Psychopathology in Children: the Transdiagnostic Contribution of Affiliative Capacity and Inhibitory Control

Isabella Palumbo
Recent initiatives have focused on integrating transdiagnostic biobehavioral models of clinically-relevant processes with quantitatively-derived dimensional structural models of psychopathology. Toward this effort, affiliative capacity (AFF) and inhibitory control (IC) processes hold particular promise as they demonstrate transdiagnostic utility and stability across developmental stages and multiple measurement modalities. The current study integrates across informants and modes of measurement in a sample of 1,671 5-to-10-year-olds to probe the unique and moderating effects of IC variation on low AFF in explanation of broad, empirically derived dimensions of psychopathology. Whereas no unique associations emerged for IC, low AFF was a significant predictor of distress- and externalizing-related problems. Distinct moderating effects emerged such that in combination with low AFF, high IC protected against distress symptoms specifically, whereas low IC predicted distress and externalizing problems. Results are discussed in the context of the interface of general trait transdiagnostic risk factors with quantitatively-derived dimensional models of psychopathology.

INDEX WORDS: Affiliative capacity, Inhibitory control, Developmental psychopathology, Child Mind Institute Healthy Brain Network, Structural equation modeling
PSYCHOPATHOLOGY IN CHILDREN: THE TRANSDIAGNOSTIC CONTRIBUTION OF AFFILIATIVE CAPACITY AND INHIBITORY CONTROL

by

ISABELLA M. PALUMBO

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by

ISABELLA M. PALUMBO

Committee Chair: Robert D. Latzman

Committee: Erin B. Tone
              David A. Washburn
              Christopher J. Patrick

Electronic Version Approved:

Office of Graduate Services
College of Arts and Sciences
Georgia State University

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DEDICATION

Dedicated to The Boys.
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1 INTRODUCTION

In recent years, transdiagnostic models have become an increasingly prominent approach to identifying fundamental processes underlying the comorbidity of psychopathology (Nolen-Hoeksema & Watkins, 2011; Insel & Cuthbert, 2009; Barlow, Allen, & Choate, 2004; Ehring & Watkins, 2008; Harvey, Watkins, Mansell, & Shafran, 2004; Kring & Sloan, 2010; Mansell, Harvey, Watkins, & Shafran, 2009). These models indicate the existence of a hierarchy of basic emotional, cognitive, and behavioral processes that have neurobiological, as well as psychological, referents and foster new dimensional conceptualizations of clinical phenomena, that contrast with the current categorical, and highly comorbid, nosology. Despite several theoretical and clinical advantages (e.g., Mansell et al., 2009), however, recent models have difficulty simultaneously assessing the mechanisms by which one trait transdiagnostic risk factor contributes to multiple disorders (i.e., multifinality) and how the moderating influences of another dispositional risk factor determine which specific cluster of disorders or symptoms will manifest (i.e., divergent trajectories) (Nolen-Hoeksema & Watkins, 2011).

There may be critical developmental periods, such as young childhood, in which some moderating risk factors have particularly strong influence in determining the trajectory of symptom development and expression. Understanding such developmental risk factors of psychopathology through a transdiagnostic approach is an important avenue of focus for early identification and intervention efforts. The focus of this approach lies on common underlying processes, rather than the large number of unique symptoms of discrete disorders, thereby identifying fundamental and far-reaching risk factors.
Several factors make transdiagnostic approaches especially relevant for understanding psychopathological problems in youth (Harvey, 2013). A large number of clinically-relevant symptoms emerge as early as 6-10 years, and nearly half of all lifetime diagnoses start by the age of 14 (Kessler et al., 2008). Moreover, the high rates of comorbidity seen in adults are often higher in young samples, both within- (e.g., multiple anxieties) and across-class (e.g., diagnoses of both anxiety and conduct disorder), (Angold, Costello, & Erkanli, 1999; Garber & Weersing, 2010), indicating the need to examine influential moderating factors present in childhood that determine more delineated psychopathological outcomes observed in adulthood. Specifically, socioemotional and cognitive processes are particularly compatible with child models of psychopathology, as they can be readily measured across various developmental periods in conjunction with dynamic environmental effects. In particular, an extant literature demonstrates the stability of social affiliation and attachment (hereafter referred to as ‘affiliative capacity’) and inhibitory control as they emerge in childhood and persist into adulthood, while also examining their influence as both risk and protective factors (e.g., Tone & Tully, 2014; Fox et al., 2005; Burt et al., 2008).

Socioemotional traits capturing low affiliative capacity (AFF) have been implicated transdiagnostically, manifesting as observable symptoms such as social apathy and lack of concern for others, evident in both internalizing and externalizing disorders (e.g., Blanchard et al., 2001; Fanning et al., 2012, respectively). Such evidence of multifinality suggests the presence of additional moderating risk factors that shape divergent developmental trajectories. Individual differences in inhibitory control (IC), for example, have been implicated in the specific development of numerous psychopathologies (Quay 1988, 1993, 1997; Gray, 1987). Measurements of trait behavioral inhibition and activation in toddlerhood and early childhood
have been shown to predict anxiety disorders in middle childhood and adolescence (Rosenbaum et al., 1993; Kagan & Snidman, 1999; Gladstone et al., 2005), as well as later antisocial behavior (Raine et al., 1998; Oldehinkel et al., 2004), respectively. Some moderators (i.e., inhibitory control) may produce symptoms on their own without the added vulnerability stemming from a transdiagnostic risk factor (i.e., low AFF); however, they do not fully explain the frequent comorbidity between psychopathologies (e.g., conduct disorder and anxiety; ADHD and depression). Importantly, not all children who display over- or undercontrolled inhibition develop internalizing or externalizing problems, further supporting the interactive relationship among transdiagnostic risk factors. Taken together, a general trait risk factor (i.e., AFF) may explain comorbidity and multifinality, while a moderating trait risk factor (i.e., IC) may explain how individuals develop specific disorders via divergent trajectories (Nolen-Hoeksema & Watkins, 2011).

Despite the burgeoning literature regarding transdiagnostic factors and the development of psychopathology, as well as the challenges posed and concrete approaches to improve the transdiagnostic model (e.g., Patrick & Hajcak, 2016), little work has been done to empirically test this interactive heuristic, as Nolen-Hoeksema and Watkins (2011) proposed (e.g., Kessel et al., 2016). Specifically, this study proposes the multifinality associated with low AFF, a dispositional transdiagnostic risk factor, to be a result of divergent trajectories dependent upon the differential moderating effects of IC. Research aimed towards elucidating these interactive effects in childhood is crucial for a more thorough understanding of the cause, nature, and implications of risk and protective factors contributing to the development and emergence of psychopathology.
1.1 The Structure of Psychopathology

The historical view of psychiatric disorders as discrete, categorical entities as defined by current diagnostic nosologies (e.g., DSM-5; American Psychological Association, 2013), has been contested by evidence that many disorders are highly comorbid and exist on a continuum. Consistent with the transdiagnostic approach, this suggests that mental disorders may have more in common regarding underlying processes than current diagnostic nosologies suggest, or that there may be a more parsimonious structure of psychopathology (Castellanos-Ryan et al., 2016; Zald & Lahey, 2017). As such, a large reliable literature explains this extensive comorbidity among categorical diagnoses by organizing psychopathology within quantitative structural models (Krueger, 1999; Krueger & Markon, 2006a; Caspi et al., 2014; Laceulle et al., 2015; Kotov et al., 2017; Krueger et al., 2018).

Quantitative models are sets of statistical equations describing and predicting psychological phenomena that hold particular promise for empirical comparison of different nosologies (Krueger & Markon, 2006a). Empirical comparisons among quantitative structural models of adult psychopathology have indicated that common forms of psychopathology can be understood in terms of a factor model (Krueger & Markon, 2006a, 2006b) that strongly resembles the influential factor model of child psychopathology proposed in the 1960s (Achenbach, 1966; Achenbach & Edelbrock, 1984). Specifically, this model is organized into two broad, correlated liability dimensions, Internalizing and Externalizing, capturing substantial common psychopathological variance.

Internalizing psychopathology represents a spectrum characterized by a propensity to experience mood and anxiety symptoms, whereas the externalizing dimension conveys risk for disinhibited, antisocial, and/or substance use disorders. This two-factor model of
psychopathology has been demonstrated to be robust across age, sex, ethnicity, culture, informant and sample type (Achenbach, 1966; Krueger, Capsi, Moffitt, & Silva, 1998; Krueger, Chentsova-Dutton, Markon, Goldberg, & Ormel, 2003; Slade & Watson, 2006; Kramer, Krueger, & Hicks, 2008; Lahey et al., 2008; Eaton, Krueger, & Oltmanns, 2011; Eaton et al., 2012; Forbush & Watson, 2012). However, since Achenbach’s (1966) seminal research, competing structural models have been proposed represent psychopathology more accurately across developmental ages and gender, and within both clinical and community populations, for example: a three-factor model (e.g., Krueger, 1999; Krueger & Markon, 2006a, 2006b; Doyle et al., 2016), as well as a number of general psychopathology ($p$ factor) models (e.g., Caspi et al., 2014; Lahey et al., 2012; Olino et al., 2014; Martel et al., 2017).

