higher levels of PSY were associated with reduced BOLD response to big punishment in the bilateral amygdala, bilateral dorsal striatum (i.e., caudate and putamen), and left OFC.

Unique Associations

When CP and PSY were entered simultaneously into a multivariate regression, significant results emerged only within the bilateral amygdala and only to the receipt of punishment (Table 10). Specifically, increased CP was negatively associated with BOLD response to punishment in the amygdala after accounting for the co-occurrence of PSY. All other bivariate associations were reduced to non-significance.

Summary

When CP groups were differentiated based on the presence of psychopathic features, fewer group differences emerged. Contrary to hypotheses, there was no variation seen in responsivity to reward and group differences surfaced only in responsiveness to big punishment. In line with prediction, both CP groups evidenced lower reactivity to punishment within the amygdala; however, contrary to hypotheses, only CP PSY+ significantly differed from HC and there were no differences between CP PSY+ and CP PSY- youth. These findings were echoed in regression analyses that demonstrated significant negative associations between amygdala reactivity to punishment and CP severity, even after accounting for co-occurring psychopathic features. This same pattern of group differences emerged in response to punishment within the putamen, though the direction of activation was contrary to prediction. Specifically, CP PSY+ youth demonstrated significantly lower activation within this region relative to HC though differences between subgroups of CP youth failed to reach significance.

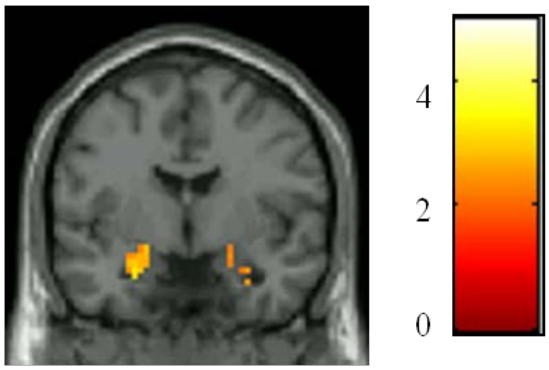
In sum, results reiterate a reduced sensitivity to punishment that is most consistently evidenced in the amygdala. Importantly, these findings remained significant after controlling for potential confounds. Moreover, there was no evidence that reduced reactivity to punishment was specific to a subgroup of CP youth psychopathic features.

Table 9. Suprathreshold clusters for CP PSY group differences: 3x4 ANOVA

Brain region	R/L	Voxels	Peak Coordinates (MNI) X	Y	Z	F	*p*-value
Group X Condition Interaction							
Amygdala	L	39	-19	-6	-19	5.01	0.000
Amygdala	R	29	31	3	-22	3.90	0.000
Putamen	L	62	-25	12	3	4.28	0.000

Note. R=right; L=left.

a.



b.

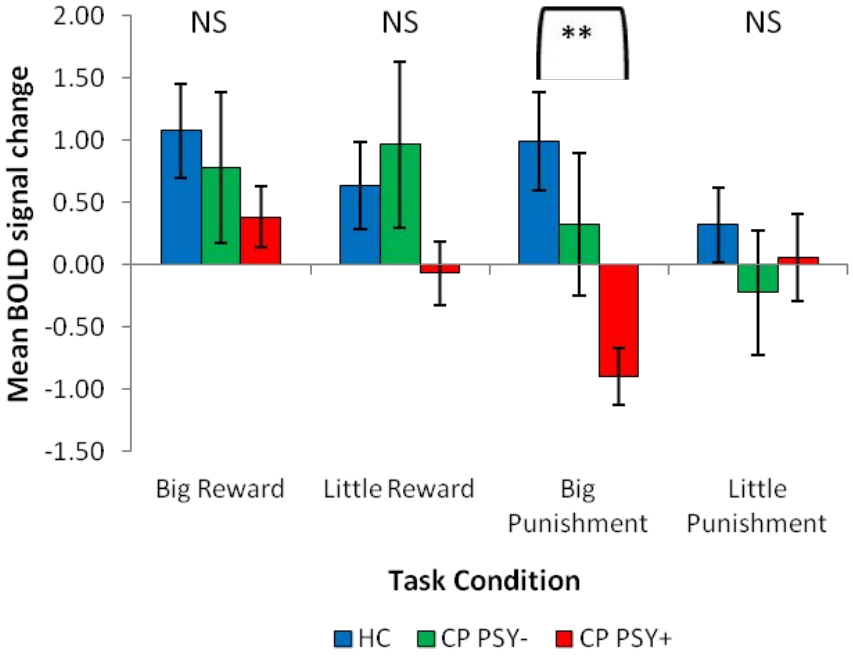
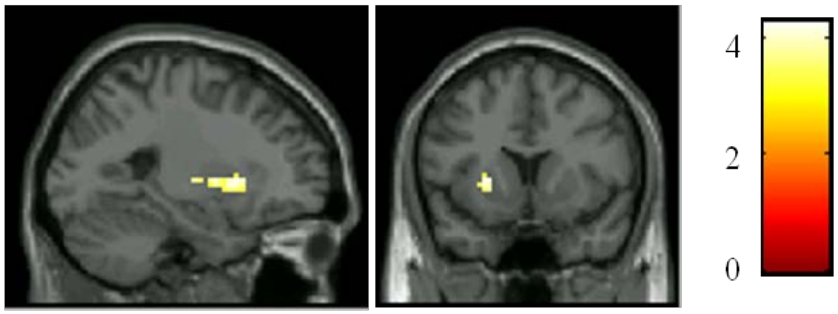


