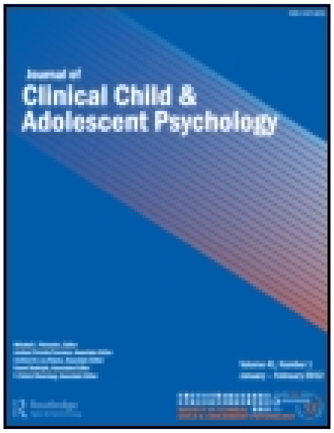

Journal of Clinical Child & Adolescent Psychology
Publication details, including instructions for authors and subscription information:
http://www.tandfonline.com/loi/hcap20

Combining Neural and Behavioral Indicators in the Assessment of Internalizing Psychopathology in Children and Adolescents

Jason S. Moser [a] , C. Emily Durbin [a] , Christopher J. Patrick [b] & Norman B. Schmidt [b]
[a] Department of Psychology , Michigan State University
[b] Department of Psychology , Florida State University
Published online: 31 Jan 2014.

To cite this article: Jason S. Moser , C. Emily Durbin , Christopher J. Patrick & Norman B. Schmidt (2015) Combining Neural and Behavioral Indicators in the Assessment of Internalizing Psychopathology in Children and Adolescents, Journal of Clinical Child & Adolescent Psychology, 44:2, 329-340, DOI: 10.1080/15374416.2013.865191

To link to this article: http://dx.doi.org/10.1080/15374416.2013.865191

Journal of Clinical Child & Adolescent Psychology, 44(2), 329–340, 2015

ISSN: 1537-4416 print/1537-4424 online
DOI: 10.1080/15374416.2013.865191

Combining Neural and Behavioral Indicators in the Assessment of Internalizing Psychopathology in Children and Adolescents

Jason S. Moser and C. Emily Durbin
Department of Psychology, Michigan State University

Christopher J. Patrick and Norman B. Schmidt
Department of Psychology, Florida State University

Anxiety and mood disorders are among the most prevalent mental health problems affecting our youth. We propose that assessment and treatment efforts in this area can benefit from a focus on developmentally sensitive neurobehavioral trait constructs, that is, individual difference constructs with direct referents in both neurobiology and behavior across the lifespan. This approach dovetails with the National Institute of Mental Health's Research Domain Criteria initiative, which aims to improve classification and treatment of psychopathology by delineating dimensions of functioning that transcend measurement domains and traditional diagnostic categories. We highlight two neurobehavioral dimensions with clear relevance for understanding internalizing problems at differing ages: (a) defensive reactivity and (b) cognitive control. Individual differences in defensive reactivity are posited to reflect variations in sensitivity of the brain's negative valence systems, whereas differences in cognitive control are theorized to reflect variations in neural systems dedicated to regulating behavior and affect. Focusing on these target constructs, we illustrate a psychoneurometric approach to assessment of internalizing psychopathology entailing use of neural, self-report, and behavioral indicators. We address the feasibility of the psychoneurometric approach for clinical application and present results from a pilot study demonstrating expected associations for neural, parent-report, and behavioral measures of defensive reactivity and cognitive control with internalizing symptoms in preschoolers. Together, our conceptual and empirical analyses highlight the promise of multimethod, dimensional assessment of internalizing psychopathology in the lab and in the clinic.

Anxiety and depression represent the most common psychological problems reported across the lifespan (Beesdo, Knappe, & Pine, 2009; Costello, Mustillo, Erkanli, Keeler, & Angold, 2003; Kessler, Chiu, Demler, & Walters, 2005; Lewinsohn, Hops, Roberts, Seeley, & Andrews, 1993). Indeed, anxiety problems are the primary reason for referral of children and adolescents for mental health services (Beidel, 1991). Fifteen to 20% of our youth in the United States are estimated to suffer from an anxiety disorder (Beesdo et al., 2009), and nearly 20% are expected to experience a major depressive episode by age 18 (Lewinsohn et al., 1993). These internalizing (anxiety and depressive) problems are associated with a range of impairments in adaptive functioning in children and adolescents, including social and academic problems as well as increased risk for suicide and comorbid conditions (Gould et al., 1998; Rohde, Lewinsohn, & Seeley, 1994). Their co-occurrence, which is extremely common (Sørensen, Nissen, Mors, & Thomsen, 2005; Stark & Laurent, 2001), is even more problematic, as youth suffering from both anxiety and depressive problems show greater chronicity, higher rates of recurrence and suicide, greater functional impairment, poorer treatment outcomes, and greater utilization

Correspondence should be addressed to Jason S. Moser, Department of Psychology, Michigan State University, East Lansing, MI 48824. E-mail: jmoser@msu.edu

of mental health care (Birmaher et al., 1996). Of importance, internalizing problems in childhood and adolescence appear to set the stage for continued adjustment problems into adulthood (Rohde et al., 1994; Weissman et al., 1999). Given the impact of anxiety and depression across the lifespan, it is critical to identify those at risk early.

Our aims in this article are to describe risk identification using a multimethod developmental approach and to discuss the clinical feasibility of adopting this approach. To move the assessment of internalizing problems toward a multilevel analytic framework, it will be critical to focus systematic investigative effort on constructs that can bridge clinical problems with neurobiological systems. That is, neural systems need to be understood not just unto themselves but as they relate to the development and maintenance of behavior problems, and to strategies for preventing and ameliorating such problems (cf. Cuthbert & Insel, 2010; Sanislow et al., 2010).

We propose a *psychoneurometric* approach (Patrick, Durbin, & Moser, 2012; Patrick et al., 2013) that reconceptualizes clinical disorders in terms of dispositional constructs that can be linked to neurobiological systems and measures. Rather than focusing on discrete diagnostic conditions as targets for neurobiological analysis, the psychoneurometric approach focuses on clinically relevant neurobehavioral traits (i.e., hypothesized dispositions with direct referents in neurobiology and behavior) as bridging constructs. Self-report or behavioral measures of these target constructs serve as initial referents for identifying reliable indicators in the domain of neurophysiology. Our objective in this review is to describe how this approach can contribute to the assessment of anxiety and depressive disorders in a developmental context.

Operating from this perspective, we highlight two constructs of central importance to internalizing psychopathology that have well-established referents in developmental psychology and known biomarkers: defensive reactivity and cognitive control. Individual differences in defensive reactivity are posited to reflect variations in sensitivity of the brain's negative valence systems, whereas differences in cognitive control are theorized to reflect variations in neural systems dedicated to regulating behavior and affect. These constructs are relevant to multiple internalizing disorders, and understanding them in neurobiological and developmental terms will be crucial to a complete account of internalizing psychopathology. Important to the aims of this special issue, we address the feasibility of assessing these neurobehavioral constructs in children and adolescents in the clinic. Furthermore, we provide an empirical demonstration of this psychoneurometric approach in preschool-aged children.

DEFENSIVE REACTIVITY AND COGNITIVE CONTROL AS CORE NEUROBEHAVIORAL CONSTRUCTS OF RELEVANCE TO INTERNALIZING PROBLEMS

The emotional state of fear has been conceptualized in terms of reactivity of the brain's defensive motivational system, which functions to prime evasive action in the presence of threat cues (Davis, 1992; Fanselow, 1994; Lang, 1995; LeDoux, 1995). The idea of constitutional variations in general fearfulness is plausible from a biological-evolutionary perspective, insofar as tendencies toward greater versus lesser defensive reactivity have differing adaptive value across alternative environmental contexts (cf. Lykken, 1995). Individual differences in fear have been featured prominently in theories of temperament. Timidity (i.e., lack of approach and presence of withdrawal) in novel situations, as well as arousal in response to novel stimuli, and social reticence are central to Kagan's (1994) concept of behavioral inhibition in children, which he viewed as a risk factor for the development of anxiety disorders. Kochanska (1997) also emphasized variations in dispositional fear as an important moderator of the effect of socialization processes on conscience development (Kochanska, Gross, Lin, & Nichols, 2002).