The common three-factor model of psychopathology, consisting of separable fear and distress factors alongside an externalizing factor, was proposed by Krueger (1999); since, an extensive body of literature robustly demonstrates evidence for this model with excellent fit indices (e.g., Eaton et al., 2012; Slade & Watson, 2006; Watson, 2009; Vollebergh et al., 2001; Slade & Watson, 2006; Beesdo-Baum et al., 2009). While these fear and distress factors are generally highly correlated (e.g., children, $r = .86$, Vollebergh et al., 2001; $r = .87$, Doyle et al., 2013; adults, $r = .71$, Eaton et al., 2013; $r = .80$, Kotov et al., 2015), employing a single overarching internalizing factor presumptively implies that the component disorders share a similar developmental etiology, trajectory, and risk factors.

Research has demonstrated that some disorders are more likely to co-occur than others, and that fear and distress disorders possess dissociable underlying neurobiological mechanisms and cognitive processes (Clark & Watson, 2006; Kendler et al., 2007; Etkin & Wager, 2007). For example, major depressive disorder and generalized anxiety (i.e., distress disorders) have high
rates of comorbidity (e.g., Kendler et al., 2007), both of which often co-occur with post-traumatic stress disorder (e.g., Grant et al., 2008; Post et al., 2011). In contrast, evidence suggests that the fear dimension disorders are unique from distress dimension disorders in that specific phobia, social phobia, and panic disorder were the least likely to co-occur with other anxiety/emotional disorders, yet the co-occurrence among these disorders were high (Brown et al., 2001; Ollendick, et al., 2002). Indeed, empirical evidence supports the consideration of separable expressions of fear and distress dimensions observed at the diagnostic level.

Unique underlying physiological and cognitive processes further emphasize the differentiation between fear and distress disorders. After accounting for common variance, fear disorders may be characterized by attention biases away from threat (i.e., threat avoidance), while distress disorders are characterized by attention biases towards threat (i.e., threat vigilance) (e.g., Salum et al., 2013; Waters et al., 2014). This is further confounded by unique consideration for what constitutes “threat” and demands such attention. Reliably, individuals with distress disorders have evidenced elevated baseline startle responses to aversive stimuli, as well as hyper-responsivity to neutral or ‘safe’ stimuli, compared to healthy controls (Morgan et al., 1995; Ray et al., 2009; Vaidyanathan, Patrick, & Cuthbert 2009, for review), whereas subjects with fear disorders show potentiated startle response solely in the presence of their specific phobia (Globisch et al., 1999; Lang et al., 2007; Vaidyanathan, Patrick, & Cuthbert 2009).

In addition to neurocognitive support for this differentiation, a reliable genetic literature also supports this model. Kendler et al., (2003) identified unique genetic risk underlying externalizing disorders, as well as two additional major sources of risk: 1) a common factor with substantial genetic variance shared between major depression and generalized anxiety disorder, and 2) a common genetic factor representing phobias and fear disorders. Thus, empirical
evidence suggests different etiology and underlying fundamental processes influencing the expression of fear and distress disorder symptoms alongside a correlated but unique externalizing factor.

1.1.1 Integration of transdiagnostic models with quantitative structure of psychopathology

Within recent decades, the investigation into dimensional quantitative structural models of psychopathology has coincided with the emergence of transdiagnostic models demarcating risk factors contributing to the comorbidity among categorical diagnoses and underlying broad dimensional factors of psychopathology. Specifically, the integration of basic research concerning emotion and cognition with developmental approaches to psychopathology has been an important advancement in the field.

Recent initiatives, such as the NIMH’s Research Domain Criteria (RDoC; Insel & Cuthbert, 2009), have attempted to shift focus towards multi-modally assessed transdiagnostic neurobehavioral processes that are thought to be relevant to and underlie human behavior, generally, and psychopathology more specifically. Whereas categorical clinical disorders are narrow-scope heterogeneous clusters of symptoms, intermediate phenotypes are conceived as neurocognitive and affective processes that are causally linked to the development of symptoms, as well as problems of neural circuitry and functioning (Cannon & Keller, 2006).

The RDoC matrix includes six broad domains representing major systems of emotion, cognition, motivation, and social behavior comprising lower-order constructs responsible for capturing distinctive neurodevelopmental aspects of their respective domain. Of particular interest for the current research are the Affiliation and Attachment (i.e., AFF) and Inhibition/Suppression (i.e., IC) constructs subsumed within the Social Processes and Cognitive
Systems domains, respectively. Consideration of affiliation and inhibitory control RDoC constructs allows for the construction of standardized and replicable transdiagnostic phenotypic indicators that may serve as a critical link between biobehavioral systems and quantitative structural models of psychopathology. However, the way in which these transdiagnostic processes interactively contribute to the liability and development of psychopathology remains unclear.

Through the support of an empirical transdiagnostic model (i.e., RDoC), a robust literature surrounding the neural bases of AFF and IC, and the associated risk for developing psychopathological symptoms, positions AFF and IC as ideal risk factors for examining the mechanisms underlying divergent trajectories and resulting multifinality. All told, considering the proposed study’s aims within the RDoC framework addresses the inherent need for multi-modal research on distinct sets of traits corresponding to RDoC process constructs – replicable across animal, child, and adult literatures – to serve as an interface between matrix constructs and clinical problems (e.g., Patrick & Hajcak, 2016; Latzman, Green, and Fernandes, 2017; Palumbo & Latzman, 2018; Kessel et al., 2016; Kozak & Cuthbert, 2016).

1.2 Affiliative Capacity as a Transdiagnostic Risk Factor

Among the various transdiagnostically relevant processes underlying psychiatric disorders, deficits in social processes has been shown to be of particular importance in both youth and adulthood, manifesting as symptoms, outcomes, or both. Low levels of social motivation and attention to social cues starting in early childhood may have severe consequences on cognition and psychopathology (Calkins & Fox, 2002; Oh et al., 2008; Coplan et al., 2013). For example, both internalizing and externalizing psychopathology and poor peer relations have been found to be bidirectional risk factors for one another (Deater-Deckard, 2001). This suggests
an interactive, cyclical pattern that emerges in childhood that may contribute to a maladaptive trajectory extending into adulthood (Deater-Deckard, 2001; Dodge et al., 2003; Dougherty, 2008).

Affiliative capacity is reliant upon accurate detection of and attention to social cues, as well as social learning and memory associated with the formation and maintenance of interpersonal relationships. Indeed, while affiliation is a behavioral consequence of social motivation, the degree of motivation varies across individuals (Kenrick, Griskevicius, Neuberg, & Schaller, 2010; Neel, Kenrick, White, & Neuberg, 2016). Disruptions in dispositional AFF can be observed transdiagnostically, expressed as symptoms at bipolar extremes. High AFF can manifest clinically as over-attachment and fear of abandonment, apparent in clinical phenomena such as borderline personality disorder and dependent personality disorder (Levy, 2005; Bornstein, 1998; Gude et al., 2004). Conversely, low dispositional AFF links to broad internalizing and externalizing dimensions and often manifests as a general lack of interpersonal effectiveness (e.g., low agreeableness, inability to establish peer relationships, social anhedonia, a blunted social responsiveness and emotional expressivity, and a lack of empathy) (e.g., Cusi et al., 2011; Frick et al., 2014, respectively).

In recent years, a burgeoning research literature has emerged surrounding the operationalization, contributing risk factors, and resulting psychopathological outcomes of low dispositional AFF (e.g., Palumbo, Perkins, et al., under review; Waller et al., 2019). Through this effort, component traits of AFF, such as low empathy, social withdrawal and anhedonia/apathy, and low agreeableness, have evidenced parallel associations with distress-based internalizing, particularly, and externalizing symptomology (e.g., Reichel & Beaudoin, 1998). For example, reduced levels of empathy have been found in individuals endorsing greater severity of
depressive symptoms (Cusi et al., 2001) and externalizing problems (Hughes et al., 2000; Miller & Eisenberg, 1988; Caplin & Cole, 2005).