Figure 12. Activation in the bilateral amygdala is associated with CP PSY group X task condition interaction

a) Region in the bilateral amygdala significant at $p < 0.05$, corrected using 3DclusterSim threshold for contiguous voxels (Left amygdala: 39 voxels, $F(6,244) = 5.01$; Right amygdala: 29 voxels, $F(6,244) = 3.90$). Slice shown at x = -21, y =-3, z =-18; *b*) Bar graphs depict extracted mean blood oxygen level-dependent (BOLD) response across all voxels within the cluster along with standard errors.

** = $p < 0.01$. The *p*-values are based on Games-Howell pairwise comparisons for extracted mean BOLD response. NS=non-significant.

a.



b.

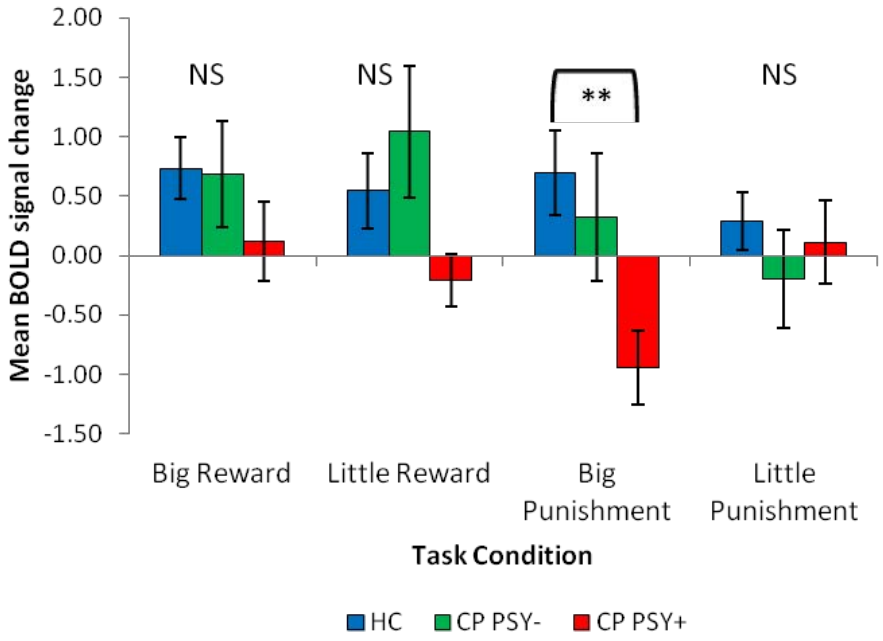


Figure 13. Activation in the left putamen is associated with CP PSY group X task condition interaction

a) Region in the putamen significant at $p < 0.005$, corrected using 3DclusterSim threshold for contiguous voxels ($F(6,244) = 4.28$, 62 voxels). Slices shown at x = -12, y =3, z =15 (MNI peak voxel); *b*) Bar graphs depict extracted mean blood oxygen level-dependent (BOLD) response across all voxels within the cluster along with standard errors.
* = $p < 0.05$. The *p*-values are based on Games-Howell pairwise comparisons for extracted mean BOLD response. NS=non-significant.

Table 10. Suprathreshold clusters for CP and PSY severity: Uunivariate and multivariate regressions

				Peak Coordinates (MNI)			
	Brain Region	R/L	Voxels	X	Y	Z	*z*-score
Bivariate Associations							
Big Punishment							
CP (- association)	SEE TABLE 8						
PSY (- association)	Amygdala	L	41	-28	0	-22	3.96
	Amygdala	R	27	31	3	-22	3.67
	Caudate/Putamen	L	21	25	9	0	3.09
	Caudate/Putamen	R	49	-16	22	9	3.09
	OFC	L	44	-25	34	-6	3.63
Unique Associations							
Big Punishment							
CP controlling for PSY (- association)	Amygdala	R	28	22	6	-19	2.52

Note. R=right; L=left; CP=conduct problems; PSY=psychopathic features; + = positive; - = negative.

4.4 AIM 2: ARE ABNORMALITIES IN REWARD AND/OR PUNISHMENT PROCESSING ASSOCIATED WITH RESPONSIVENESS TO TREATMENT?

The following sets of analyses were conducted to examine the association between individual differences in BOLD response to reward and punishment and treatment responsiveness. As described above, overall treatment effectiveness, effect of brain function and the interaction between treatment group and brain function were examined. For these analyses, brain function was defined as those clusters reaching significance in group level analyses. Prior to examining potential associations between abnormalities in reward/punishment processing and treatment responsiveness, information regarding the success of random assignment and service use is presented.

Random Assignment and Service Use

As described above, participants were randomly assigned to one of two treatment conditions (SNAP versus TAU) as a part of a larger treatment study, which demonstrated moderate treatment effects (Burke & Loeber, 2014). To verify that randomization was successful among the current subsample of participants, groups were compared on all study variables of interest. Table 11 presents the means and standard deviations for all study variables at baseline and post-treatment follow-up for youth participating in SNAP and youth participating in TAU. Both treatment groups were equivalent on all demographic and baseline measures.