Other theorists have focused on placing fear proneness within broader structural models of temperament, often as part of a higher order Negative Emotionality factor that typically also includes dispositional anger- and sadness-proneness (Shiner, 1998). For example, Goldsmith and Campos (1982) characterized fearfulness as one of five basic dimensions of temperament, and Buss and Plomin (1984) identified fear proneness as one of two basic trait expressions of negative emotional reactivity (the other being anger) that emerge within the 1st year of life.

The content domain of dispositional fear, and the extent to which it has primarily been treated as a lower order manifestation of a more general distress-proneness dimension (Negative Emotionality [NE]), or alternatively in the form of narrower constructs such as behavioral inhibition (BI) or shyness, has varied somewhat in the literature. Various models derived from parent-report methods have emphasized differing manifestations of trait fear within the broader domain of NE (e.g., specific fears of situations or animals vs. social anxiety/social reticence); thus, each may be emphasizing somewhat different components of a broader dispositional fear construct. However, even conceptions that focus on narrower constructs, such as BI or shyness, appear to represent complex configurations of traits. BI includes elements of both high NE and low positive emotionality (Laptook et al., 2008), and shy behavior can reflect high anxiety (social-evaluative shyness), isolation emerging from peer rejection, or low social interest (Asendorpf, 1993). To provide a more coherent target for linkage with neurobiological constructs, it will be important to understand the nature and structure of dimensions underlying fear proneness, taking into account developmentally appropriate manifestations of fear.

It remains to be seen whether parsing the construct of trait fear into these lower order traits will result in greater predictive validity to distinct neurophysiological indices or improved discriminant validity with respect to differing internalizing disorders. Evidence from structural analyses of internalizing disorder diagnoses and symptoms in youngsters (Higa-McMillan, Smith, Chorpita, & Hayashi, 2008; Lahey et al., 2008) generally supports the distinction between "fear" and "distress" disorders documented in the adult literature (e.g., Krueger, 1999; Watson, 2005). The evidence for this distinction across ages suggests that elements of worry and perhaps shyness and social-evaluative concerns may cluster together with depressive disorders and generalized anxiety disorder, whereas other fearful tendencies such as physical caution and object fear may relate more strongly to phobic disorders.

Regarding the concept of cognitive control, theorists since the earliest days of psychology have recognized a broad dimension of human variation encompassing tendencies toward behavioral restraint versus disinhibition. William James (1890) noted in his classic *Principles of Psychology* that "there is a type of character in which impulses seem to discharge so promptly into movements that inhibitions get no time to arise" (p. 1144). Along similar lines, contemporary theorists in the domains of personality and psychopathology have identified individual difference constructs ranging from "ego control" (Block & Block, 1980) to "constraint" (Tellegen, 1985) to "novelty seeking" (Cloninger, 1987) to "syndromes of disinhibition" (Gorenstein & Newman, 1980). The concept of behavioral restraint versus impulsivity is also featured prominently in developmental theories of temperament (e.g., Buss & Plomin, 1975; Kochanska, 1997; Rothbart & Ahadi, 1994).

In adults, low cognitive control has been considered in theories of both internalizing and externalizing, that is, as a factor contributing to difficulty inhibiting impulses and overlearned responses, including tendencies toward aggression and impulsivity, and to negative emotional dysregulation characteristic of internalizing (Carver, Johnson, & Joormann, 2008). In youth, low levels of cognitive control have been repeatedly associated with externalizing problem behavior, and in some studies to internalizing (e.g., Eisenberg et al., 2009). The link between internalizing and cognitive control in children is less clear, however. As in adults, high cognitive control may enable children to effectively regulate negative emotion, thus reducing internalizing risk. Alternatively, given links between high effortful control and tendencies toward guilt/shame in children (Rothbart, Ahadi, & Hershey, 1994) high cognitive control may in fact predispose to internalizing problems during some periods in development.

In addition, the relationship of cognitive control to internalizing may vary as a function of fear proneness at certain points in development. For example, neurobehavioral models suggest that protracted development of neural capacity for cognitive control may couple with peripubertal increases in neural sensitivity to fear to increase risk for internalizing problems at the transition to adolescence (Casey et al., 2010). This is supported by work showing that low effortful control interacts with high fear proneness to predict internalizing symptoms in late childhood/early adolescence (Muris, Meesters, & Blijlevens, 2007; Oldehinkel, Hartman, Ferdinand, Verhulst, & Ormel, 2007).

BEHAVIORAL ASSESSMENT OF DEFENSIVE REACTIVITY AND COGNITIVE CONTROL

Laboratory task paradigms may be particularly useful for formulating bottom-up models of core mechanisms underlying variations in defensive reactivity/fear proneness. Laboratory methods have significant incremental advantages beyond parent report measures (Durbin, 2010) because (a) they circumvent biases in parent report associated with parental psychopathology (e.g., Durbin & Wilson, 2012; Richters, 1992); (b) they circumvent limitations in parental knowledge/awareness of children's fearful tendencies (e.g., due to constraints on observation resulting from parents' tendency to keep children away from threatening stimuli); and (c) they define constructs of interest at the level of specific observable patterns of behavior (rather than inferences about subjective state), allowing for closer comparison with constructs assessed in the animal literature such as freezing, withdrawal, and exploration. Thus, they provide an important link to neuroscience on the biological bases of fearful temperament in other animals.

Existing research utilizing batteries of laboratory tasks (e.g., Durbin, 2010; Durbin, Hayden, Klein, & Olino, 2007; Durbin, Klein, Hayden, Buckley, & Moerk, 2005; Hayden, Klein, Durbin, & Olino, 2006; Olino, Klein, Dyson, Rose, & Durbin, 2010) has covered a range of manifestations of traits related to fear/fearlessness and inhibitory control. Tasks used for assessing fear proneness include contact-with-stranger tasks, performance tasks involving presentation of negative feedback or in which concerns about social scrutiny are heightened, exposure to typically fear-eliciting stimuli (e.g., scary objects, animals) or ambiguous/novel stimuli, or instructed engagement in acts that tend to elicit physical caution (such as walking across a balance beam). Procedures for assessing inhibitory control include tasks involving turn-taking, delay of gratification, and temptation to engage in impulsive behavior. Individual differences in responses within these tasks have been linked to teacher- and parent-reported internalizing and externalizing problems (Dougherty et al., 2011; Hayden, Klein, & Durbin, 2005), and family history of mood disorders (Durbin et al., 2005; Olino et al., 2010). Other researchers have employed tasks focusing on motor slowing, inhibition of dominant behaviors, and patience in response to delays as indicators of effortful control (e.g., Kochanksa, Murray, Jacques, Koenig, & Vandegeest, 1996), or measures from cognitive psychology designed to tap executive functioning skills (e.g., Diamond & Taylor, 1996; Hongwanishkul, Happaney, Lee, & Zelazo, 2005).

Lab measures of fear proneness in preschoolers have been linked to familial risk for internalizing disorders (e.g., Olino et al., 2010), child anxiety disorders (e.g., Dougherty et al., 2011), and genetic polymorphisms (Hayden et al., 2007). Moreover, laboratory research on dispositional fear (e.g., Dyson, Olino, Durbin, Goldsmith, & Klein, 2012) indicates that this construct is differentiable from individual differences in other negative emotions. The use of laboratory tasks is also helpful for defining narrower fear phenotypes that may have differential associations with neurobiological or psychopathological constructs.

NEUROPHYSIOLOGICAL ASSESSMENT OF DEFENSIVE REACTIVITY AND COGNITIVE CONTROL

Extant research provides a strong base for incorporating neurophysiological measures of defensive reactivity and cognitive control into the study of internalizing psychopathology across development. Fear-potentiated startle and right-sided asymmetric brain activation are well-documented indices of dispositional defensive reactivity. The error-related negativity component of the human event-related potential, on the other hand, appears to provide a reliable index of individual differences in cognitive control processes relevant to learning and performance.