Over the last few decades, it has become apparent that internalizing symptoms are contemporaneous correlates of passive, social withdrawal and disaffiliation (e.g., Rubin, Coplan, & Bowker, 2009; Boivin et al., 1995; Morison & Masten, 1991; Ollendick et al., 1990; Hymel et al., 1990; Rubin et al., 1995) while externalizing may be conceptualized as relating to active, agentic disaffiliation (e.g., Patrick, Fowles, & Krueger, 2009). Agreeableness, as operationalized by the Five Factor Model (Digman, 1990; Goldberg, 1990), overlaps with affiliation and captures dispositional traits relating to both social (e.g., “can be cold and aloof”), as well as agentic (e.g., “sometimes rude to others”) manifestations. Low levels of dispositional Agreeableness (i.e., Antagonism) has been associated with distress-based internalizing and externalizing psychopathology to a similar degree (Malouff et al., 2005; Sleep et al., 2018; Watts et al., 2019; John et al., 1994), indicating commonality between agentic and social disaffiliation through shared deficits in compassion, altruism, and trust within interpersonal relationships.

Callousness, the most commonly studied expression of low AFF, is a trait characterized by a disinterest in forming and maintaining close relationships, a lack of empathy for other’s distress, and uncaring and unemotional behaviors that are attributable to the reduced sensitivity to the emotions and needs of others (Frick, Barry, & Bodin, 2000; Frick et al., 2003; Patrick, Fowles, & Krueger, 2009; Waller & Hyde, 2018; Hyde et al., 2015; Barry et al., 2000; Berg et al., 2013). An immense literature implicates callous traits as a unique risk factor in the development of externalizing psychopathology (for reviews, see Frick & White, 2008; Hawes, Prince, & Dadds, 2014), as well as distinct emotional, cognitive, and temperamental characteristics that distinguish high callous-youth from other antisocial youth (Frick et al., 2008).
Further these traits have been moderately positively associated with internalizing symptoms (Essau et al., 2006; Barker & Salekin, 2012) and internalizing-related temperamental traits (Latzman et al., 2013; Berg et al., 2013) even after controlling for demographics and conduct problems (Hipwell et al., 2007; Enebrink et al., 2005).

More recently, it has been proposed that callousness comprises subfactors which embody dispositional trait dimensions representing a callous lack of empathy and guilt, an uncaring disregard for others, and an unemotional demeanor (e.g., Frick, 2004). Previous studies have demonstrated that a two-factor model, consisting of callous and uncaring subscales, provides a better fit to the data than a three-factor model (including an unemotional scale) (Roose et al., 2010; Gao & Zhang, 2006; Houghton, Hunter, & Crow, 2013; Waller et al., 2015; Hawes et al., 2014). A differential pattern of associations exists between ICU scales and personality and psychopathology outcome variables of interest, such that callous and uncaring traits correlate in a similar way, and the unemotional scale evidences distinct associations (Latzman et al., 2013; Berg et al., 2013; Cardinale & Marsh, 2017, review). For example, callous and uncaring scales both evidence positive associations with anxiety and depression, as well as with aggressive and rule-breaking behavior, across multiple informants (Berg et al., 2013; Waller et al., 2015a; Gao & Zhang, 2016), whereas the unemotional scale was generally unrelated.

While it is well established that affiliative capacity, and its proxy callousness, predicts externalizing problems, it is important to address the existing literature demonstrating inconsistent findings between internalizing psychopathology and low AFF (Sevecke and Kosson 2010). Theoretically, low anxiety and depression characterize youth with high callous traits, whereas those who are high in anxiety and depression evidence low callous traits (Frick & Ellis, 1999). Empirically, callousness has been negatively associated with internalizing symptoms (i.e.,
high callousness associated with less symptomatology; e.g., Barry et al., 2000; Pardini et al.,
2012), or unrelated (Fanti, 2013; Pardini & Loeber, 2008; Frick, Lilienfeld, Ellis, Loney, &
Silverthorn, 1999; Pardini, 2006). Research finding positive associations with callousness and
internalizing disorders have, importantly, considered distress and fear symptoms separately, such
that distress disorders, as opposed to fear-specific psychopathology were associated with greater
callousness (e.g., Waller et al., 2015b). These positive relationships found between callous scores
and distress symptoms suggest that callous traits may relate specifically to self- and informant-
reports of children being socially withdrawn, isolated, or low in mood, consistent with the
conceptualization of low AFF more broadly.

Whereas callousness may be an imperfect proxy for AFF, there is an absence of a single
empirically supported or standardized measure capturing all aspects of AFF, as conceptualized
by RDoC. In an attempt to address this limitation, Palumbo, Latzman, and Patrick (under review)
developed and validated a psychometric index of AFF, to be described further below, that
captures low affiliative traits thought to be a precursor for callousness (Waller et al., 2019). This
index evidenced positive associations with both internalizing and externalizing-related behavior,
consistent with the larger literature, which remained significant after accounting for other
dispositional traits, such as fearlessness and disinhibition. Through the use of this RDoC-
conformant index of AFF, the current study seeks to clarify the common and unique associations
with fear, distress, and externalizing psychopathology.

1.3 Inhibitory Control as a Unique Predictor and Moderator

As with AFF, transdiagnostic deficits in cognitive and behavioral IC have been
considered within emotional and behavioral disorders (Gotlib & Joorman, 2010; Mathews &
MacLeod, 2005; Venables et al., 2018; Utendale & Hastings, 2011). Inhibitory control, defined here as the cognitive processes for intentional control or suppression of a response in the service of higher order or longer-term goals (Nigg, 2000), has evidenced robust associations with psychopathology in youth and adulthood (e.g., Latzman et al., 2016; Hecht & Latzman, 2017; for a review see, Snyder, Miyake, & Hankin, 2015). This definition is in line with that of inhibition proposed within the three-component model of executive functioning (EF; Miyake et al., 2000; Friedman et al., 2008; Latzman & Markon, 2010) and has been considered as the underlying processes influencing executive function processes more broadly (Barkley, 1997; Friedman et al., 2008; Hecht & Latzman, 2017; Miyake & Friedman, 2012). When considered simultaneously with the additional two components, updating and shifting, to model a common, higher-order EF construct, inhibition correlates virtually perfectly with this common EF factor (loading of 1.0; Friedman et al., 2008), such that there is no remaining inhibition-specific variance. Further investigation into the proportion of variance in each EF component due to the common EF factor reveals that 99%, 43%, and 44% of the variance is explained in inhibition, updating, and shifting, respectively. These results can be understood as EF being dependent upon IC with some added task-demand specific variance.

Heritability studies have indicated that genetic influences mediate almost all of the variance captured by the common EF factor (A = 99%; Friedman et al., 2008). Importantly, updating and shifting also have significant genetic influences specific to each factor indicating correlated, yet separable EF processes with distinct underpinnings. These results are in line with neuroimaging studies in which investigation beyond the frontal regions activated by all three components of executive function, there were no other brain regions activated by inhibition, specifically, whereas unique regions were evident for updating and shifting tasks (Collette et al.,
Thus, individual differences in IC appear to be very closely related to, or underlie what is common among executive functions, such that this construct may serve as a fundamental, unifying component of executive control from which other executive deficits stem (e.g., Zacks & Hasher, 1994; Friedman et al., 2008; Barkley, 1997; Miyake & Friedman, 2012).

Nigg (2000) further identified separable processes underlying IC including, but not limited to, interference control, which is the suppression of interference due to resource or stimulus competition, and behavioral inhibition, which is the suppression of a prepotent response. Individual differences in interference control and behavioral inhibition may reflect variations in cooperation of two neural systems in response to visual cues and execution of prepotent responses. The first, a posterior attentional system, is responsible for the automatic orientation of visual attention in response to motion, change, or other salient visual cues that primes communication with neural systems responsible for the execution of an appropriate response (i.e., bottom-up processing). The anterior system controls effortful or intentional attentional focusing (i.e., top-down) in response to both visual cues and goal-directed strategy consideration (Nigg, 2000). The effective communication of these two neural systems reflects an ability to deliberately 1) suppress attention to distractors that may slow the primary response, 2) suppress internal stimuli that may interfere with the current operations of working memory, and 3) suppress attention and override a prepotent response to a competing stimulus in service of carrying out a goal-directed response (Nigg, 2000).

Friedman and Miyake (2004) successfully modeled behavioral operationalizations of Nigg’s IC processes via well-established and validated neurocognitive IC tasks (i.e., antisaccade, stop-signal, stroop, flanker; Miyake et al., 2000) that evidenced strong positive associations with each other, and with other measures of inhibition and executive function. Specifically, tasks such
as Stop-Signal and Go/No-go successfully measured prepotent response inhibition, whereas Flanker and other attention-related tasks capture variance related to resistance to distractor interference. In service of capturing the multi-dimensional aspect of IC, the proposed study is focused on distinct neurocognitive indicators of Nigg’s conceptualization of IC, further supported by Miyake’s task-based models.