Of those enrolled in SNAP, children attended an average of 6.63 (SD=4.73) of the 12 child sessions and parents attended an average of 5.89 (SD=4.57) of the 12 parent sessions; this did not significantly differ from those in the larger treatment sample. While over 50% of children

included in the current dissertation attended 8 or more child sessions and over 50% of parents attended 8 or more parent sessions, there were 4 children (21%) who attended no child sessions and 4 (21%) parents who attended no parent sessions. As the larger treatment evaluation was implemented with an intent-to-treat design, all participants were retained in the analyses after randomization, regardless of their level of service use.

Of those assigned to TAU, only 2 (13.3%) children were engaged in wrap around services by the 3-month follow-up assessment and this was comparable to percentage of youth engaged in the larger treatment sample (16 out of 122, 13.1%). An additional 5 (33.3%) children engaged in lower intensity mental health services by the 3-month follow-up, including outpatient mental health treatment and other behavioral health services. This was also comparable to the larger treatment sample.

Effects of brain function on treatment outcome

Separate repeated measures ANOVAs were conducted for each of the clusters that significantly differentiated groups in the analyses described above (Aim 1) and the effects of interest are shown in Table 12. As predicted, there was an overall effect of intervention as indicated by the interaction between time (CP at baseline, CP at 3-month) and treatment group (Figure 14). Post-hoc paired sample t-tests revealed a significant reduction in CP from baseline to 3-month follow-up for youth participating in SNAP ($t(18)=5.14$; $p<.001$), whereas youth in the TAU group did not experience any significant change in CP across this same period ($t(14)=1.13$; $p>.25$). This is in line with hypotheses and indicates that youth participating in SNAP experienced significant reductions in CP over time relative to those youth in TAU.

Contrary to prediction, there was no association between brain function and CP nor was there a significant interaction between time, treatment group and brain function, suggesting that brain function did not moderate intervention effects on CP over time.

In a second set of analyses effects of interest were examined using binary logistic regression with treatment responders versus non-responders as the dependent variable. Expanding on the findings described above, there was a consistent trend level main effect of treatment indicating that relative to youth receiving TAU, youth assigned to SNAP were more likely to respond to treatment as defined by a 5 or more point reduction (0.5 SD) in CP over time as measured by the CBCL. However, consistent with the aforementioned analyses there was no evidence for a main effect of brain function or a treatment group by brain function interaction.

Summary

Consistent with hypotheses and findings from the larger treatment study (Burke & Loeber, 2014), results confirm the overall effectiveness of the SNAP intervention. However, contrary to prediction, abnormalities in responsivity to reward/punishment were unassociated with level of CP at follow-up and there was no evidence of moderation. Thus, regardless of individual differences in responsivity to reward/punishment, youth assigned to SNAP were more likely to experience significant reductions in CP over time.

Table 11. Means and standard deviations for all study variables by treatment group

	SNAP				TAU			
	Baseline (n=19)		Follow-up (n=19)		Baseline (n=15)		Follow-up (n=15)	
	Mean	*SD*	Mean	*SD*	Mean	*SD*	Mean	*SD*
Age	11.02	*1.02*	10.77	*1.27*	10.57	*1.28*	11.29	*1.03*
Race (African-American)	95%	---	---	---	80%	---	---	---
Public Assistance (yes/no)	63%	---	---	---	73%	---	---	---
Family Income	Between $15,000 - $19,999		---	---	Between $15,000 - $19,999		---	---
IQ Composite	91.63	*10.98*	---	---	91.73	*12.02*	---	---
ADHD symptoms	67.79	*7.97*	65.00	*9.06*	66.73	*8.82*	63.79	*8.78*
Internalizing symptoms	61.79	*9.18*	63.40	*10.18*	63.20	*9.15*	60.32	*6.63*
Conduct Problems	78.11	*8.42*	73.33	*8.00*	75.47	*7.60*	69.16	*7.40*
APSD CU	6.95	*2.01*	7.57	*1.83*	7.20	*2.31*	7.06	*1.91*
APSD Narcissism	7.26	*2.40*	7.14	*2.96*	7.13	*1.96*	7.00	*2.66*
APSD Impulsivity	6.89	*1.76*	7.43	*1.34*	6.80	*1.74*	6.13	*1.54*
APSD Total	22.74	*5.12*	23.64	*4.55*	22.93	*5.02*	21.50	*4.73*

Note. SNAP=Stop-Now-And-Plan; TAU=Treatment as Usual; SD=standard deviation; ADHD=Attention Deficit Hyperactivity Disorder; APSD=Antisocial Process Screening Device; CU=Callous-Unemotional Traits; Means designated with different subscript letters are significantly different from each other ($p<.05$) based on post-hoc independent sample t-tests. There were no significant differences at between groups at baseline.