Fear-Potentiated Startle (FPS)

FPS, defined as the potentiation of the startle eyeblink reflex during aversive stimulation, is thought to index activity of the brain's defensive motivational system (Lang, Bradley, & Cuthbert, 1990, 1997). A substantial body of animal research demonstrates that startle potentiation is mediated by the brain's fear/defense circuit, centered in the amygdala (Davis, 2000; Davis, Antoniadis, Amaral, & Winslow, 2008; LeDoux & Schiller, 2009). In humans, FPS is reliably observed during exposure to a range of aversive stimuli, including images of unpleasant scenes such as those involving threat to oneself or injury to others (Bradley, Codispoti, Cuthbert, & Lang, 2001). As in animals, aversive visual cuing is known to elicit activation of the brain's fear/defense circuit, including the amygdala (Sabatinelli, Bradley, Fitzsimmons, & Lang, 2005), and it is this circuitry activation that is theorized to potentiate the startle reflex (Lang et al., 1990). Consistent with the conceptualization of FPS as an index of defensive reactivity, enhanced FPS has been demonstrated in adolescents at risk for anxiety disorders (Grillon, Dierker, & Merikangas, 1998), adult phobic patients (McTeague & Lang, 2012), and individuals high on scale measures of trait fear (Vaidyanathan, Patrick, & Bernat, 2009).

Elicitation of FPS in young children (<10 years) has been inconsistent, primarily because of problems identifying age-appropriate stimuli. Children also have smaller muscles around their eyes that can lead to poor signal strength, and retention of data can be challenging because of excessive movement artifacts and noncompliance with task procedures that are more common in children (Balaban & Berg, 2007). In response to these concerns, Quevedo, Smith, Donzella, Schunk, and Gunnar (2010) developed a task using child appropriate film clips that was successful in producing comparable FPS across a wide age range of individuals, from early childhood (3 years of age) to adulthood (*M* age 2 years). The film clips were chosen to be more engaging for the children and displayed child-centered content (e.g., Disney characters and themes). It is yet unclear whether FPS recorded in this task relates to internalizing psychopathology. Nonetheless, existing data support the utility of FPS as a measure of defensive reactivity with relevance for the expression of internalizing across the lifespan.

Resting EEG Asymmetry

Right-lateralized brain activation, measured by resting electroencephalogram (EEG) activity, has also been implicated as an index of defensive reactivity across the lifespan. Right parietal regions are involved in vigilance and threat detection (Compton et al., 2003; Corbetta & Shulman, 2002), and enhanced right versus left parietal activation has been linked to individual differences in fear proneness (indexed behaviorally) in children. Likewise, enhanced right parietal activity appears to characterize adults high in fear-related symptoms (Nitschke, Heller, Palmieri, & Miller, 1999). Thus, across the lifespan, right-lateralized parietal brain activation operates as an indicator of defensive reactivity.

Error-Related Negativity (ERN)

Cognitive control involves engagement of processes in frontal brain regions (Miller & Cohen, 2001), including the anterior cingulate cortex, which has been found to signal conflict from competing response options and errors to coordinate a distributed frontal network for cognitive control implementation, thereby optimizing the flexible adjustment of behavior (Botvinick, 2007; Ridderinkhof, Ullsperger, Crone, & Nieuwenhuis, 2004). Brain event-related potential (ERP) studies have identified the ERN as a robust marker of anterior cingulate cortex–mediated cognitive control processes invoked by performance errors (Holroyd & Coles, 2002; Yeung, Botvinick, & Cohen, 2004). The ERN is clearly evident in adolescents as well as adults (Davies, Segalowitz, & Gavin, 2004) and, more recently, has been observed in young children (i.e., ages 5–11; Kim, Iwaki, Imashioya, Uno, & Fujita, 2007; Torpey, Hajcak, Kim, Kujawa, & Klein, 2012; Wiersema, van der Meere, & Roeyers, 2007). The ERN thus represents a neurophysiological marker of cognitive control across development.

Enhanced ERN characterizes both anxious children (i.e., age 8–17; Hajcak, Franklin, Foa, & Simons, 2008; Ladouceur, Dahl, Birmaher, Axelson, & Ryan, 2006) and adults (Olvet & Hajcak, 2008), suggesting exaggerated neurophysiologic-mediated cognitive control functions. Of importance, however, recent work suggests that the association between the ERN and internalizing may change across development. Specifically, Meyer, Weinberg, Klein, and Hajcak (2012) demonstrated, as in adults, enhanced ERN for anxious versus nonanxious older children (11–13 years), whereas somewhat smaller ERN was evident for anxious versus nonanxious younger children (8–10 years). In a recent follow-up study (Torpey et al., 2013), this research group showed that children even younger in age (6 years) characterized as highly fearful showed reduced ERN in comparison with typically developing less fearful peers. In turn, this finding of decreased cognitive control function as indexed by ERN in fearful children coincides with evidence from self-report research indicating that youth with internalizing problems are characterized by low cognitive/effortful control (e.g., Eisenberg et al., 2009).

This age-related change in the direction of association between ERN and internalizing may reflect differential developmental trajectories of defensive reactivity and cognitive control. As previously mentioned, neurobehavioral models suggest that protracted development of neural capacity for cognitive control may couple with peripubertal increases in neural sensitivity to fear to increase risk for internalizing problems at the transition to adolescence (Casey et al., 2010). Indeed, mean levels of cognitive/effortful control increase from adolescence to early adulthood (Donnellan, Conger, & Burzette, 2007; Roberts, Caspi, & Moffitt, 2001), whereas fearful tendencies, particularly in female individuals, tend to peak at peri-puberty (Durbin et al., under review), before cognitive/effortful control is fully developed. The observation of reduced ERN in highly fearful children is consistent with the possibility that weak cognitive control may increase proneness to anxiety in early development. By contrast, enhanced ERN in older anxious youth may reflect either a shift in core capacity for cognitive control (from lower to higher) or, alternatively, neurophysiologic compensation for insufficient capacity for cognitive control in anxious youth at later stages of development.

CLINICAL FEASIBILITY OF MEASURING NEUROBEHAVIORAL CONSTRUCTS OF RELEVANCE TO INTERNALIZING PSYCHOPATHOLOGY

Although we have argued for a multimethod approach to the assessment of internalizing problems using self- and informant-reports, behavioral observation, and neurophysiology (e.g., FPS & EEG/ERP), we acknowledge the barriers to employing such a battery of tests. In particular, the costs associated with collecting neurophysiological data include purchase and maintenance of recording equipment and time and expenses for training in appropriate use. However, purchase prices for neurophysiological data collection systems have decreased in recent years, and cost-effective systems are readily available from several companies such as BIOPAC and Emotiv. Many such systems do not require specially shielded rooms and can thus yield quality data in a variety of settings. In fact, recent efforts have been devoted to creating low-cost systems suitable for recording neurophysiology in various real-world settings, including ambulatory systems for monitoring activity while walking outdoors (Debener, Minow, Emkes, Gandras, & Vos, 2012). The technology is thus becoming more affordable and more flexible for application in clinical settings.

Of importance, recording of measures such as FPS, resting EEG asymmetry, and ERN can also be achieved quite efficiently. Recording FPS involves application of only two electrodes beneath one eye (Blumenthal et al., 2005). EEG asymmetry and ERN can be recorded with just two lateral/parietal scalp electrodes (P3 and P4; e.g., Nitschke et al., 1999) and one fronto-central electrode (FCz; e.g., Weinberg, Olvet, & Hajcak, 2010), accompanied by a small number of other additional reference electrodes for electrical grounding and artifact detection purposes. With electrode positioning provided by a spandex or stretch-lycra cap, recording these three measures could be done at a low cost and with minimal setup time. Two desktop computers or laptops—one for stimulus presentation and another for data collection—would be required and could be stationed in a single room or two adjacent rooms. These computers could also be placed on rollaway carts to provide for recording in alternative locations, with easy storage when not in use. With this straightforward system, only one clinician or support staff member would be needed to conduct the assessment.