The aforementioned variability in IC has been used to describe internalizing and externalizing behavior (Gray, 1987; Quay, 1988a, 1988b, 1993, 1997), through emphasis on the interaction between behavioral activation (i.e., bottom-up posterior system) and behavioral inhibition (i.e., top-down anterior system). Specifically, an underactive inhibitory system (i.e., low IC) has been implicated in conduct problems, antisocial behavior, attention problems, and substance use (Friedman et al., 2007; Young et al., 2009; Dolan, Bechara & Nathan, 2008; Finn et al., 2009; for meta-analytic reviews, see Morgan & Lilienfeld, 2000; Ogilvie et al., 2011), whereas an overactive inhibitory system (i.e., high IC) has been observed in individuals reporting internalizing symptoms (depression, Snyder, 2013; anxiety, Shwartz, Snidman, & Kaga, 1999; Grahek et al., 2018). Further, psychometric measurements of trait inhibition in toddlerhood and early childhood have predicted distress disorders in early and middle childhood (Biederman et al., 1990, 1993; Hirshfeld et al., 1992; Rosenbaum et al., 1993) and adolescence (Hayward et al., 1998; Schwartz, Snidman, & Kagan 1999), as well as externalizing disorders in later development (Utendale & Hastings, 2011; Utendale et al., 2011; Young et al., 2009; Olson et al., 1999). Resulting emotional and behavioral problems may stem from the role of IC in determining the emotion and intensity experienced, as well as determining how an individual respond to that emotion (Joorman, 2018; Latzman, Shishido, Latzman, & Clark, 2016).
Individual differences in IC abilities have been implicated in socioemotional and behavioral information processing and differential liability for psychopathological symptoms. Thus, the unique distinguishable nature of the associations with psychopathology position IC not only as an independent predictor, but also an invaluable moderating transdiagnostic risk factor in detangling parallel associations between low dispositional AFF and internalizing and externalizing symptomatology. Although a recent study has examined the interactive relationship between low AFF (i.e., callousness) and IC in the explanation of externalizing problems (Waller et al., 2017), to date, investigation into the integration of transdiagnostic factors and resulting divergent trajectories has yet to be initiated. The current study is the first to probe the unique risk of inhibitory dysfunction on the transdiagnostic risk for low AFF in the explanation of quantitatively-derived externalizing and internalizing psychopathology.

1.4 Current Study

Identifying and integrating risk and protective factors present in childhood is crucial for understanding and differentiating divergent developmental trajectories of psychopathology. Specifically, the integration of social and cognitive processes with developmental approaches to psychopathology has been an important advancement in the field. As an extensive literature demonstrates AFF and IC as being transdiagnostic and stable across developmental stages (i.e., early childhood, adolescence, adulthood) and multiple methods of measurement (e.g., self-report, task-based, neurophysiology), these dispositional traits hold promise for elucidating the unique and interactive effects underlying the developmental liability for, and divergent trajectories of, internalizing and externalizing psychopathology. As described below, parent-report measures of AFF, in conjunction with interview-based symptoms of psychopathology, and neurocognitive
indicators of IC allows for the unique opportunity to investigate interactive effects of RDoC constructs, with the additional advantage of integrating across units of analysis.

A major aim of RDoC (Cuthbert & Insel, 2013) is to advance the conceptualization and understanding of how neural processes relate to psychological phenomena with a particular emphasis on 1) multilevel, multimodal datasets that include genetics, neuroimaging and physiology, self-report, and behavioral measures, and 2) large samples to allow for well-powered multi-variate analyses. A significant limitation in the pursuit of this endeavor is the lack of available studies that have been designed and sufficiently powered to examine these moderating effects influencing divergent psychopathological outcomes.

To this end, the Child Mind Institute (CMI) has launched the Healthy Brain Network (HBN), an ongoing initiative focused on creating and sharing a biobank of data from 10,000 New York area participants (ages 5-21; Alexander et al., 2017). Attributable to its large sample and comprehensive assessment battery, the Child Mind Institute Healthy Brain Network (CMI-HBN; Alexander et al., 2017) study provides a unique opportunity to accomplish the following aims: 1) Integrate multiple methodologies to assess latent psychopathology, AFF, and IC (via clinician interview, parent-report, and task-based methods, respectively); 2) Model the three-factor quantitative structure of psychopathology in young children; 3) Examine affiliative and IC correlates of resulting latent psychopathology dimensions (i.e., fear, distress, and externalizing); 4) Investigate the moderating influence of individual variation in IC capacity on dispositional AFF in the explanation of divergent trajectories and multifinality of psychopathology.

Specifically, the proposed study would be the first to use a multi-modal approach across sources (i.e., parent and child) to gain a greater understanding of a) how an individual trait transdiagnostic risk factor (i.e., AFF) leads to multiple psychopathologies (i.e., multifinality) and
b) how specific psychopathology emerges from the moderating effects of individual differences in IC (i.e., overcontrolled or undercontrolled; *divergent trajectories*). Through these aims, the proposed research will integrate dysfunctions in both social and cognitive processes, to enhance our ability to understand the basis of and liability for divergent trajectories in the development of psychopathology.

As previous studies have demonstrated the significance of examining subfactors of trait AFF in relation to psychopathology (Berg et al., 2013; Waller et al., 2015a; Gao & Zhang, 2016; Kimonis et al., 2008; Waller et al., 2015b), the current study will comparatively consider a one- and two-factor structure of AFF using an exploratory factor analysis (EFA) approach at the item level. Consistent with the empirically supported two-factor model of callousness (Waller et al., 2015b; Houghton et al., 2013; Hawes et al., 2014), we expected a two-factor model to better explain the data and to reflect a coldhearted demeanor and lack of empathy (Factor 1) and a social disregard or withdrawal (Factor 2).

It is expected that both transdiagnostic latent AFF factors, modeled using parent-report indicators, will be positively associated with both distress and externalizing symptoms (i.e., deficient AFF associated with psychopathology), with AFF Factor 1 evidencing stronger associations than AFF Factor 2 (Waller et al., 2015; Frick et al., 2008; Latzman et al., 2013). Regarding fear symptoms, due to the lack of studies examining this association specifically, we did not propose a hypothesis regarding the directionality of the associations. Additionally, consistent with previous research, IC is expected to correlate similarly with fear and distress and differentially associate with externalizing dimensions (positively and negatively, respectively; Grahek et al., 2018; Ogilvie et al., 2011).
Finally, it is hypothesized that the results will evidence a differential moderating effect, such that, in those with low AFF, greater IC will predict distress symptoms specifically (Rothbart, Ellis, Posner, 2004; Eisenberg et al., 2000; Eisenberg et al., 2005), and weaker IC will predict externalizing symptoms (Song et al., 2016; Waller et al., 2017), with stronger associations for Factor 1 compared to uncaring across all dimensions of psychopathology. All proposed study details (i.e., number of subjects, procedures, assessments), plans for analyses, and hypotheses were pre-registered through the Open Science Framework (OSF; https://osf.io/hnbcr/?view_only=b5a526f783444a49981231a7e739c436).

Taken together, the present research aims to elucidate unique and interactive transdiagnostic associations between AFF and IC in the explanation of psychopathology in children. Understanding transdiagnostic processes in psychopathology is critically important, both theoretically and clinically; greater understanding of how both individual risk factors lead to multiple disorders and how specific disorders emerge from that risk factor will help identify who is most at risk for what disorders and how that risk develops and changes over the lifespan.

2 METHODS

2.1 Participants

Participants comprised 1,671 children, ages 5-10 years ($M_{age} = 8.07$, $SD = 1.63$ years; 34.4% female), recruited and tested through the CMI-HBN consortium project described above (Alexander et al., 2017). The racial composition of the sample includes 50.0% Caucasian, 16.5% Black/African American, 11.1% Hispanic, and 22.4% Biracial or Other. Participants were provided with study information and children and parents provided written assent and consent, respectively.
2.2 Psychopathology

2.2.1 Kiddie Schedule for Affective Disorders and Schizophrenia (K-SADS; Kaufman et al., 1997).

The K-SADS is a semi-structured diagnostic interview developed to assess current and past episodes of psychopathology in children and adolescents according to criteria outlined in the fourth edition of the Diagnostic and Statistical Manual of Mental Disorders (DSM-IV; American Psychological Association, 2000). Parents and children responded to both open and closed questions and diagnostic ratings were made through clinician consensus (N = 1360). Participants were rated as either endorsing symptom criteria for the disorder, or not, for both past and current periods. Lifetime diagnostic symptom counts were computed by identifying whether each participant endorsed each symptom, either currently, in the past, or both, for each disorder. Of the 1360 children, 23.7% endorsed at least one symptom of distress disorders, 39.9% endorsed at least one symptom of fear disorders, and 89.6% of participants endorsed at least one symptom of externalizing disorders. Due to low endorsement of symptoms, and thus considerably low base rates, substance use disorders were not included in subsequent analyses.