†Baseline group differences on the aggressive behaviors subscale, rule breaking subscale and externalizing composite were also examined. Groups were equivalent on each scale ($p>.50$)

Table 12. Effect of treatment, brain function and the interaction between treatment and brain function: Repeated measures ANOVAs

Group Analysis	Condition	Brain Region (voxels)	Time X TX Group	Brain Function	Time X TX Group X Brain Function
CPCU	Reward & Punishment	Left mPFC (BA10; 8 voxels)	8.16**	0.20	1.18
	Reward	Left Amygdala (22 voxels)	6.67*	0.07	0.17
	Reward	Left Caudate (14 voxels)	6.58*	0.10	0.25
	Punishment	Left Amygdala (22 voxels)	5.44*	0.70	0.07
	Punishment	Left Caudate (14 voxels)	8.55**	0.96	2.26
CP PSY	Punishment	R/L Amygdala (68 voxels)	6.65*	0.39	0.35
	Punishment	Left Putamen (62 voxels)	11.92**	0.11	4.43

Note. TX=treatment; X=interaction; CPCU=conduct problems, callous-unemotional traits; CP PSY=conduct problems, psychopathic features; mPFC=medial prefrontal cortex; R/L=right and left.
* = $p < 0.05$; ** = $p < 0.01$

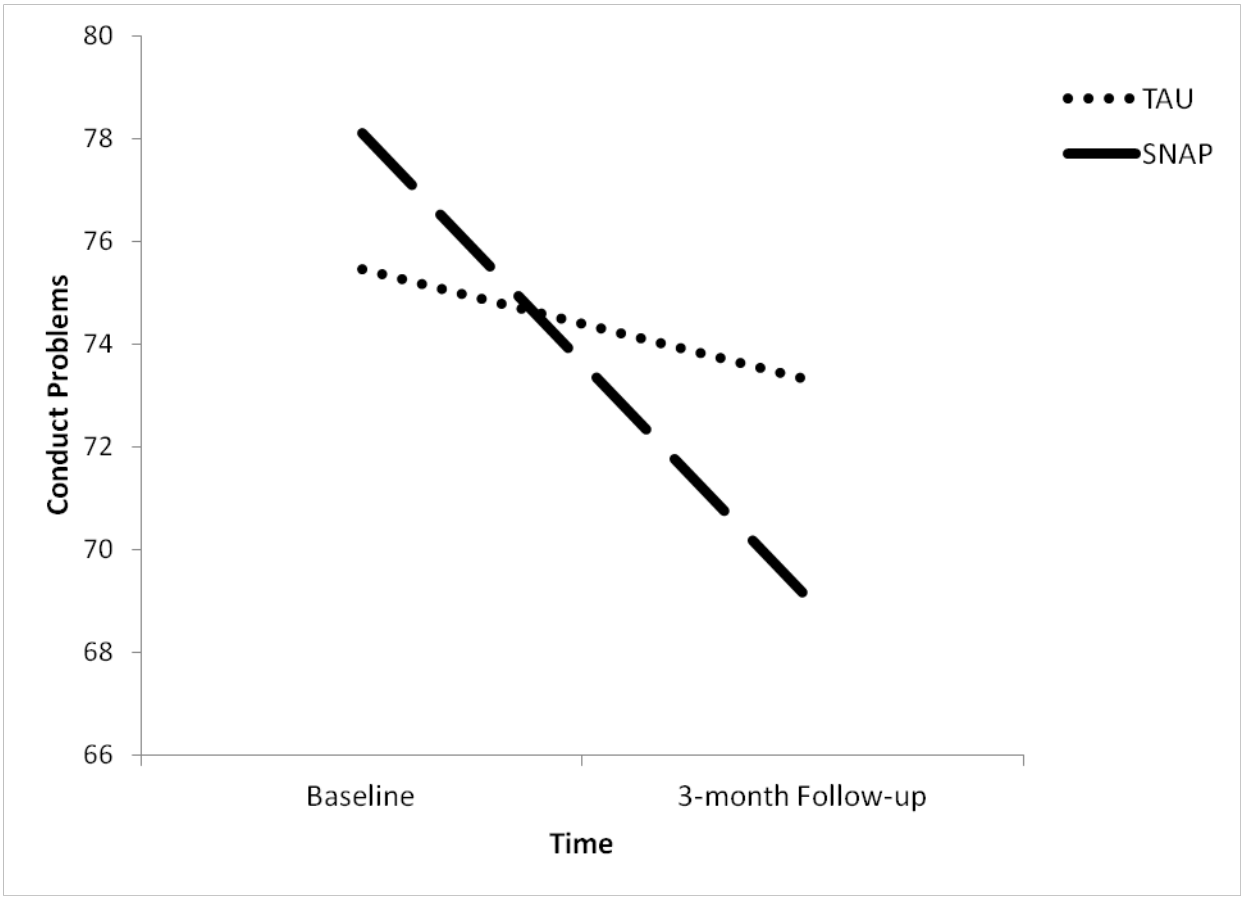


Figure 14. Interaction between time and treatment group reveal effectiveness of SNAP intervention relative to TAU

Post-hoc paired sample t-tests revealed significant differences between baseline levels of CP and CP at 3-month follow-up for those youth participating in SNAP ($t(33)=5.14$; $p<.001$). No differences were seen between levels of CP at baseline and 3-month follow-up for those youth in TAU ($t(33)=1.13$; $p>.25$).