Collecting neurophysiological data is also quite noninvasive and generally well tolerated by patients across the lifespan, as evidenced by the exponential increase in psychopathology studies examining neurophysiology over the past several decades. These attributes also make EEG/ERP data collection more feasible for clinicians. EEG is already commonly collected in hospitals for testing seizure-related conditions and may serve as a natural bridge to using such methods with mental health patients. In fact, EEG/ERP has been utilized extensively in some of the most complex clinical cases, including paralyzed and "locked-in" patients, to provide such patients with a means for communicating through brain–computer interfaces (e.g., Birbaumer, 2006). With respect to internalizing problems in particular, there is a wealth of data, previously reviewed, to suggest that EEG/ERP and FPS measures are clinically feasible with this population across the lifespan.

With regard to behavioral observations, assessments of this type are already commonly utilized by clinicians engaged in parent training and family therapy, as well as in some assessment contexts (such as classroom observations or exposure-based treatments for social anxiety). Many emotionally evocative lab tasks could easily be conducted within a clinical setting, as most do not require expensive equipment or additional personnel. For example, social-evaluative concerns can be elicited readily using performance tasks employing simple stimuli (such as games, puzzles, or cognitive tasks). Individual differences in cognitive control can be assessed using delay tasks and simple games such as Simon Says that are easily administered in an individual or group therapy session. We anticipate that future clinicians will have neurophysiological and behavioral observation methods more readily at their disposal to help advance assessment and treatment of internalizing problems across development.

Translating this model to intervention, the aforementioned neurobehavioral traits would serve as the targets for treatment rather than broad and heterogeneous diagnostic categories. Treatment would thus become transdiagnostic in nature, with applications to a range of individuals suffering from internalizing-related problems. Because our approach is multimethod, treatment response would not be constrained to diagnostic status but, rather, would be indexed by changes across self-report, neurophysiology, and behavior. Our dimensional approach also allows for interventions to be preventative for those at risk as well as ameliorative for those suffering from active impairments.

Treatments targeting core mechanisms already exist for internalizing psychopathology. For instance, attention bias modification procedures that direct attention to emotionally neutral versus threatening stimuli have been developed for internalizing problems such as social phobia (e.g., Amir et al., 2009). However, rather than applying modification procedures based on diagnostic status, our approach suggests that individuals could be selected into treatment at differing extremes along the dimension of defensive reactivity. We also suggest that FPS, rather than self-report, could be used to determine the most fear-evoking visual or imaginal cues for use in vivo or imaginal exposure exercises with individuals high in defensive reactivity, for example, in a computerized habituation procedure using images from the International Affective Picture System (Lang, Bradley, & Cuthbert, 1999). Changes across all measures of defensive reactivity—FPS, EEG asymmetry, self-report, and behavior—could then be tracked as indicators of treatment success.

As for cognitive control, cognitive training/remediation programs designed to improve cognitive functions and reduce symptoms would be natural interventions to use to target our neurobehavioral trait constructs. For example, Siegle, Ghinassi, and Thase (2007) demonstrated the promise of cognitive training in depression; following from this, our focus would be on selecting individuals based on neurobehavioral cognitive-control metrics rather than diagnosis. Similar sorts of cognitive training paradigms have recently been suggested for anxiety-related problems, with some specifically targeting error-related processes (Sylvester et al., 2012), which can be operationalized using ERN. Finally, better understanding the normative development of these neurobehavioral constructs would help to identify critical periods of development in which intervention or prevention strategies can produce optimal impact on these dispositions and affiliated risk for internalizing problems.

EMPIRICAL DEMONSTRATION

In this next section, we present pilot data from a collaborative project involving three of the four authors (JSM, CED, CJP) in which we have begun to apply the psychoneurometric approach to the study of internalizing psychopathology in preschool-aged children (ages 3–7). Our focus on young children is motivated by the importance of identifying core liabilities relevant to internalizing psychopathology prior to the onset of manifest disorder so as to distinguish between processes that are etiologically relevant (i.e., causes) and those that are the outcome of emergent psychopathology. This distinction is critical for theoretical models of the role of these trait processes in the development of risk. However, even dimensions that reflect outcomes of pathological processes (rather than their causes) may still be useful targets for treatment. Second, our model presumes that behavioral measures may provide closer phenotypic targets for neurophysiological measures (as compared to questionnaires), and empirical research on child temperament has produced a range of laboratory methods for eliciting and assessing individual differences in behaviors reflecting fear proneness and cognitive control. Many of these methods focus on the identification of behavioral phenotypes similar to those employed in the animal literature (e.g., freezing as an index of fear). By contrast, such measures are largely lacking for adolescents and adults. Thus, for both theoretical and methodological reasons, we believe that early developmental periods can serve as an important starting point and continuing referent for work of this kind. However, the real power of this approach will be revealed to the extent that it can be applied in future studies across the lifespan.

Sample

Children and their parents undergo extensive diagnostic, psychometric, observational, and neurophysiologic assessments as part of a larger ongoing project examining the development and familial transmission of anxiety and depressive problems. We focus here on associations between neurophysiological measures and behavioral lab task and self-report measures showing the most promise in the children. Thirty-one children (13 female; *M* age = 5.73 years, *SD* = 1.38) completed at least one of the neurophysiological tasks and had data available from the laboratory behavioral assessment. Most children (91.3%) came from families with annual household incomes equal to or less $60,000. Most mothers (66.7%) had an associates degree or less, and most fathers (56.3%) had attended some college or less. Data submitted to each analysis were from a subset of the total sample, as some data were lost due to of excessive artifacts, poor behavioral performance on the ERN task, or because the child did not complete one of the neurophysiological tasks (e.g., time constraints, task not yet available). Thus, sample sizes vary for the differing associations reported on next. Significant as well and nonsignificant effects of moderate to large size are reported to illustrate the potential of our novel approach.

Laboratory Behavioral Assessment

We employed a battery of 15 tasks designed to tap individual differences in defensive reactivity, cognitive control, and near-neighbor constructs, drawn from prior investigations of child temperament (e.g., Durbin, 2010; Durbin et al., 2007; Durbin et al., 2005) or specifically designed for this study. Tasks were selected because they have been shown to be sensitive to risk for internalizing disorders (Durbin et al., 2005), capable of assessing stable elements of these traits (Durbin et al., 2007), or (for new tasks) because of their theoretical relevance to the constructs of interest. For example, fear-eliciting tasks included contact with a stranger, performance procedures involving receipt of negative feedback or heightened social scrutiny concerns, exposure to typically fear-eliciting stimuli (e.g., scary objects, animals, ambiguous stimuli), and instructed engagement in acts that elicit physical caution, such as walking across a balance beam. Trained raters coded each task for every instance of facial, vocal, and bodily indicators of fear; these were weighted by their intensity (low, moderate, high) and summed, and an overall composite was computed as the weighted sum across all 15 tasks. Prior studies using this coding scheme (Durbin, 2010; Durbin et al., 2007; Durbin et al., 2005) have demonstrated good to excellent interrater reliability for traits assessed using this approach.

Further evidence for the value of these behavioral measures comes from data demonstrating their effectiveness in predicting later emergence of internalizing problems in a sample of 70 children aged 3 to 6½. Lab-assessed fear proneness was measured at baseline, and mothers completed Child Behavior Checklist (CBCL) ratings 6 months later. Baseline fear proneness in response to the lab tasks predicted higher CBCL anxious/depressed scores at 6-month follow-up ($r = .32$, $p < .01$). This effect was significant and of similar magnitude across a variety of methods for quantifying internalizing problems based on CBCL ratings (i.e., withdrawn/depressed: $r = .31$, $p < .01$; *DSM* anxiety scale: $r = .42$, $p < .001$; Internalizing: $r = .31$, $p < .01$). Moreover, in a hierarchical regression analysis, lab-assessed fear proneness (entered in the second step) remained a significant predictor of CBCL anxious/depressed scores at 6-month follow-up after controlling for baseline CBCL scores ($p < .05$; entered in the first step of the regression).