2.3 Affiliative Capacity

Following procedures used to develop dispositional trait scales from other item sets (e.g., Hall et al., 2014; Brislin et al., 2015, Sellbom et al., 2016; Brislin et al., 2018), existing parent-report measures within the larger CMI-HBN protocol were used to create a psychometric index of AFF (N = 1430; Palumbo et al., under review). Item content of the AFF scale reflects core characteristics such as a lack of empathy, social disregard, and a coldhearted demeanor. Given the numerous deficiencies of coefficient alpha documented in the psychometric literature (Dunn et al., 2013; Deng & Chan, 2016; Peters, 2014), an additional measure of internal scale
reliability, McDonald’s omega, is reported; internal reliability (Cronbach’s alpha and McDonald’s omega) in this sample were .86 and .88, respectively.

2.4 Inhibitory Control

2.4.1 Task-Based Neurocognitive Measures.

The Adaptive Cognitive Evaluation (ACE; Rodondi et al., 2017) is a mobile assessment battery that presents standard neuropsychological paradigms to assess fundamental domains of cognitive function. The ACE assessments have integrated adaptive psychometric staircase algorithms into each cognitive task (Garcia-Perez, 2001), that allows for a personalized assessment reliant upon an individual’s cognitive performance on each task. Task difficulty is dynamically adjusted after each trial to ensure that each participant’s performance converges to an ~80% accuracy level to reflect true differences in cognitive ability and not disparities in the testing parameters or biases related to ceiling/floor effects. Reliability and validity efforts show robust support for the use of mobile assessment methods (Rodoni et al., 2017). Specifically, previous work involving 15,000 participants demonstrate comparable performance outcomes across mobile and traditional lab/clinic-based diagnostics (Lee et al., 2012). Further, ACE developers have shown high test-retest reliability across developmental age groups, as well as construct validity in comparison to standard lab-based assessments (Raz et al., 2006).

In service of measuring IC, the ACE battery includes three tasks designed to assess an individual’s ability to selectively process information that is relevant to the immediate goals, while ignoring goal-irrelevant distractions ($N = 794$). In a Flanker task (Eriksen & Eriksen, 1974), participants are required to indicate the left–right orientation of a centrally presented stimulus while inhibiting attention to the potentially incongruent stimuli that surround it (i.e., the flankers, two on either side). In the adapted ACE version, participants are responding to letters
(e.g., CCACC or DDDDD; indicating ‘A’ and ‘B’ with the left key and ‘C’ and ‘D’ with the right). Participants also completed the Boxed task, a visual scan task designed to measure directed attention and inhibition in the context of distractors. In this task, individuals are required to find a green box that is open at the top (indicated by the left key) or bottom (by right key). Within each trial, the green target box is surrounded by distractor red boxes that can be open from either of the four sides or distractor green boxes open from the left or right. Finally, participants completed the Sustained Attention and Impulsivity Task (SAIT), analogous to the Sustained Attention and Response Task (SART; McVay & Kane, 2009, 2012), a variant of the Go/No-Go task commonly used to measure IC. Consistent with the SART task paradigm, the Go stimulus occurred more frequently than the No-Go stimulus in order to establish a prepotent response set that required application of IC to override.

3 ANALYTIC APPROACH

3.1 Measurement Models

All models were estimated using the MPlus package (Version 7.4; Muthen & Muthen, 1998-2014), with full-information maximum likelihood (FIML) estimation to accommodate missing data by estimating a likelihood function for each individual based on all available data. This method has been validated and deemed appropriate for handling incomplete data within latent moderated structural equations (Cham et al., 2017). The CFA model of psychopathology was fitted using the MLR estimator, which does not assume normally distributed variables, such as with diagnostic symptom counts (Brown, 2006). All other models were estimated using maximum likelihood (ML) estimation. Goodness of fit for each model was evaluated with the
root mean square error of approximation (RMSEA), comparative fit index (CFI), and the likelihood ratio $\chi^2$ test.

To examine the structure of psychopathology in youth, a three-factor CFA model was fitted comprising fear, distress, and externalizing factors, demarcated by specific diagnostic symptom counts, as described above. In an attempt to elucidate the nature of AFF, item-level exploratory factor models were fitted using a goemin (oblique) rotation to extract a one- and two-dimensional model. Comparative fit indices and factor content were considered to determine which model to retain in the full structural models.

Currently, concerns regarding the utility of neurocognitive task-based indicators in capturing individual differences in IC (e.g., low between-subjects reliability, inconsistency due to a large number of derived component and difference scores, low intercorrelations; Draheim et al., 2019; Hedge et al., 2018; Engle et al., 1999) limit the ability to propose strongly-supported hypotheses about the component indicators of latent IC. Based on the current literature, a number of indicators have been derived from such neurocognitive tasks in attempt to address such concerns, optimize individual differences, and increase reliability (e.g., component scores, difference scores, integrative scores; Draheim et al., 2019; Engle et al., 1999). Therefore, based on theoretical and empirical considerations, an iterative approach, described in more detail below, was taken towards operationalizing IC.

The following indicators were derived for each neurocognitive task: reaction time (RT) and accuracy for each component condition (e.g., Flanker congruent and incongruent trials), total task RT and accuracy, RT cost (i.e., RT for condition 2 minus RT for condition 1), error rate cost (i.e., accuracy for condition 1 minus accuracy for condition 2), and task efficiency (reaction time/accuracy, computed per condition and for total task performance). Intercorrelations among
task indicators were examined to identify those which showed potential to create a cohesive latent construct. To limit the number of competing models, additional consideration was given towards recommendations provided within the literature (e.g., Draheim et al., 2019). For example, as Draheim and colleagues recommend the use of accuracy scores over difference scores, a model consisting of total reaction time was chosen over a model consisting of Flanker total reaction time cost, although the intercorrelations were similar in magnitude.

From among the base sample of 1,671, 1,360 subjects had diagnostic interview data, 1,430 had parent-reported AFF data, and 794 had neurocognitive task data. For participants missing data within one of the measurement modalities, full information maximum likelihood estimation (as implemented in Mplus 8) was used to generate imputed score values.

### 3.2 Full Structural Model

Structural equation modeling (SEM) was used to examine unique and interactive associations between AFF and IC in the explanation of internalizing and externalizing-related psychopathology. To estimate the unique predictive power of the trait transdiagnostic constructs of interest, the three-factor psychopathology model was regressed onto the AFF and IC factors. Finally, to examine the moderating effect of IC on AFF in the differential development of psychopathology, latent CFA-based fear, distress, and externalizing factors were regressed on regression-estimated AFF factor score(s) along with IC interaction terms (i.e., AFF*IC, created via the XWITH function in Mplus).

The major aim of the current study regarded the explanation of quantitatively-derived models of psychopathology via unique and interactive effects of latent transdiagnostic constructs. If allowed to be freely estimated, the estimates of the observed variables that each measurement model comprised would be influenced by the both the latent factors and component observed
variables in other measurement models (e.g., Flanker accuracy influenced by lifetime MDD symptom count and also by the Distress latent factor). Therefore, the estimates of each measurement model were retained and fixed in order to maintain focus on how each latent factor behaved within the full structural model.

### 3.3 Power Analysis

Regarding the necessary sample size to achieve adequate power in complex SEM models, various rules-of-thumb have been advanced, including: a) a minimum sample size of $N = 200$ (Boomsma, 1982, 1985; Hoogland & Boomsma, 1998; Boomsma and Hoogland, 2001; Kline, 2005; Kline, 2011), b) 5 or 10 subjects per estimated parameter (Bentler & Chou, 1987; see also Bollen, 1989), c) 10 subjects per variable (Nunnally, 1967), and d) 50 subjects per latent factor (Hair et al., 2014). According to these estimates, the recommended sample sizes for the proposed model would be: a) 200, b) 450, c) 230, and d) 300, respectively. However, more conservative estimates indicate larger sample sizes are necessary, considering the model’s estimators and data type; for example, 200-500 subjects were recommended for ML estimates using categorical data (i.e., item level data comprising AFF factors; Bandalos, 2014), and a sample size greater than 400 was suggested for continuous non-normal missing data (i.e., KSADS symptom-level data; Savalei & Bentler, 2005; Yuan & Bentler, 2000). Taken together, the present sample size of 1,671 far exceeds the maximum recommended sample size to account for categorical, continuous non-normal, and missing data (i.e., $N = 500$).
4 RESULTS