5.0 GENERAL DISCUSSION

A primary objective of this dissertation was to characterize the BOLD response to the receipt of reward and punishment among subgroups of boys with early-onset CP. It was hypothesized that youth with CP, regardless of their level of CU traits (or psychopathic features), would exhibit hyper-reactivity to reward in the VS relative to HC. Contrary to hypotheses, boys with CP and low CU traits exhibited reduced reactivity to big reward in the DS (i.e., caudate) relative to both HC and youth with CP and CU, who evidenced increased activation to reward in this same region. Moreover, youth with CP and low levels of CU traits exhibited a similar pattern of hypo-activation to reward in the amygdala and mPFC relative to HC and these differences were not evident when subgroups were characterized by the presence of psychopathic features. Taken together, results provide some initial evidence for potential differences in the mechanisms underlying reward processing in subgroups of youth with and without CU traits.

Abnormalities in punishment processing were expected in all ROIs examined and were hypothesized to be most pronounced in a subgroup of CP youth with elevated levels of CU traits (and psychopathic features). Results provided partial support of hypotheses and, consistent with the behavioral literature, were indicative of a primary deficit within this domain. Results were most reliable and robust with regard to responsivity to punishment in the amygdala. As predicted, boys with CP demonstrated reduced reactivity to punishment in this region relative to HC who evidenced significant activation. Additionally, CP youth evidenced reduced activation

in the striatum following the receipt of punishment; though, this was less consistent across analyses and in the opposite direction of hypotheses. Also contrary to prediction, there was no evidence to support that punishment insensitivity was most pronounced in CP youth with CU traits or psychopathic features. Moreover, no consistent differences emerged within regulatory regions (e.g., ACC, OFC) suggesting abnormalities during initial encoding are specific to subcortical regions. Lastly, differences in neural response were specific to *big* reward and *big* punishment and this may be a reflection of the task design rather that the magnitude of the monetary gain/loss. Specifically, small reward and punishment may be less salient given the possibility of larger reward/punishment. Results are discussed within the context of the broader literature below.

The second aim of the current dissertation was to evaluate the extent to which individual differences in reward and/or punishment processing were associated with responsiveness to intervention. This objective was notably exploratory in nature and sought to test the notion that abnormalities in reward and/or punishment processing may influence the impact of a multi-modal intervention that focuses on behavioral principles associated with reward and punishment contingencies. Contrary to hypotheses, reactivity to reward and punishment among CP youth was unrelated to level of CP following treatment and abnormalities in neural processing failed to moderate the effectiveness of SNAP intervention. Though small sample sizes and reduced power may have contributed to null effects, results provide support for the success of this multi-modal, empirically supported intervention among boys with early-onset CP and aberrant reward/punishment processing. These findings are discussed in greater detail below.

5.1 NEURAL ABNORMALITIES IN REWARD PROCESSING

Group differences in reward processing emerged within the striatum, providing some evidence for abnormalities in response to reward among youth with CP. However, contrary to prediction, differences were specific to the DS, namely the caudate, and were unrelated to VS reactivity. This suggests group variation in reward processing may be less related to the emotional experiences of reward (Cardinal, et al., 2002) and instead specific to responsivity to uncertain reward and the acquisition of reward-action associations (Delgado, Miller, Inati, & Phelps, 2005; Elliott, Newman, Longe, & William Deakin, 2004). Moreover, group differences emerged in the unexpected direction and *between* subgroups of CP youth, specific to the presence or absence of CU traits. Boys with CP and CU demonstrated increased activation in the caudate, no different than that of HC, but significantly *greater* than boys with CP and low levels of CU traits. Results also provide additional evidence for hypo-activity to reward among boys with CP and low levels of CU, who demonstrated reduced activation to reward in the amygdala and mPFC relative to HC. These deficits may have important implications for reward-based learning (Cardinal, et al., 2002; Fareri, et al., 2008; Matthys, Vanderschuren, & Schutter, 2012a) and suggest that CP youth with low levels of CU traits could experience difficulty in this regard.

At the same time, it is important to note that the aforementioned group differences were reduced to non-significance after controlling for potential confounds, with some suggestion that deficits in responsivity to reward were uniquely associated with clinically significant internalizing problems. This is particularly interesting given emerging literature that documents associations between internalizing problems, namely depression, and reduced responsivity throughout reward-related circuitry (Forbes, et al., 2006; Forbes & Dahl, 2005; Forbes, Shaw, & Dahl, 2007). In light of research documenting high rates of comorbidity between CP and

internalizing disorders (Campbell, et al., 2000; Loeber & Keenan, 1994), future studies may aim to disentangle whether potential deficits in reward processing represent a shared or unique etiology. As such, the utilization of alternative comparison groups (e.g., youth with internalizing problems only) may help to elucidate these findings.

It is also important to highlight that the hypo-activity to reward seen among CP youth with low CU stands in direct contrast to youth with CP and CU, who demonstrated more normative responsivity to reward in the caudate. Moreover, in continuous analyses CU traits were uniquely associated with increased activation in the caudate after controlling for CP, though this fell just below the cluster threshold. Additionally, whole-brain analyses found youth with CP and CU to exhibit hyper-activation to reward within the cingulate and postcentral gyrus. While these analyses were notably exploratory in nature and identify regions outside of the reward-related circuitry that could be less functionally significant, this pattern of over-activation in this subgroup may warrant further inquiry. Along these lines, recent neuroimaging work reports similar inconsistencies among samples of CP youth with regard to hyper- versus hypo-activation within reward related circuitry (e.g., Bjork, et al., 2010; Rubia, et al., 2009), which may be related to a failure to examine CU traits. Thus, while there continues to be debate about whether CP is driven by over- versus under-reactivity to reward (Quay, 1993; Zuckerman, 1996), it may be important to consider potential differences in the mechanisms underlying reward function *between* subgroups of CP youth with and without CU traits and/or with and without co-occurring internalizing problems.