FPS

Based on difficulties with eliciting FPS in children using still visual images, as previously reviewed, we used the Quevedo et al. (2010) study as the basis for selecting 12 film clips (four pleasant, four unpleasant, four neutral) developed in our laboratory for use with children in this age range as affective foreground stimuli. Film clips were drawn from a range of live actor and cartoon movies produced for children and adolescents (e.g., *Harry Potter, The Incredibles*). Each film clip lasted approximately 1 min, during which time white noise bursts were presented through headphones at random points. The startle blink response was recorded from under the left eye, time-locked to the presentation of the noise bursts. The difference in startle response elicited by negative as compared to neutral film clips served as the primary FPS measure of interest.

Resting EEG Asymmetry

EEG was recorded during four consecutive 1-min periods of rest, alternating between eyes open and eyes closed (Towers & Allen, 2009). Parietal alpha asymmetry scores reflecting relative power of activity within the alpha frequency band over left versus right recording sites were extracted. Lower alpha values are indicative of greater relative brain activity; thus, in what follows, higher asymmetry scores reflect greater right-sided activation (Shankman et al., 2011).

ERN

The ERN was measured using a developmentally appropriate version of the Eriksen flanker task (Eriksen & Eriksen, 1974), known as the "fish" flanker task (Rueda, Posner, Rothbart, & Davis-Stober, 2004), in which stimuli consisted of yellow cartoon fish swimming to the left and right on a blue, ocean-like background. Analyses of the ERN focused on 5- to 7-year-olds because younger children have difficulty performing the task successfully. Children were instructed to respond to the central target stimulus while ignoring flanking stimuli as quickly and as accurately as possible. The ERN was then extracted from EEG activity over the fronto-central recording sites time-locked to the execution of an incorrect response.

Questionnaires

To index traits and symptoms relevant to internalizing psychopathology, we administered the informant-based Child Behavior Questionnaire (CBQ; Rothbart, Ahadi, Hershey, & Fisher, 2001) and Child Behavior Checklist (CBCL; Achenbach & Rescorla, 2009) to parents; mother-reports are the focus of analyses reported here, as fewer fathers returned these measures. CBQ scales have demonstrated adequate internal consistency and good test–retest reliability (Rothbart et al., 2001). For purposes of the current presentation, we report results from the Fear scale of the CBQ and the Anxiety/Depression scale from the CBCL. The CBCL in particular has received significant empirical attention, and it is also commonly used in practice. For these reasons, we demonstrate its relationship to neurophysiological and behavioral lab task indicators that have real potential to be implemented in the clinical context.

Results

Table 1 displays preliminary findings from our lab-based assessment battery. Although nonsignificant due to small sample size, the relationship between individual differences in fear proneness as assessed by lab tasks and by FPS was in the predicted direction and of moderate magnitude. Likewise, associations between the CBQ fear score and CBCL anxious/depressed scores and FPS were nonsignificant but in the expected direction and of comparable size. All correlations indicated that higher fear behaviors were associated with larger FPS magnitude.

TABLE 1
Associations Between Neural and Behavioral Measures in The Pilot Study

	ASYM	*ERN*	*Lab*	*CBQ*	*CBCL*
FPS	.13 (13)	.30 (6)	.31 (10)	.38 (17)	.34 (17)
ASYM		.73* (9)	.37 (12)	.52* (15)	.38 (15)
ERN			.60* (13)	.22 (10)	.40 (10)
Lab				.12 (15)	.05 (15)
CBQ					.23 (24)
CBCL					

Note: Sample sizes are presented within parentheses. FPS = Fear Potentiated Startle; ASYM = Parietal asymmetry; ERN = Error-Related Negativity; Lab = Behavioral laboratory assessment; CBQ = Child Behavior Questionnaire; CBCL = Child Behavior Checklist.
*$p < .05$.

The association between lab-assessed fear proneness and right parietal asymmetry score was in the expected direction and of moderate magnitude, suggesting that greater right parietal activity was associated with higher fear behaviors. The association between CBQ fear score and right parietal asymmetry was also in the expected direction, statistically significant, and represents a large effect. Similarly, the association between the CBCL indicator of anxious and depressive psychopathology was in the expected direction, and of moderate magnitude. All relationships confirm that fear- and anxiety-related traits and symptoms are associated with overactive right parietal resting activation.

The association between individual differences in lab-assessed fear proneness and ERN amplitude was in the expected direction, statistically significant, and large, indicating smaller ERN response for high versus low fear children. (The ERN is a negative going ERP component and thus a positive association indicates a negative relationship.) The association between ERN amplitude and the CBQ fear score was, on the other hand, nonsignificant and small. The ERN's relationship to the CBCL indicator of anxious and depressive symptoms was in the expected direction and moderate in size. All of these correlations indicated that children exhibiting higher fear and greater internalizing tendencies were characterized by reduced cognitive control function.

Across neurophysiological measures, smaller ERN was strongly associated with greater right parietal asymmetry scores. Smaller ERN was also moderately associated with FPS. Thus, the neurophysiologic indicator of cognitive control—ERN—covaried with both of the two neurophysiologic indicators of defensive reactivity suggesting that reduced frontal control function was associated with enhanced defensive reactivity. Of interest, however, the two proposed indicators of defensive reactivity—FPS and right parietal asymmetry—were only modestly associated with one another.

Together, the current preliminary findings provide an effective illustration of how neurobehavioral constructs relevant to internalizing-related problems can be assessed across domains of behavior, physiology, and informant report. Although many of the effects were nonsignificant due to small sample size, the magnitude and direction of the effects are promising, especially given that most of the reported relationships span measurement domains (e.g., behavioral observation and neurophysiology), and thus are expectedly modest because of inherent issues related to method variance. Our aim for this ongoing work is to substantially expand the sample to enhance power for detecting the predicted associations thereby allowing us to more fully realize the promise of our psychoneurometric approach. Specifically, we will evaluate how composites of neurophysiological measures can be assembled to improve convergence with behavioral measures and informant report. Moreover, we will examine how neurophysiological measures can be combined with behavioral and informant measures to enhance prediction across domains, and potentially to improve prospective prediction of internalizing symptoms (see Patrick et al., 2012, and Patrick et al., 2013, for more fully developed examples applied to adult externalizing problems). Future data collection in our lab will continue to focus on determining the predictive validity of these early measurements, and, in particular, to evaluate the predictive validity of the neurophysiological measures and their incremental validity relative to lab-task or parent-report measures alone.

SUMMARY AND CONCLUDING REMARKS

In acknowledging the need to advance assessment and treatment of internalizing psychopathology for our youth, we have proposed a psychoneurometric approach the objective of which is to integrate information across behavioral, neurophysiological, and self-report assessments. This tactic has a number of notable features. First, it addresses the issue of diagnostic comorbidity by focusing on broad dispositional variables that differing disorders share. Second, it addresses the conceptual gap between diagnostic phenotypes and biological systems by placing investigative emphasis on neurobehavioral trait constructs rather than disorders. Finally, it provides a two-way path along which behavioral conceptions can guide efforts to identify clinically relevant neurobiological circuits or processes and reciprocally along which knowledge gained about relevant neurobiological circuits/processes can feed back into behavioral conceptions of clinical disorders.

To realize the promise of this approach, moderate to large sample studies will be needed to establish reliable neurobehavioral indicators of constructs such as defensive reactivity and cognitive control with relevance to internalizing psychopathology. For reasons of practicality, we encourage the use of lower cost, less invasive technologies such as EEG/ERP or visceral–somatic measures (e.g., skin conductance, startle blink) that are widely accessible to investigators in the field. Such methods are more likely to be implemented in clinical contexts as well. Regarding treatment implications, in particular, our approach provides a framework for generating and testing more targeted interventions aimed at addressing underlying mechanisms directly, in contrast to relying on extant treatment packages for diffuse disorder categories.