4.1 Measurement Models

4.1.1 Psychopathology.

Consistent with the larger literature, the current study fitted a three-factor CFA model of psychopathology via lifetime diagnostic symptom counts. Maximum likelihood estimation with robust standard errors (MLR) was used to account for the non-normality of symptom count data. As expected, the correlated three-factor model fit the data adequately (RMSEA = .037, CFI = .876, TLI = .825, SRMR = .039, $\chi^2 = 92.836, p < 0.001$). The Fear factor adequately reflected shared variance among lifetime symptom counts of panic/agoraphobia, specific phobia, separation anxiety, and social anxiety (loadings ranging from .34 to .51). Distress was defined by common variance among MDD, GAD, and PTSD (loadings .50, .43, and .35, respectively). Finally, Externalizing comprised ADHD, ODD, and CD (loadings .42, .72, .42, respectively). A strong positive association was evident between Fear and Distress ($r = .797, p < 0.001$) and each of these scales showed a moderate positive association with Externalizing ($rs = .319$ and .521, respectively, $ps < 0.001$; see Figure 4.1).
**Figure 4.1. Confirmatory Factor Analysis of K-SADS Psychopathology Lifetime Symptom Counts (RMSEA = .037, CFI = .876, TLI = .825, SRMR = .039, $\chi^2 = 92.836, p < 0.001$); K-SADS = Kiddie Schedule Affective Disorders and Schizophrenia. N = 1360.**

### 4.1.2 Affiliative Capacity.

The current study comparatively considered a one- and two-dimensional models, estimated via item-level EFA using a goemin (oblique) rotation and maximum likelihood (ML) estimation. Although the two-factor model was a better fit for the data (RMSEA = .059, CFI = .949, TLI = .925, SRMR = .031, $\chi^2 = 317.031, p < 0.001$) than the one-factor model (RMSEA = .086, CFI = .867, TLI = .840, SRMR = .057, $\chi^2 = 759.440, p < 0.001$), the two factors appeared to capture variance associated with keying of items (i.e., one factor reflecting entirely negatively-keyed items while the other reflected entirely positively-keyed items; see Appendix A). Given that the shared variance among each factor’s items appeared to be methodological rather than substantive, the two factors evidenced significant content overlap and the partitioning of the AFF
construct was not conceptually supported. For example, whereas “Does not feel guilty after misbehaving” (CBCL 26) and “The feelings of others are unimportant to him/her” (ICU 21) loaded on factor 1, reverse-keyed equivalent items, “Feels bad or guilty when she/he has done something wrong” (ICU 5) and “Considerate of other people’s feelings” (SDQ 1), loaded on factor 2. Thus, the one-factor model was retained for further analysis.

To improve fit further and to increase reliability of the resulting AFF factor, modification indices and item descriptors were reviewed to evaluate whether items were similar enough to justify correlating their associated residuals. The residual variance of the following two item pairs overlapped (i.e., measured something in common other than the variance measured by the latent AFF factor represented in the model): ICU 12 (“Seems very cold and uncaring”) and ICU 6 (“Does not show emotions”), which appear to represent individuals being perceived as unemotional \( r = .29, p < 0.001 \), and ICU 4 (“Does not care who s/he hurts to get what s/he wants”) and CBCL 16 (“Cruelty, bullying, or meanness to others”), which capture variance related to aggression and exploitation \( r = .28, p < 0.001 \). The resulting one-factor model with correlated residuals demonstrated similar item loadings and improved fit \( (RMSEA = .075, CFI = .901, TLI = .877, SRMR = .051, \chi^2 = 578.562, p < 0.001) \) and was thus retained within the full structural models (see Figure 4.2).
Figure 4.2. Exploratory Factor Analysis of Affiliative Capacity (RMSEA = .075, CFI = .901, TLI = .877, SRMR = .051, $\chi^2 = 578.562, p < 0.001$; ICU = Inventory of Callous Unemotional Traits, CBCL = Child Behavior Checklist, SDQ = Strengths and Difficulties Questionnaire * indicates reverse-keyed items. N=1430.

4.1.3 Inhibitory Control

As described above, an iterative process was taken towards operationalizing IC. Eight competing models consisted of the various combinations of Boxed total accuracy and total reaction time, Flanker total accuracy and reaction time, SAIT total accuracy and reaction time (see Appendix B). As each model was just-identified, fit comparisons were made via AIC and sample size-adjusted BIC, as well as consideration for balance of factor loadings and analytical recommendations (e.g., Mangus et al., 2019; Draheim et al., 2019). Two comparable models fit considerably better than the remaining six: Model 1 consisted of Boxed total accuracy, Flanker total accuracy, and SAIT reaction time to Go trials ($AIC = 6103.012$; $ss$ adj $BIC = 6116.526$); Model 2 comprised Boxed total accuracy, Flanker total accuracy, and SAIT total accuracy ($AIC$...
Although Model 2 demonstrated marginally better fit, the factor loadings for Model 1 were more balanced across indicators (0.746, 0.748, and -0.648, respectively) than in Model 2 (0.827, 0.711, 0.664). Further, Mangus et al., (2019) demonstrate the advantage of using joint models of accuracy and reaction time in service of improving measurement precision, particularly in young children. Thus, Model 1 (Figure 4.3) was retained for further analyses within the full SEM model.

![Diagram](image)

*Figure 4.3. Confirmatory Factor Analysis of Neurocognitive Task-Based Indicators (df = 0; model just-identified); SAIT = Sustained Attention and Impulsivity Task. N=794*

### 4.2 Full Structural Equation Model.

As described above, all component measurement models (i.e., psychopathology, AFF, IC), and their respective fixed estimates, were considered simultaneously in a full structural model using ML estimation to examine main effects of AFF and IC in the prediction of psychopathology symptom dimensions, as well as the moderating effect of IC on the relationship between AFF and dimensions of psychopathology. Further, given age and sex variation in the sample, both models statistically covaried out age and sex.
4.2.1 *Unique Predictive Effects of Affiliative Capacity and Inhibitory Control on Psychopathology*

To probe the unique effects of AFF and IC in the prediction of broad dimensions of psychopathology, Fear, Distress, and Externalizing dimensions were regressed onto AFF and IC, simultaneously. As shown in Figure 4.4, neither AFF nor IC were unique significant predictors of Fear ($\beta_{\text{AFF}} = .077, p = .084; \beta_{\text{IC}} = -.060, p = .357$). AFF, however, evidenced significant predictive power for Distress ($\beta_{\text{AFF}} = .176, p < .001$) and Externalizing ($\beta_{\text{AFF}} = .524, p < .001$); importantly, the unique effect of AFF on Distress and Externalizing was in the same direction indicating that low AFF is a significant risk factor for greater symptomatology within both dimensions of psychopathology. Main effects of IC did not meet traditional cutoffs for statistical significance for Distress ($\beta_{\text{IC}} = -.085, p = .191$) nor Externalizing ($\beta_{\text{IC}} = -.052, p = .252$).

*Figure 4.4. Main Effect of Affiliative Capacity and Inhibitory Control on Factors of Psychopathology; N = 1671.*
4.2.2 Moderating Effect of Inhibitory Control on the Relationship between Affiliative Capacity and Psychopathology

To test for possible moderating effects of IC on the relationship between AFF and psychopathology factors, Fear, Distress, and Externalizing were regressed simultaneously onto AFF, IC, and the product term of these two latent factors (i.e., AFF*IC). Consistent with hypotheses, IC did not evidence a significant moderating effect on the relationship between AFF and Fear ($\beta_{\text{AFFxIC}} = -.140, p = .06$). Conversely, the AFF*IC interaction term emerged as a significant predictor of Distress ($\beta_{\text{AFFxIC}} = .168, p < .05$), such that in individuals with low AFF, greater symptomatology was predicted by low IC, whereas high IC served as a protective factor against Distress symptoms (Figure 4.5). Finally, there was a significant moderating effect of IC on AFF in the prediction of Externalizing problems ($\beta_{\text{AFFxIC}} = .101, p < .05$). Probing of this relationship through simple slope analyses revealed low AFF as a robust predictor of Externalizing symptoms, though exacerbated in the presence of low IC (Figure 4.6).

![Figure 4.5. Simple slopes plot of interaction between Affiliative Capacity & Inhibitory Control in the prediction of Distress](image-url)
Figure 4.6. Simple slopes plot of interaction between Affiliative Capacity & Inhibitory Control in the prediction of Externalizing

5 DISCUSSION

Given the rise in transdiagnostic models as an increasingly prominent approach to understanding psychopathology (e.g., Kotov et al., 2017; Krueger et al., 2018; Insel et al., 2010), the current study was undertaken to demonstrate the multifinality associated with (low) affiliative capacity, and the potentially moderating effect of inhibitory control to explain the development of specific dimensions of psychopathology. Through integration of multiple units of analysis and careful operationalization of AFF and IC in an RDoC-conformant manner (i.e., Affiliation and Attachment and Cognitive Control constructs, respectively), the current study demonstrates the utility in marrying RDoC with quantitatively-derived models of psychopathology (i.e., HiTOP) to facilitate progress in elucidating the etiology and common, as well as distinct, risk factors of psychopathology at various levels of specificity (Kozak & Cuthbert 2017; Latzman, DeYoung, & The HiTOP Neurobiological Foundations Workgroup, in press; Michelini, Palumbo, DeYoung, Latzman, & Kotov, under review). Further, investigation into such transdiagnostic processes, and the interplay among them, in children allows for
identification of developmental risk factors prior to the emergence of clinically significant impairment.