5.2 NEURAL ABNORMALITIES IN PUNISHMENT PROCESSING

Amygdala

Group differences were expected be most pronounced and diffuse with regard to punishment processing. Results provide confirmation for reduced reactivity to punishment among boys with early-onset CP. Both group and continuous analyses support hypotheses and consistently found boys with CP to demonstrate reduced activation in the amygdala following the receipt of punishment. Moreover, these findings remained significant after accounting for important confounds (i.e., income, IQ, etc.). While other neuroimaging studies in this area have provided some support for amygdala dysfunction in response to punishment (e.g., Finger, et al., 2011), these studies have utilized relatively complex tasks that incorporate multiple phases of learning (i.e., encoding, acquisition, extinction) and often examine the neural response to removal of reward as opposed to the introduction of punishment (Bjork, et al., 2010; Rubia, et al., 2009). To our knowledge, this dissertation represents the first neuroimaging study to examine basic responsivity to the receipt of punishment in the form of monetary loss among CP youth in late childhood. Current findings build upon behavioral work in this area which consistently finds children with CP have lower reactivity to inherently aversive stimuli or positive punishment (e.g., lound tones; Herpertz, et al., 2001; van Goozen, et al., 2004), by demonstrating a similar insensitivity to negative punishment (i.e., loss of money). This reduced sensitivity to punishment has been well-documented across childhood and adolescence, with recent work suggesting that these deficits are present as early as 3 years of age and serve to predict criminal offending in adulthood (Gao, Raine, Venables, Dawson, & Mednick, 2010). Taken together, this provides evidence that reduced emotional arousal to both positive (i.e., introduction of something aversive) and negative (i.e., removal of something pleasurable) punishment may hinder the

development of conditioned associations between cues of impending punishment and distress, ultimately increasing the likelihood of the development and persistence of CP (Kochanska, 1994).

In line with findings from the current dissertation, the amygdala has been a recent focus of the neuroimaging literature within this population, with studies consistently demonstrating links between amygdala dysfunction and heightened levels of CP in youth. This is consistent with theory proposing deficient processing within this region, particularly among youth with elevated CP and CU (Blair, 2007; Kiehl, 2006). For example, studies have shown structural differences in gray matter volume of the amygdala among youth with CP (De Brito et al. 2009; Huebner et al. 2008; Sterzer et al. 2007) and adults with a history of early-onset CP (Pardini et al. 2013). Other work in this area has focused on amygdala reactivity during emotion processing tasks, specifically reactivity to emotional faces, and find youth with CP and high levels of CU traits or psychopathic features to evidence reduced amygdala reactivity relative to controls (for review see Hyde, Shaw, & Hariri, 2013; Jones, Laurens, Herba, Barker, & Viding, 2009; Marsh, et al., 2008). However, contrary to prediction, the current dissertation found no differences between subgroups of CP youth, whether defined by the presence of CU traits or psychopathic features. Noteworthy, the majority of previous research in this area compares youth with CP and CU traits (or psychopathic features) to HC, making it impossible to discern whether significant group differences are driven by the presence of CP or CU. The current dissertation is one of the only investigations to examine potential differences in neural processing between subgroups of CP youth (see also Hyde, 2012 for studies examining emotion processing among subgroups; Viding, et al., 2012). Moreover, CP subgroups within the current study were indistinguishable in terms of demographic and other clinically relevant variables (e.g., internalizing problems,

ADHD) and differed only on their levels of CU traits and/or psychopathic features. Thus, in light of the rigorous study design, failure to detect significant within group differences is indicative of similar punishment processing among these subgroups of CP youth and suggests that previous findings may be attributable to the presence of CP as opposed to CU or psychopathic features.

Striatum

In addition to robust associations between CP and reduced activation in the amygdala, the current dissertation also provided some evidence for reduced reactivity to punishment within the striatum, though this varied by location and subgroup. Specifically, CPCU- evidenced reduced activation in the caudate relative to HC (no differences with CPCU+) while CP PSY+ exhibited decreased activation in the putamen compared to HC (no differences with CP PSY-). Inconsistency of results may reflect the lack of complete overlap between CU and PSY group classifications and certainly warrant caution with regard to interpretation. However, it is also important to note that the direction of these findings are contrary to previous work in the area (Finger, et al., 2008; Gatzke-Kopp, et al., 2009) and emerging theory (Glenn & Yang, 2012). Specifically, past research has documented *increased* activation within the DS following punishment and this has been interpreted as an inability to appropriately process the absence of reward. In other words, CP youth may be processing punishment as if it was (or should be) reward due to ineffective error monitoring or a failure to process contingency change. This is thought to increase their propensity to continuously engage in perseverative, reward-focused action and may impair the ability to flexibly respond to the environment (Newman & Lorenz, 2002). Results in the current dissertation may reflect the unpredictable nature of the task design (i.e., no learning or contingency change) and thus, findings can only speak to an inherently

reduced responsivity to punishment that may contribute to difficulties with error monitoring in the presence of competing reward and punishment.