In closing, we emphasize that the methodological approach we proposed is intended as a complement to, rather as a substitute for, other available research strategies. Specifically, we view the psychoneurometric approach as a paradigm for linking clinical disorders to neurobehavioral systems, rather than as a prescription for a specific program of research. Although representing only one approach to the multimethod assessment of internalizing psychopathology in youth, we hope it can serve as a model for more fully appreciating our most common mental health problems.

REFERENCES

Achenbach, T., & Rescorla, L. (2009). Child Behavior Checklist (CBCL/1.5-5 and CBCL/6-18). In *Handbook of psychiatric measures* (pp. 296–301). Washington, DC: American Psychiatric Publications.

Amir, N., Beard, C., Taylor, C. T., Klumpp, H., Elias, J., Burns, M., & Chen, X. (2009). Attention training in individuals with generalized social phobia: A randomized controlled trial. *Journal of Consulting and Clinical Psychology, 77*, 961.

Asendorpf, J. B. (1993). Abnormal shyness in children. *Journal of Child Psychology and Psychiatry, 34*, 1069–1083.

Balaban, M. T., & Berg, W. K. (2007). Measuring the electromyographic response: Development issues and findings. In L. A. S. McMaster & S. J. S. Brock (Eds.), *Developmental psychophysiology theory, systems and methods* (pp. 257–285). Cambridge, UK: Cambridge University Press.

Beesdo, K., Knappe, S., & Pine, D. S. (2009). Anxiety and anxiety disorders in children and adolescents: developmental issues and implications for *DSM–V. The Psychiatric Clinics of North America, 32*, 483.

Beidel, D. C. (1991). Social phobia and overanxious disorder in school-age children. *Journal of the American Academy of Child & Adolescent Psychiatry, 30*, 545–552.

Birbaumer, N. (2006). Breaking the silence: Brain–computer interfaces (BCI) for communication and motor control. *Psychophysiology, 43*, 517–532.

Birmaher, B., Ryan, N. D., Williamson, D. E., Brent, D. A., Kaufman, J., Dahl, R. E., & Nelson, B. (1996). Childhood and adolescent depression: A review of the past 10 years. Part I. *Journal of the American Academy of Child & Adolescent Psychiatry, 35*, 1427–1439.

Block, J., & Block, J. H. (1980). The role of ego-resiliency and ego-control in the organization of behavior. In W. A. Collins (Ed.), *Minnesota Symposium on Child Psychology* (Vol. 13, pp. 39–101). Hillsdale, NJ: Erlbaum.

Blumenthal, T. D., Cuthbert, B. N., Filion, D. L., Hackley, S., Lipp, O. V., & Van Boxtel, A. (2005). Committee report: Guidelines for human startle eyeblink electromyographic studies. *Psychophysiology, 42*, 1–15.

Botvinick, M. M. (2007). Conflict monitoring and decision making: reconciling two perspectives on anterior cingulate function. *Cognitive, Affective, & Behavioral Neuroscience, 7*, 356–366.

Bradley, M. M., Codispoti, M., Cuthbert, B. N., & Lang, P. J. (2001). Emotion and motivation I: defensive and appetitive reactions in picture processing. *Emotion, 1*, 276.

Buss, A. H., & Plomin, R. (1975). *A temperament theory of personality development*. New York, NY: Wiley.

Buss, A. H., & Plomin, R. (1984). *Temperament: Early developing personality traits*. Hillsdale, NJ: Erlbaum.

Carver, C. S., Johnson, S. L., & Joormann, J. (2008). Serotonergic function, two-mode models of self-regulation, and vulnerability to depression: What depression has in common with impulsive aggression. *Psychological Bulletin, 134*, 912.

Casey, B., Jones, R. M., Levita, L., Libby, V., Pattwell, S. S., Ruberry, E. J., & Somerville, L. H. (2010). The storm and stress of adolescence: Insights from human imaging and mouse genetics. *Developmental Psychobiology, 52*, 225–235.

Cloninger, C. R. (1987). A systematic method for clinical description and classification of personality variants. *Archives of General Psychiatry, 44*, 573–588.

Compton, R. J., Banich, M. T., Mohanty, A., Milham, M. P., Herrington, J., Miller, G. A., & Heller, W. (2003). Paying attention to emotion: An fMRI investigation of cognitive and emotional Stroop tasks. *Cognitive, Affective, & Behavioral Neuroscience, 3*, 81–96.

Corbetta, M., & Shulman, G. L. (2002). Control of goal-directed and stimulus-driven attention in the brain. *Nature Reviews Neuroscience, 3*, 201–215.

Costello, E. J., Mustillo, S., Erkanli, A., Keeler, G., & Angold, A. (2003). Prevalence and development of psychiatric disorders in childhood and adolescence. *Archives of General Psychiatry, 60*, 837.

Cuthbert, B. N., & Insel, T. R. (2010). Toward new approaches to psychotic disorders: The NIMH Research Domain Criteria project. *Schizophrenia Bulletin, 36*, 1061–1062.

Davies, P. L., Segalowitz, S. J., & Gavin, W. J. (2004). Development of response-monitoring ERPs in 7-to 25-year-olds. *Developmental Neuropsychology, 25*, 355–376.

Davis, M. (1992). The role of amygdala in conditioned fear. In J. Aggleton (Ed.), *The amygdala: Neurobiological aspects of emotion, memory and mental dysfunction* (pp. 255–305). New York, NY: Wiley.

Davis, M. (2000). The role of the amygdala in conditioned and unconditioned fear and anxiety. In J. Aggleton (Ed.), *The amygdala: A functional analysis* (Vol. 2, pp. 213–287). Oxford, UK: Oxford University Press.

Davis, M., Antoniadis, E. A., Amaral, D. G., & Winslow, J. T. (2008). Acoustic startle reflex in rhesus monkeys: a review. *Reviews in the Neurosciences, 19*, 171–186.

Debener, S., Minow, F., Emkes, R., Gandras, K., & Vos, M. (2012). How about taking a low-cost, small, and wireless EEG for a walk? *Psychophysiology, 49*, 1617–1621.

Diamond, A., & Taylor, C. (1996). Development of an aspect of effortful control: Development of the abilities to remember what I said and to "Do as I say, not as I do". *Developmental Psychobiology, 29*, 315–334.

Donnellan, M. B., Conger, R. D., & Burzette, R. G. (2007). Personality development from late adolescence to young adulthood: Differential stability, normative maturity, and evidence for the maturity-stability hypothesis. *Journal of Personality, 75*, 237–264.

Dougherty, L. R., Bufferd, S. J., Carlson, G. A., Dyson, M., Olino, T. M., Durbin, C. E., & Klein, D. N. (2011). Preschoolers' observed temperament and psychiatric disorders assessed with a parent diagnostic interview. *Journal of Clinical Child & Adolescent Psychology, 40*, 295–306.

Durbin, C. E. (2010). Modeling temperamental risk for depression using developmentally sensitive laboratory paradigms. *Child Development Perspectives, 4*, 168–173.

Durbin, C. E., Hayden, E. P., Klein, D. N., & Olino, T. M. (2007). Stability of laboratory-assessed temperamental emotionality traits from ages 3 to 7. *Emotion, 7*, 388.

Durbin, C. E., Hicks, B. M., Blonigen, D. M., Johnson, W., Iacono, W. G., & McGue, M. (under review). *Personality trait change across late childhood to young adulthood: Evidence for nonlinearity and sex differences in change*. Manuscript under review.

Durbin, C. E., Klein, D. N., Hayden, E. P., Buckley, M. E., & Moerk, K. C. (2005). Temperamental emotionality in preschoolers and parental mood disorders. *Journal of Abnormal Psychology, 114*, 28.