In service of this effort, the current study took a multi-modal, cross-informant approach to address the critical issue of method variance. Specifically, parent-reported AFF, in conjunction with child-performed neurocognitive IC tasks, allows for the unique opportunity to investigate independent and interactive effects of transdiagnostic constructs on clinician-administered interview-based symptoms of psychopathology, with the additional advantage of integrating across units of analysis (see Cuthbert & Insel, 2013).

5.1.1 Affiliative Capacity and Inhibitory Control Correlates of Psychopathology Dimensions

In the current study, items originating from existing parent-report measures were used to model a psychometric index of AFF (Palumbo et al., under review). Contrary to a priori hypotheses, a one-factor structure of AFF better explained the data; although the two-factor structure demonstrated more reliable fit indices, the variance captured within these factors reflected the keying of items, rather than unique content. Thus, a one-factor model was retained.

AFF was unrelated to Fear, but demonstrated unique predictive power for Distress and Externalizing, such that low AFF served as a common risk for greater symptoms within both dimensions of psychopathology, albeit stronger for externalizing. This observed relationship with externalizing has been extensively supported within the broader literature (for reviews, see Frick & White, 2008; Hawes, Price & Dadds, 2014). Results are further in line with previous studies that suggest that the ambiguous associations between AFF, and related constructs (e.g., callousness), and internalizing can be clarified by considering distress-based symptoms independently of fear symptoms (e.g., Waller et al., 2015; Latzman et al., 2019; Palumbo,
Perkins et al., under review; Palumbo, Latzman, & Patrick., under review). These observed effects likely reflect common processes underlying a lack of interest in social reciprocity and interpersonal relationships, withdrawal, and low mood (Gao & Zhang, 2017), consistent with the conceptualization of low AFF more broadly and with manifest symptoms of distress and externalizing syndromes.

Through consideration of supporting literature (e.g., Washburn, Latzman, Schwartz, & Bramlett, 2015; Engle et al., 1999; Hedge, Powell, & Sumner, 2018; Draheim et al., 2019) and an extensive iterative process, IC was modeled via three neurocognitive task-based indicators: accuracy summary scores for the Boxed and Flanker tasks, as well as the mean reaction time for “go” trials within the SAIT task. Although there were no observed main effects of IC in the prediction of any of the three psychopathology dimensions, this may be due to a number of important contributing factors. First, in line with the cognitive-neuroscience literature, which emphasizes the relatively late maturation of the prefrontal brain structures crucial for IC, developmental constraints may restrict range of abilities in the current sample (Ridderinkhof, Band, & Logan, 1999; Dowsett & Livesey, 2000; Bedard et al., 2002; Williams et al., 1999). That is, the restricted range in this young sample may have limited variation in individual differences of IC that would otherwise be seen in older samples. This restricted range in IC may confound difficulties isolating the differential mechanisms driving poor performance (i.e., over-vs. under-controlled). It has also been argued that experience with neurocognitive tasks, or analogous activities of daily living, increase the acquisition of complex rules by placing demands on and increasing mastery of executive processes (Dowsett & Livesey, 2000); such exposure likely varies substantially between ages 5-10 years old. Lastly, it may be that low IC may contribute greater risk to psychopathology in the presence of other temperamental traits or
cognitive abilities, than in isolation (e.g., Muris & Ollendick, 2005; De Pauw & Mervielde, 2010; Rettew & McKee, 2005; Palumbo, Latzman, & Patrick, under review).

5.1.2 Joint Contributions of Affiliative Capacity and Inhibitory Control in the Explanation of Psychopathology

As expected, IC did not demonstrate a moderating effect on AFF in the prediction of Fear-based symptoms. Contrary to hypotheses, however, in individuals with low AFF, low IC exacerbated risk for Distress; that is, as currently operationalized, high IC appears to serve as a protective factor for Distress in the presence of low AFF. This unexpected finding may be attributable to the current operationalization of high IC reflecting adaptive abilities, rather than the excessive degree of inhibition that motivates problematic behavior. Specifically, the mechanisms underlying poor performance (i.e., the tendency to be over- or under-controlled) may not be considered independently but, rather, are contributing comparably to low IC.

Coupled with low AFF, the results of the current study suggest that poor IC appears to exacerbate risk for externalizing problems. Notably, low AFF appears to be a robust predictor of externalizing psychopathology, such that low AFF provides the antagonistic element that is salient to antisocial-aggressive expressions of externalizing proneness, irrespective of degree of disinhibition. Whereas both low AFF (i.e., callousness or meanness) and low IC (i.e., disinhibition) have been extensively reported as correlates of externalizing proneness (Frick & White, 2008; Hawes, Price & Dadds, 2014; Nelson & Foell, 2018; Krueger et al., 2007; Krueger, McGue, & Iacono, 2001), the current results suggest the possibility that, in young children, low IC may contribute to externalizing only in the presence of low AFF, rather than in isolation. These findings are in line with a recent study (Palumbo, Latzman, & Patrick, under review) that demonstrated the association between disinhibition and externalizing psychopathology in young
children varied by level of AFF, operationalized as dispositional meanness. Importantly, Palumbo and colleagues included an externalizing composite that specifically captured oppositional, rule-breaking, and aggressive behaviors, whereas attention problems were considered separately. Taken together, the major processes underlying disinhibited externalizing (i.e., substance use and inattention/hyperactivity) may be distinct from those influencing antagonistic externalizing. This is consistent with the externalizing spectrum model (Krueger et al., 2007), as well as the more recently developed Hierarchical Taxonomy of Psychopathology (HiTOP; Kotov et al., 2017); however, further research is needed to confirm such a distinction.

Although the hypothesis of divergent developmental trajectories was only partially supported in the present study (i.e., in the presence of low AFF, low IC predicts risk for both distress and externalizing), these results are in line with the current state of the field and serve to highlight outstanding gaps in the literature. There is a critical need to clarify underlying mechanisms of poor IC, as broader-level analyses likely obscure differential associations with broad dimensions of psychopathology. For example, Naragon-Gainey and Simms (2018) found that, whereas internalizing and externalizing psychopathology evidenced parallel associations with conscientiousness and disinhibition (negative and positive, respectively), two operationalizations of constructs similar to IC, unique associations with the lower-order facets emerged. Specifically, whereas distress disorders and antagonistic externalizing disorders were both negatively associated with conscientiousness (high IC), these associations were uniquely driven by feelings of low self-efficacy/competence and low deliberation or impulsivity, respectively. Overall, the current results, and supporting literature, indicate the pressing need to identify and utilize measures that isolate components of inhibitory control in service of
elucidating specific mechanisms underlying poor IC that contribute to the differential development of psychopathology.

5.2 Limitations & Future Directions

Some notable limitations of the present study must be acknowledged, which highlight important avenues for future research. First, the current work was limited by the availability of measures within the larger HBN study protocol. While large, publicly accessible datasets, such as the CMI-HBN project, are advantageous, they pose limitations on what data are available for use. For example, it is recommended that new data collection efforts, which aim to optimize AFF measurement, carefully consider which instruments are selected for inclusion, being sure to include explicit assessment of socioemotional affiliation-related content to more fully capture the AFF dimension. For example, the inclusion of items regarding the desire, yet inability, to affiliate (e.g., “I have difficulty maintaining interpersonal relationships”), may allow for effective partitioning of AFF factors (i.e., coldhearted demeanor/lack of empathy and social disconnect/withdrawal). It may then be possible to further elucidate unique associations among processes within the affiliative domain and broad dimensions of psychopathology. However, it is recommended that multi-measure, integrative, item-level factor analysis continue to be the analytic approach (e.g., Palumbo, Perkins et al., under review; Patrick, Iacono, & Venables, 2019) as this allows for maximization of construct reliability while systematically removing error that would otherwise be integrated through the use of manifest variables.

Another limitation of the current operationalization of AFF is the purpose underlying the previous development of this index (Palumbo, Latzman, & Patrick under review). Initially, this scale was developed as a child-analogous measure of psychopathic meanness and is therefore located in the callousness vector space. Whereas meanness/callousness can be utilized as a proxy
for low AFF, it likely reflects a component piece of a broader affiliative construct and requires further revision to be more fully situated within the conceptualization of socioemotional affiliation more broadly. Further, as this index was developed to be unidimensional, as is supported in the current study, consideration of item content and revision may facilitate the parcellation of, and investigation into unique correlates of subfactors of AFF.

In addition, despite the advantageous use of multiple informants, it is possible that parents may not be accurate reporters of a child’s level of AFF as many of the emotional and cognitive items reflect internalized processes and traits that may not be directly observable or communicated by the child. Future studies may consider integrating data from multiple informants into a single construct in order to remove any variance associated with a single reporter and isolate variance related to the construct of interest.