Regulatory Regions

Also contrary to hypotheses, no group differences were detected in response to punishment within regulatory regions (e.g., ACC, mPFC, OFC). While there was some evidence to suggest reduced activation across reward and punishment conditions within the mPFC, this was specific to CP youth with low levels of CU and was not consistent across analyses. Prior work in this area has demonstrated abnormalities in the ACC (Gatzke-Kopp, et al., 2009), mPFC (Bjork, et al., 2010; Finger, et al., 2008) and OFC (Finger, et al., 2011; Rubia, et al., 2009) among youth with CP; however, the direction of these findings has varied (i.e., increased versus decreased activation among CP youth relative to HC) and this may be attributable to variation in task and analysis design. For example, while Rubia et al. (2009) utilized a rewarded continuous performance and compared responsivity to rewarded responses relative to responses without reward, Finger and colleagues (2008) used a response-reversal task and examined reactivity to punished errors versus rewarded responses. Along these lines, the current dissertation separately examined responsivity to the initial encoding of unpredictable reward and punishment within the context of a card guessing task. Because this task does not require learning to modify a previously rewarded response or set-shifting, it may be less likely to highlight potential group differences in regulatory regions like the ACC or OFC that are noted for their involvement in error monitoring and contingency learning (e.g., Rogers, et al., 2004). Conversely, it may be that prior to the transition to adolescence, differences in regulatory function are less pronounced. Specifically, risk-taking behaviors in adolescence are believed to arise due to an imbalance between more rapidly developing subcortical regions (i.e., striatum, amygdala) and protracted

development of regulatory circuits in the frontal cortex (Somerville, Jones, & Casey, 2010; Steinberg, 2008). This dual-process is at its height during adolescence, with more recent suggestion that differences in the development of these systems are particularly pronounced among youth with CP (Bjork & Pardini, 2014). Thus, we may expect evidence of aberrant processing within regulatory regions to be more prominent in adolescence.

5.3 CLINICAL IMPLICATIONS FOR INTERVENTION

While the current dissertation failed to find associations between individual differences in reward/punishment processing and response to intervention, results reiterate findings from Burke and Loeber (2014) and confirm the effectiveness of SNAP, a multimodal, empirically-supported intervention. Specifically, youth with CP who were assigned to SNAP experienced a significant reduction in level of externalizing behavior over time relative to CP youth experiencing treatment as usual. Importantly, It should also be noted that within the larger treatment sample, CU traits failed to moderate treatment effectiveness, further emphasizing the utility of this intervention among youth with CP and CU (Pardini, Byrd, Kimonis, Burke, & Loeber, in preparation). While moderation analyses were exploratory in nature given the small sample size, results emphasize the utility of this intervention in youth with early-onset CP despite abnormalities in reward and punishment processing.

While these results are promising, intervention efforts typically boast effect sizes that are still small to moderate (e.g., Matthys, et al., 2012b; McCart, Priester, Davies, & Azen, 2006). This may be related to the 'one size fits all' approach and a failure to assess and treat child-specific deficits at an individual level. Given the noted heterogeneity that exists among youth

with CP, efforts to tailor interventions to meet child-specific needs may increase the effectiveness of social learning-based interventions. Some researchers have proposed assessing children with CP for potential deficits in reward/punishment processing prior to treatment initiation, in order to modify or individualize the treatment approach (see Matthys, et al., 2012b). For example, treatment for youth with deficits in punishment processing may focus on increasing the use of praise and reward systems that facilitate the reinforcement of positive, prosocial behaviors (see Dadds and Salmon 2003). Evan as the current dissertation failed to identify an association between reward/punishment processing and responsiveness to intervention, this avenue of research may warrant continued investigation. Moreover, an examination of how treatment induced changes in specific parenting behaviors serve to interact with identified deficits in reward and/or punishment processing may help to further elucidate more complex moderation mechanisms and ultimately, amplify treatment effectiveness.

5.4 LIMITATIONS AND FUTURE DIRECTIONS

The current study offers additional insights into the characterization of abnormalities in reward/punishment processing in CP youth and is the first known investigation to examine these mechanisms among subgroups of CP youth with and without CU traits relative to matched HC. Moreover, it is one of the only studies to explore how individual differences in responsivity to reward/punishment may influence responsiveness to treatment. Nonetheless, findings from the current dissertation should be considered in the context of several limitations. First and foremost, it is important to reiterate that the sample size in the current dissertation is notably small. While primary comparisons at baseline utilized a sample size almost double that of prior imaging

research in this area, efforts to examine potential difference between subgroups of youth with CP resulted in relatively small group sizes and could undermine attempts to detect significant effects. Moreover, analyses examining associations between reward/punishment processing and treatment responsiveness were notably exploratory in nature given the small number of CP youth who completed both an fMRI scan and treatment. This combined with significant variability in responsivity to reward/punishment within groups necessitates continued investigation and attempted replication in larger samples.