Durbin, C. E., & Wilson, S. (2012). Convergent validity of and bias in parent reports of child emotion. *Psychological Assessment, 24*, 647–660.

Dyson, M. W., Olino, T. M., Durbin, C. E., Goldsmith, H. H., & Klein, D. N. (2012). The structure of temperament in preschoolers: A two-stage factor analytic approach. *Emotion, 12*, 44.

Eisenberg, N., Valiente, C., Spinrad, T. L., Cumberland, A., Liew, J., Reiser, M., & Losoya, S. H. (2009). Longitudinal relations of children's effortful control, impulsivity, and negative emotionality to their externalizing, internalizing, and co-occurring behavior problems. *Developmental Psychology, 45*, 988.

Eriksen, B. A., & Eriksen, C. W. (1974). Effects of noise letters upon the identification of a target letter in a nonsearch task. *Perception & Psychophysics, 16*, 143–149.

Fanselow, M. S. (1994). Neural organization of the defensive behavior system responsible for fear. *Psychonomic Bulletin & Review, 1*, 429–438.

Goldsmith, H. H., & Campos, J. J. (1982). Toward a theory of infant temperament. In R. N. Emde & R. J. Harmon (Eds.), *The development of attachment and affiliative systems* (pp. 161–193). New York, NY: Plenum.

Gorenstein, E. E., & Newman, J. P. (1980). Disinhibitory psychopathology: A new perspective and a model for research. *Psychological Review, 87*, 301.

Gould, M. S., King, R., Greenwald, S., Fisher, P., Schwab-Stone, M., Kramer, R., & Shaffer, D. (1998). Psychopathology associated with suicidal ideation and attempts among children and adolescents. *Journal of the American Academy of Child & Adolescent Psychiatry, 37*, 915–923.

Grillon, C., Dierker, L., & Merikangas, K. R. (1998). Fear-potentiated startle in adolescent offspring of parents with anxiety disordersf. *Biological Psychiatry, 44*, 990–997.

Hajcak, G., Franklin, M., Foa, E., & Simons, R. (2008). Increased error-related brain activity in pediatric obsessive-compulsive disorder before and after treatment. *American Journal of Psychiatry, 165*, 116–123.

Hayden, E. P., Dougherty, L. R., Maloney, B., Durbin, C. E., Olino, T. M., Nurnberger, J. I., Jr., & Klein, D. N. (2007). Temperamental fearfulness in childhood and the serotonin transporter promoter region polymorphism: A multimethod association study. *Psychiatric Genetics, 17*, 135–142.

Hayden, E. P., Klein, D. N., & Durbin, C. E. (2005). Parent reports and laboratory assessments of child temperament: A comparison of their associations with risk for depression and externalizing disorders. *Journal of Psychopathology and Behavioral Assessment, 27*, 89–100.

Hayden, E. P., Klein, D. N., Durbin, C. E., & Olino, T. M. (2006). Positive emotionality at age 3 predicts cognitive styles in 7-year-old children. *Development and Psychopathology, 18*, 409.

Higa-McMillan, C. K., Smith, R. L., Chorpita, B. F., & Hayashi, K. (2008). Common and unique factors associated with *DSM–IV–TR* internalizing disorders in children. *Journal of Abnormal Child Psychology, 36*, 1279–1288.

Holroyd, C. B., & Coles, M. G. (2002). The neural basis of human error processing: reinforcement learning, dopamine, and the error-related negativity. *Psychological Review, 109*, 679.

Hongwanishkul, D., Happaney, K. R., Lee, W. S., & Zelazo, P. D. (2005). Assessment of hot and cool executive function in young