Several limitations surrounding IC also warrant discussion and further research. One notable limitation of the current operationalization of IC is the nature of the task-based indicators. Though the tasks included in the larger HBN protocol demonstrate considerable experimental reliability, with robust and easily replicable experimental effects (Hedge, Powell, & Sumner, 2018), this can largely be attributed to low between-subjects variability (Dang, King, & Inzlicht, 2020). Inopportunely, between-subjects variability is necessary to detect individual differences in task performance and thus questions the utility of such tasks in correlational research. Although the indicators used in the current study are not without their own limitations, they have been shown to be preferable to difference scores (i.e., a subject’s performance in one condition is subtracted from their performance in another condition), which fail to overcome these concerns and are poorly suited for the purpose of differential and developmental research (Draheim et al., 2019). Further, it is important to note that the latent modeling approach
facilitates the isolation of variance within these indicators associated with IC processes, while parceling out error-related or non-related variance, thereby increasing construct reliability (Washburn et al., 2015; Engle et al., 1999).

Consistent with suggestions for future research (Draheim et al., 2019; Mangus et al., 2019), the current study operationalized IC through the joint use of accuracy and reaction time data, which has been shown to result in modest improvements in the measurement precision and reliability of IC abilities, particularly in early school-aged children (Mangus et al., 2019). This combined approach further reduced floor and ceiling effects that often occur when accuracy data alone are considered. Although integration of such indicators in the current study (i.e., Boxed and Flanker accuracy and SAIT reaction time) may improve between-subject reliability, the underlying mechanisms behind subject performance (i.e., over- or under-controlled) may therefore be less well captured.

Future researchers may consider operationalizing AFF and IC by fully integrating multiple units of analysis and multiple informants into each of their cohesive constructs. Previous work indexing AFF (Palumbo et al., under review) and IC (Patrick et al., 2013; Venables et al., 2018) successfully integrated neurophysiological indicators, task-based performance, and psychometric scale measures to 1) address concerns regarding method variance, and 2) operationalize such constructs in a manner that facilitates the interface between biological (i.e., RDoC) and quantitatively-derived psychiatric nosologies (i.e., HiTOP) (Latzman et al., in press; Perkins, Latzman, & Patrick, 2019).

Finally, the current analyses were exclusively cross-sectional in nature. To establish trait measures as predictive risk factors for psychopathology, follow-up assessments of psychopathology at later time points will be needed. Alternatively, although indirect,
developmental risk may be assessed through the comparison of unique and interactive effects within different age cohorts. Fortunately, the HBN project was designed as a prospective-longitudinal study, with an age range of 5-21 years, and therefore additional follow-up assessments and availability of older cohorts (i.e., young adolescence and young adulthood) will be available in the future.

5.3 Conclusions

Limitations notwithstanding, the current study provides notable insights into the unique contributions of fundamental transdiagnostic biobehavioral processes, and the interplay between them, in the explication of dimensions of psychopathology in young children. Specifically, in a large sample of young children, low AFF predicted risk for distress, as opposed to fear-based internalizing, as well as externalizing symptomatology, which was further exacerbated by the presence of low IC. These results provide an example of the way in which transdiagnostic biobehavioral processes may interface with quantitatively-derived dimensions of psychopathology in service of clarifying common and distinct risk factors of psychopathology at various levels of specificity and illuminating the utility of a unified, dimensional, and neurobiologically-grounded psychological nosology. Looking forward, by incorporating additional empirically-supported, developmentally sensitive report, neurophysiological, and task-based measures, AFF and IC may be used to refine understanding of psychopathological risk across development, beyond current methods.
REFERENCES


predispositions to childhood aggression at age 11 years. *Archives of General Psychiatry*, 55(8), 745-751.


indicator of fear and distress disorders and affiliated traits. *Psychological bulletin, 135*(6), 909.


### Appendix A

<table>
<thead>
<tr>
<th>Item content</th>
<th>Factor 1</th>
<th>Factor 2</th>
</tr>
</thead>
<tbody>
<tr>
<td>ICU 4: Doesn’t care who is hurt to get what they want</td>
<td>.68</td>
<td>--</td>
</tr>
<tr>
<td>CBCL 26: Doesn’t feel guilty after misbehaving</td>
<td>.65</td>
<td>--</td>
</tr>
<tr>
<td>CBCL 16: Cruel, bullies, mean to others</td>
<td>.61</td>
<td>--</td>
</tr>
<tr>
<td>ICU 12: Seems cold and uncaring</td>
<td>.60</td>
<td>--</td>
</tr>
<tr>
<td>ICU 18: Shows no remorse when done something wrong</td>
<td>.49</td>
<td>--</td>
</tr>
<tr>
<td>ICU 21: Others’ feelings are unimportant</td>
<td>.43</td>
<td>--</td>
</tr>
<tr>
<td>ICU 6: Doesn’t show emotion</td>
<td>.34</td>
<td>.11</td>
</tr>
<tr>
<td>ICU 24: Does things to make others feel good*</td>
<td>-.23</td>
<td>.86</td>
</tr>
<tr>
<td>ICU 17: Tries not to hurt others’ feelings*</td>
<td>--</td>
<td>.75</td>
</tr>
<tr>
<td>ICU 8: Is concerned about others’ feelings*</td>
<td>--</td>
<td>.78</td>
</tr>
<tr>
<td>SDQ 1: Considerate of others’ feelings*</td>
<td>--</td>
<td>.62</td>
</tr>
<tr>
<td>ICU 16: Apologizes to persons s/he has hurt*</td>
<td>--</td>
<td>.60</td>
</tr>
<tr>
<td>ICU 5: Feels bad/guilty when done something wrong*</td>
<td>--</td>
<td>.51</td>
</tr>
</tbody>
</table>

*Appendix A. Exploratory Factor Analysis of Two-factor Affiliative Capacity (RMSEA = .059, CFI = .949, TLI = .925, SRMR = .031, $\chi^2 = 317.031$, $p < 0.001$); Loadings with $p < .01$ are reported. ICU = Inventory of Callous Unemotional Traits, CBCL = Child Behavior Checklist, SDQ = Strengths and Difficulties Questionnaire * indicates reverse-keyed items. N=1430.*
Appendix B

<table>
<thead>
<tr>
<th>Model</th>
<th>AIC</th>
<th>ss adj BIC</th>
<th>Boxed Loading</th>
<th>Flanker Loading</th>
<th>SAIT Loading</th>
</tr>
</thead>
<tbody>
<tr>
<td>$B_{ACC}, F_{ACC}, S_{ACC}$</td>
<td>6096.51</td>
<td>6110.02</td>
<td>0.83</td>
<td>0.71</td>
<td>0.66</td>
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<tr>
<td>$B_{ACC}, F_{ACC}, S_{RT}$</td>
<td>6103.01</td>
<td>6116.53</td>
<td>0.75</td>
<td>0.75</td>
<td>-0.65</td>
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<tr>
<td>$B_{ACC}, F_{RT}, S_{ACC}$</td>
<td>6284.43</td>
<td>6297.94</td>
<td>0.94</td>
<td>-0.50</td>
<td>0.58</td>
</tr>
<tr>
<td>$B_{ACC}, F_{RT}, S_{RT}$</td>
<td>6221.51</td>
<td>6235.03</td>
<td>-0.66</td>
<td>0.74</td>
<td>0.65</td>
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<tr>
<td>$B_{RT}, F_{ACC}, S_{ACC}$</td>
<td>6411.82</td>
<td>6425.34</td>
<td>-0.38</td>
<td>0.69</td>
<td>0.68</td>
</tr>
<tr>
<td>$B_{RT}, F_{ACC}, S_{RT}$</td>
<td>6317.91</td>
<td>6331.42</td>
<td>0.45</td>
<td>-0.56</td>
<td>0.86</td>
</tr>
<tr>
<td>$B_{RT}, F_{RT}, S_{ACC}$</td>
<td>6386.02</td>
<td>6399.53</td>
<td>0.72</td>
<td>0.79</td>
<td>-0.37</td>
</tr>
<tr>
<td>$B_{RT}, F_{RT}, S_{RT}$</td>
<td>6223.09</td>
<td>6246.61</td>
<td>0.67</td>
<td>0.82</td>
<td>0.59</td>
</tr>
</tbody>
</table>

Appendix B. Inhibitory control model fit comparisons. Two competing models bolded; retained final model italicized. $B_{ACC} = $ Boxed accuracy; $B_{RT} = $ Boxed reaction time; $F_{ACC} = $ Flanker accuracy; $F_{RT} = $ Flanker reaction time; $S_{ACC} = $ SAIT accuracy; $S_{RT} = $ SAIT reaction time. $N = 794$. 