Second, it should be noted that CU traits and psychopathic features were measured using the APSD, a measure that while consistently used in the literature, has been noted for its lack of internal consistency (Munoz & Frick, 2007; Poythress, et al., 2006). This scale was used with the intention to examine the new DSM-5 specifier 'lack of prosocial emotions' as an indicator of the presence CU traits (American Psychiatric Association, 2013). While this represents an important advancement in the literature, future studies may want to utilize alternative measures and/or create a composite that takes advantage of different measures and informants. Along these lines, while parent- and child-report were combined in the current study to make use of multiple informants, the addition of teacher-report would be ideal so as to provide important information about these features in an alternative setting. Finally, the current investigation is one of the only studies to examine potential differences in groups characterized by CU versus psychopathic features. A comparison of results based these classification criteria revealed minimal differences, though the only variation between subgroups was specific to the presence of CU traits. Thus, as future research continues to investigate potential differences in these subgroups, it will be important to explicitly delineate these classifications as they are often used interchangeably throughout the literature.

Next, the current dissertation focused on reward and punishment processing in a clinical sample of boys with severe CP in late-childhood, limiting the degree to which these results can be generalized to community samples, girls and/or adolescents. As such, future research is needed to examine the extent to which potential abnormalities are characteristic of youth with mild to moderate CP as well as samples of girls. Moreover, given the noted changes in neural function that occur during the transition to adolescence (Bjork & Pardini, 2014; Steinberg, 2008), it will be important to investigate neural processing in comparable samples of adolescents. Along these lines, it is unclear whether the abnormalities documented in the current investigation are stable and/or reliably predict risk for the persistence of CP. Very few studies have examined within individual change in neural functioning over time and how this relates to future CP. Thus, little is known about whether abnormalities associated with CP in late childhood reflect preexisting, stable functional abnormalities or slower developmental maturation that may resolve over time. More importantly, it remains unclear how stability versus change in aberrant neural responses is associated with the persistence or desistance of CP over time. Prospective longitudinal studies that incorporate the assessment of neural function over time are needed to address these limitations.

It is also important to note that while the current dissertation identified group based functional differences in distinct regions associated with reward and punishment processing, these regions are merely 'one piece of the puzzle' and should be considered within the context of a broader, interconnected circuitry. Recent meta-analytic findings emphasize the importance of conceptualizing behavioral constructs (e.g., risk-taking, emotional experience) as arising from aberrant processing throughout general brain networks. This was found to be superior to a 'locationist' approach focused on direct links between deficits in any one region and relevant

behavioral phenomena (Lindquist, Wager, Kober, Bliss-Moreau, & Barrett, 2012). Thus, the identification of group based differences in amygdala responsivity to punishment or striatal reactivity to reward in the current dissertation represent vulnerabilities or probabilistic associations that are believed to increase risk for CP. That is to say, the association between reduced amygdala activation to punishment and CP does not represent a direct causal relationship but instead operates as a part of a structurally and functionally interconnected neural network. Accordingly, deterministic interpretations should be cautioned against. Instead, current results highlight potential risk factors that comprise one piece of a more complex mosaic that we are still working to better delineate and understand (see Hyde, et al., 2013 for further discussion).

Along these lines, the current dissertation did not consider the role of important contextual influences and how they may interact with deficits in reward/punishment processing to increase risk for CP. For example, harsh and inconsistent parenting is thought to inadvertently reinforce CP (Patterson et al. 1992) and may also contribute to the development of CU traits or psychopathic features (Waller et al. 2013). This type of parenting combined with an insensitivity to punishment and difficulties inhibiting a reward-dominant response style may be particularly detrimental. Moreover, research suggests that parent–child interactions are bidirectional and as such, have cascading effects that serve to further entrain aberrant reward and punishment processing (Dodge and Pettit 2003; Pardini et al. 2008; Sameroff 2000). The examination of these interactive processes is particularly important to consider as we seek to further understand the development and persistence of CP. In addition, the evaluation of interactions between intervention driven changes in parenting and child specific deficits in reward/punishment processing may also help to shed light on variability in the success of intervention for these youth. Lastly, youth with deficits in reward/punishment processing may be particularly

vulnerable to deviant social influences, and emerging work suggests differences in responsivity to reward in the presence of peers (Centifanti and Modecki 2013). As such, further investigation of the role of peers, particularly during the transition to adolescence may be particularly informative.

In sum, the current dissertation demonstrates consistent deficits in punishment processing among boys with high levels of CP in late childhood. This was most robust within the amygdala and not specific to youth with CU traits or psychopathic features. Additionally, there was initial evidence of distinct reward processing mechanisms among CP youth with high versus low levels of CU traits, though it is unclear whether this is attributable to CU traits or other confounding variables (e.g., internalizing problems). Finally, although random assignment to SNAP resulted in significant reductions in CP at 3-month follow-up, individual differences in responsivity to reward and punishment were unrelated to post-treatment levels of CP and failed to moderate the effectiveness of the SNAP intervention. Future research should seek to replicate these results and build on this basic understanding of aberrant reward/punishment processing by examining reward/punishment processing within the context of learning. Moreover, gaining a better understanding the development of reward/punishment processing over time and the potential interaction between these mechanisms and relevant contextual influences (e.g., parenting) will be particularly important. As our knowledge about these mechanisms increase, this information should be used to refine and individualize prevention and intervention efforts.

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