Psychophysiologic Methods for the Study of Developmental Psychopathology

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Psychophysiology may be defined as that area of research examining the interaction of physiological systems and psychological states. It involves both the measurement of reactions of a physiological system to changes in psychological state and the influence of a physiological system on the initiation, presentation, and termination of psychological behavior. In this sense, psychophysiology is truly bidirectional, involving both input and output systems that guide, reflect, and accompany psychological behavior. A good example of this can be seen in work indicating that prolonged exposure to abuse and maltreatment can reshape the functioning of core regulatory systems (Cicchetti & Rogosch, 2001; Glaser, 2000; Hart, Gunnar, & Cicchetti, 1995). It appears that along with behavioral and psychological systems, central physiological mechanisms will also reorganize to maximally adapt to the demands of the environment (Campos, Campos, & Barrett, 1989), however aberrant. It is because of this bidirectional relationship that developmental psychophysiology holds great promise for the study of developmental psychopathology.

Developmental psychophysiology also holds the promise of helping the field expand its research boundaries to incorporate multiple levels of analyses. For example, Sroufe and Rutter (1984) contend that developmental psychopathology should emphasize four broad areas of study: (1) the origins and time course of early appearing psychopathology, (2) the varying manifestations of disorder with development, (3) the precursors and sequelae of these disorders, and (4) the relationship of maladaptation to nondisordered patterns of behavior. To do so, researchers must be able to examine and compare developmental processes that act and interact at the behavioral, cognitive, affective, and psychophysiological levels. In this way, researchers can build a multidimensional model of the mechanisms and manifestations of developmental psychopathology.

For example, in assessing risk, Cicchetti and Dawson (2002) note that risk factors can appear at varying levels, ranging from the molecular to the environmental. Although any single risk factor may not be sufficient for a disorder to
manifest, the collective risk found in the pooling of vulnerabilities across levels of functioning may lead to the larger overarching disorders described clinically. In addition, because risk factors tend to act synergistically rather than additively and are rarely found in isolation (Cicchetti & Dawson, 2002), the use of multiple levels of analysis is also critical to outlining the bidirectional nature of the physiology-behavioral link (Kagan, Snidman, McManis, Woodward, & Hardway, 2002).

However, out of either necessity or long-standing tradition, researchers often treat psychopathology as a binary system. That is, participants in studies are often divided into two exclusive groups that are labeled disordered and nondisordered. Our schemes for categorizing and diagnosing psychopathology are dependent on documenting a compendium of behaviors, affects, and cognitions that are both highly variable and dynamic in nature. Indeed, even in the case of developmental disorders with clear genetic markers, such as Down syndrome and Fragile X, the path between genotype and phenotype is so complex that a simple karyotype tells us very little about the psychological state of the individual in question. Therefore, one of the main goals for developmental psychopathology has been to create more precise and nuanced profiles of individual developmental disorders, incorporating both observed behavior and underlying developmental mechanisms. In the past 2 decades, psychophysiological measures have become a central tool in this endeavor.

The increasing use of developmental psychophysiology in developmental psychopathology research has evolved from the unique strengths of the psychophysiological approach and the insights it allows into the processes underlying or accompanying early maladaptation. Inherent in the developmental psychopathological approach is the study of the manner in which early dispositions lead to adaptations in psychological behavior over time. Trajectories of human development are an outgrowth of the interaction between a given nervous system's readiness and reactivity and the adaptations of that nervous system across time. Behavioral change is a result of initial dispositions responding to dynamic and challenging environmental contexts. Research involving measurement of physiological systems thus holds great promise for elucidating important aspects of the bidirectional influences on individual trajectories across development.

In this chapter, we start with the basic tenets and strengths of psychophysiological research. We then systematically examine and review research exploring a variety of physiological systems, detailing issues of approach and measurement. We end this chapter with some thoughts on the future directions of this type of research for the field of developmental psychopathology.

STRENGTHS OF THE PSYCHOPHYSIOLOGICAL APPROACH

The use of physiological measures in behavioral research provides a number of advantages, permitting a window onto the bidirectional influence that physiological systems have on behavior and behavior on physiology. However, it is important to note that psychophysiology does not convey a special truth to data independent of behavior. Often, investigators will claim that physiological responses are more objective than behavioral analysis. In fact, such measures are no more essential than precise behavioral measurement. As van der Molen and Molenaar (1994, p. 466) noted, "The usefulness of psychophysiological measures depends on the demonstration of the sensitivity of the measures to task manipulations derived from developmental psychology." Psychophysiology does provide, however, a means for understanding a level of processing that may not be accessible through observation alone.

Psychophysiology illuminates the link between physiology and behavior, opening up the possibility of supplementing behavioral classifications with the structure, function, and timing of underlying physiological and neural events. Psychophysiology also allows developmental researchers to incorporate a multiple-measures approach, giving them an ability to create multidimensional profiles of the areas of interest and examine associations and disassociations between physiology and behavior. Finally, this approach is exceedingly useful for preverbal and compromised populations, which are often at the heart of developmental psychopathology.

Understanding the Physiology-Behavior Connection

A major strength of the psychophysiological approach is that one can examine the action of a targeted physiological system as it changes in response to psychological challenge. The nature of that change, the manner in which physiological change energizes, arouses, or inhibits behavior, may provide insight into psychological responses to challenge. Knowledge of the underlying physiology of that system as well as an understanding of what aspects of that system are being reflected in its measurement is critical if accurate interpretation of the change in physiology is to be made. At a very basic level, it is important to understand how the physiological system works, that is, how it activates or inhibits behavior. Similarly, it is crucial to understand which mea-
sures of a particular physiological system best reflect these processes.