children: Age-related changes and individual differences. *Developmental Neuropsychology, 28*, 617–644.
James, W. (1890). *Principles of psychology*. New York, NY: Holt.
Kagan, J. (1994). *Galen's prophecy: Temperament in human nature*. New York, NY: Basic Books.
Kessler, R. C., Chiu, W. T., Demler, O., & Walters, E. E. (2005). Prevalence, severity, and comorbidity of 12-month *DSM–IV* disorders in the National Comorbidity Survey Replication. *Archives of General Psychiatry, 62*, 617.
Kim, E. Y., Iwaki, N., Imashioya, H., Uno, H., & Fujita, T. (2007). Error-related negativity in a visual go/no-go task: Children vs. adults. *Developmental Neuropsychology, 31*, 181–191.
Kochanska, G. (1997). Multiple pathways to conscience for children with different temperaments: From toddlerhood to age 5. *Developmental Psychology, 33*, 228.
Kochanska, G., Gross, J. N., Lin, M. H., & Nichols, K. E. (2002). Guilt in young children: Development, determinants, and relations with a broader system of standards. *Child Development, 73*, 461–482.
Kochanska, G., Murray, K., Jacques, T. Y., Koenig, A. L., & Vandegeest, K. A. (1996). Inhibitory control in young children and its role in emerging internalization. *Child Development, 67*, 490–507.
Krueger, R. F. (1999). The structure of common mental disorders. *Archives of General Psychiatry, 56*, 921.
Ladouceur, C. D., Dahl, R. E., Birmaher, B., Axelson, D. A., & Ryan, N. D. (2006). Increased error-related negativity (ERN) in childhood anxiety disorders: ERP and source localization. *Journal of Child Psychology and Psychiatry, 47*, 1073–1082.
Lahey, B. B., Rathouz, P. J., Van Hulle, C., Urbano, R. C., Krueger, R. F., Applegate, B., & Waldman, I. D. (2008). Testing structural models of DSM–IV symptoms of common forms of child and adolescent psychopathology. *Journal of abnormal child psychology, 36*, 187–206.
Lang, P. J. (1995). The emotion probe: Studies of motivation and attention. *American Psychologist, 50*, 372.
Lang, P. J., Bradley, M. M., & Cuthbert, B. N. (1990). Emotion, attention, and the startle reflex. *Psychological Review, 97*, 377.
Lang, P. J., Bradley, M. M., & Cuthbert, B. N. (1997). Motivated attention: Affect, activation, and action. In P. J. Lang, R. Simons, & M. T. Balaban (Eds.), *Attention and orienting: Sensory and motivational processes* (pp. 97–135). Hillsdale, NJ: Erlbaum.
Lang, P. J., Bradley, M. M., & Cuthbert, B. N. (1999). *International affective picture system: Instruction manual and affective ratings* (Technical Support A-4). Gainsville, FL: The Center for Research in Psychophysiology, University of Florida.
Laptook, R. S., Klein, D. N., Durbin, C. E., Hayden, E. P., Olino, T. M., & Carlson, G. (2008). Differentiation between low positive affectivity and behavioral inhibition in preschool-age children: A comparison of behavioral approach in novel and non-novel contexts. *Personality and Individual Differences, 44*, 758–767.
LeDoux, J. E. (1995). Emotion: Clues from the brain. *Annual Review of Psychology, 46*, 209–235.
LeDoux, J. E., & Schiller, D. (2009). What animal fear models have taught us about human amygdala function? In P. J. Whalen & E. A. Phelps (Eds.), *The human amygdala* (pp. 43–60). New York, NY: Guilford.
Lewinsohn, P. M., Hops, H., Roberts, R. E., Seeley, J. R., & Andrews, J. A. (1993). Adolescent psychopathology: I. Prevalence and incidence of depression and other *DSM–III–R* disorders in high school students. *Journal of Abnormal Psychology, 102*, 133.
Lykken, D. T. (1995). *The antisocial personalities*. Mahwah, NJ: Erlbaum.
McTeague, L. M., & Lang, P. J. (2012). The anxiety spectrum and the reflex physiology of defense: from circumscribed fear to broad distress. *Depression and Anxiety, 29*, 264–281.
Meyer, A., Weinberg, A., Klein, D. N., & Hajcak, G. (2012). The development of the error-related negativity (ERN) and its relationship with anxiety: Evidence from 8 to 13 year-olds. *Developmental Cognitive Neuroscience, 2*(1), 152.
Miller, E. K., & Cohen, J. D. (2001). An integrative theory of prefrontal cortex function. *Annual Review of Neuroscience, 24*, 167–202.
Muris, P., Meesters, C., & Blijlevens, P. (2007). Self-reported reactive and regulative temperament in early adolescence: Relations to internalizing and externalizing problem behavior and "Big Three" personality factors. *Journal of Adolescence, 30*, 1035–1049.
Nitschke, J. B., Heller, W., Palmieri, P. A., & Miller, G. A. (1999). Contrasting patterns of brain activity in anxious apprehension and anxious arousal. *Psychophysiology, 36*, 628–637.
Oldehinkel, A. J., Hartman, C. A., Ferdinand, R. F., Verhulst, F. C., & Ormel, J. (2007). Effortful control as modifier of the association between negative emotionality and adolescents' mental health problems. *Development and Psychopathology, 19*, 523–539.
Olino, T. M., Klein, D. N., Dyson, M. W., Rose, S. A., & Durbin, C. E. (2010). Temperamental emotionality in preschool-aged children and depressive disorders in parents: Associations in a large community sample. *Journal of Abnormal Psychology, 119*, 468.
Olvet, D. M., & Hajcak, G. (2008). The error-related negativity (ERN) and psychopathology: Toward an endophenotype. *Clinical Psychology Review, 28*, 1343–1354.
Patrick, C. J., Durbin, C. E., & Moser, J. S. (2012). Reconceptualizing antisocial deviance in neurobehavioral terms. *Development and Psychopathology, 24*, 1047.
Patrick, C. J., Venables, N. C., Yancey, J. R., Hicks, B. M., Nelson, L. D., & Kramer, M. D. (2013). A construct-network approach to bridging diagnostic and physiological domains: Application to assessment of externalizing psychopathology. *Journal of Abnormal Psychology, 122*, 902.
Quevedo, K., Smith, T., Donzella, B., Schunk, E., & Gunnar, M. (2010). The startle response: Developmental effects and a paradigm for children and adults. *Developmental Psychobiology, 52*, 78–89.
Richters, J. E. (1992). Depressed mothers as informants about their children: a critical review of the evidence for distortion. *Psychological Bulletin, 112*, 485.
Ridderinkhof, K. R., Ullsperger, M., Crone, E. A., & Nieuwenhuis, S. (2004). The role of the medial frontal cortex in cognitive control. *Science, 306*, 443–447.
Roberts, B. W., Caspi, A., & Moffitt, T. E. (2001). The kids are alright: Growth and stability in personality development from adolescence to adulthood. *Journal of Personality and Social Psychology, 81*, 670.
Rohde, P., Lewinsohn, P. M., & Seeley, J. R. (1994). Are adolescents changed by an episode of major depression? *Journal of the American Academy of Child & Adolescent Psychiatry, 33*, 1289–1298.
Rothbart, M. K., & Ahadi, S. A. (1994). Temperament and the development of personality. *Journal of Abnormal Psychology, 103*, 55.
Rothbart, M. K., Ahadi, S. A., & Hershey, K. L. (1994). Temperament and social behavior in childhood. *Merrill-Palmer Quarterly, 1982*, 21–39.
Rothbart, M. K., Ahadi, S. A., Hershey, K. L., & Fisher, P. (2001). Investigations of temperament at three to seven years: The Children's Behavior Questionnaire. *Child Development, 72*, 1394–1408.
Rueda, M. R., Posner, M., Rothbart, M., & Davis-Stober, C. (2004). Development of the time course for processing conflict: An event-related potentials study with 4 year olds and adults. *BMC Neuroscience, 5*, 39.
Sabatinelli, D., Bradley, M. M., Fitzsimmons, J. R., & Lang, P. J. (2005). Parallel amygdala and inferotemporal activation reflect emotional intensity and fear relevance. *Neuroimage, 24*, 1265–1270.
Sanislow, C. A., Pine, D. S., Quinn, K. J., Kozak, M. J., Garvey, M. A., Heinssen, R. K., & Cuthbert, B. N. (2010). Developing constructs for psychopathology research: research domain criteria. *Journal of Abnormal Psychology, 119*, 631.
Shankman, S. A., Klein, D. N., Torpey, D. C., Olino, T. M., Dyson, M. W., Kim, J., & Tenke, C. E. (2011). Do positive and negative temperament traits interact in predicting risk for depression? A resting EEG study of 329 preschoolers. *Development and Psychopathology, 23*, 551.

Shiner, R. L. (1998). How shall we speak of children's personalities in middle childhood? A preliminary taxonomy. *Psychological Bulletin, 124*, 308.

Siegle, G. J., Ghinassi, F., & Thase, M. E. (2007). Neurobehavioral therapies in the 21st century: Summary of an emerging field and an extended example of cognitive control training for depression. *Cognitive Therapy and Research, 31*, 235–262.

Sørensen, M. J., Nissen, J. B., Mors, O., & Thomsen, P. H. (2005). Age and gender differences in depressive symptomatology and comorbidity: An incident sample of psychiatrically admitted children. *Journal of Affective Disorders, 84*, 85–91.

Stark, K. D., & Laurent, J. (2001). Joint factor analysis of the children's depression inventory and the revised children's manifest anxiety scale. *Journal of Clinical Child Psychology, 30,* 552–567.

Sylvester, C., Corbetta, M., Raichle, M., Rodebaugh, T., Schlaggar, B., Sheline, Y., & Lenze, E. (2012). Functional network dysfunction in anxiety and anxiety disorders. *Trends in Neurosciences, 35*, 527–535.

Tellegen, A. (1985). Structures of mood and personality and their relevance to assessing anxiety, with an emphasis on self-report. In A. H. Tuma & J. D. Maser (Eds.), *Anxiety and the anxiety disroders* (pp. 681–706). Hillsdale, NJ: Erlbaum.

Torpey, D. C., Hajcak, G., Kim, J., Kujawa, A. J., Dyson, M. W., Olino, T. M., & Klein, D. N. (2013). Error-related brain activity in young children: Associations with parental anxiety and child temperamental negative emotionality. *Journal of Child Psychology and Psychiatry, 54*, 854–862.

Torpey, D. C., Hajcak, G., Kim, J., Kujawa, A., & Klein, D. N. (2012). Electrocortical and behavioral measures of response monitoring in young children during a Go/No-Go task. *Developmental Psychobiology, 54*, 139–150.

Towers, D. N., & Allen, J. J. (2009). A better estimate of the internal consistency reliability of frontal EEG asymmetry scores. *Psychophysiology, 46*, 132–142.

Vaidyanathan, U., Patrick, C. J., & Bernat, E. M. (2009). Startle reflex potentiation during aversive picture viewing as an indicator of trait fear. *Psychophysiology, 46*, 75–85.

Watson, D. (2005). Rethinking the mood and anxiety disorders: A quantitative hierarchical model for *DSM–V. Journal of Abnormal Psychology, 114*, 522.

Weinberg, A., Olvet, D. M., & Hajcak, G. (2010). Increased error-related brain activity in generalized anxiety disorder. *Biological Psychology, 85*, 472–480.

Weissman, M. M., Wolk, S., Wickramaratne, P., Goldstein, R. B., Adams, P., Greenwald, S., & Steinberg, D. (1999). Children with prepubertal-onset major depressive disorder and anxiety grown up. *Archives of General Psychiatry, 56*, 794.

Wiersema, J. R., van der Meere, J. J., & Roeyers, H. (2007). Developmental changes in error monitoring: An event-related potential study. *Neuropsychologia, 45*, 1649–1657.

Yeung, N., Botvinick, M. M., & Cohen, J. D. (2004). The neural basis of error detection: Conflict monitoring and the error-related negativity. *Psychological Review, 111*, 931.