For many years, for example, heart rate increases in mobile infants who were exposed to unfamiliar adults were assumed to reflect the state of fear in the infants. Infants were approached by an unfamiliar adult while researchers monitored cardiac activity. Increases in heart rate were thought to reflect the infant’s fear of the stranger. Increases and decreases in heart rate, however, are multiply determined. Heart rate change could be the result of metabolic, motor, or psychological change or some combination thereof. Infants who actively moved in response to stranger approach would show heart rate increases, as would an infant who would sit still and cry during this situation. Heart rate increases could not differentiate among these different behavioral responses. The lack of specificity of the physiological response and the multidetermined nature of the response raise important caveats in interpreting heart rate changes during certain types of challenge. Often, however, researchers fall back on the presumed psychological explanation for heart rate change (e.g., arousal, fear, anxiety) without first examining other potential confounding influences.

Linking multidetermined physiological responses to diffuse and nonspecific psychological states (e.g., arousal or anxiety) leads to a lack of precision in the association between the physiological change and the psychological state. This lack of precision in identifying the physiological factors involved in the increased heart rate and the lack of precision in the definition of the underlying psychological state do not facilitate further understanding of the phenomenon of interest. Thus, the very strength of the psychophysiological approach, linking physiological and behavioral change, may sometimes be a critical weakness, particularly when the underlying physiological processes are not well understood.

On the other hand, there are examples from the psychophysiology literature in which knowledge of physiological mechanisms assists in the interpretation of behavioral change. Porges (Porges & Byrne, 1992) has shown that by using complex filtering and statistical techniques, one can identify and extract the component of heart rate, reflecting parasympathetic influence. Vagal tone is a quantification of the variability in heart rate due to respiratory influences that are primarily vagal in origin. The level of vagal tone of an individual or changes in vagal tone as a result of psychological challenge may be interpreted as reflecting the influence of parasympathetic tone or vagal activity on heart rate. The obvious benefit of such precision is that it allows one to examine the relationship of this system to both higher cortical responses and other connected peripheral responses. For example, one can map out the manner in which changes in vagal tone affect brain stem nuclei and upstream cortical centers that may modulate attention. Similarly, one can examine the influence of cortical regions on the brain stem nuclei, which control parasympathetic tone. In addition, because vagus nerve activity affects multiple organ sites, one can begin to describe the manner in which individual differences in vagal tone affect physiological and psychological organization and preparedness for action and behavior. Finally, the precision of physiological description and links to specific psychological behaviors allows one to develop models for how certain initial dispositions may adapt to changing environmental challenges.

Assessing Function through the Timing of Physiological Change

Yet another strength of the psychophysiological approach can be found in its ability to reflect the importance of timing of physiological events underlying or accompanying behavior. Each physiological system commonly measured in psychophysiological research has its distinct time course, which affects and is affected by psychological challenge and behavioral response. For example, recording brain electrical activity (i.e., electroencephalogram, EEG) during repeated stimulus presentation allows the creation of event-related potentials (ERPs), which reflect the timing of neural processing. These ERPs may reflect the immediate processing of sensory information at the millisecond level as well as higher-order cortical processing at the level of hundreds of milliseconds. Continuing the time line, measures of the autonomic nervous system (e.g., heart rate) provide information at the level of seconds, and activity in the limbic-hypothalamic-pituitary-adrenal (LHPA) axis is at the level of minutes. The varying time course for different physiological systems directly reflects their function in the individual’s response to psychological challenge, be it to evaluate the stimulus (milliseconds), divert resources such as blood and oxygen to muscle to respond (seconds), or organize a response to provide energy toward restoring homeostasis in the body (minutes). The timing of physiological responses links directly to the behaviors under study and may provide insight into the function of the behavior in response to the particular challenge.

Providing Multidimensional Biobehavioral Profiles

The use of multiple measures applied to experimental settings allows for a richer and more nuanced analysis of data, particularly when interested in performance differences across two or more groups. A central strategy in
developmental psychopathology research is to contrast the performance of a clinical or high-risk group on a particular task with that of a healthy control group. The addition of multiple measures allows for the addition of analyses that focus on individual differences across two or more physiological systems, which are often both theoretically and statistically stronger avenues for discovery. Perhaps as important, researchers can now look to between-group differences in within-group response patterns. This allows for the examination of individual and group profiles, which may produce a more stable or informative picture of a given disorder than would isolated bits of data. This is in line with the call for more holistic, person-oriented research strategies (e.g., Bergman & Magnusson, 1997; von Eye & Bergman, 2003) that focus on the significance of single variables and of patterns in development, the developmental study of syndromes (typical patterns), and the detection of “white spots” in development in characterizing the individual as an “organized whole.”

This is not to say that each individual measure, even if a core indicator of the disorder or maladjustment, need be deviant or abnormal. Rather, a great deal of insight can be gained in finding patterns of normality and abnormality across measures as well as in creating broad behavioral and psychophysiological profiles. That is, disorder or risk may manifest in the dysregulation of responses across systems rather than alterations within an individual system (Bauer, Quas, & Boyce, 2002). An early example can be seen in Ax’s (1970) work demonstrating that Schizophrenia is marked by poor coordination across systems (in this case, heart rate and respiration) rather than dysregulation within a single system.

It is in this endeavor that developmental psychopathology can benefit from its developmental roots. In the case of psychophysiological measures, their use in the study of psychopathology should not come with the expectation that the measure(s) will necessarily be patently deviant. There may be cases, such as institutionalization (Carlson & Earls, 1997), in which differences are apparent, but it is just as likely that a measure falls within the normal developmental distribution. The greatest information may be found when the measure is placed in the larger context of a physiological or behavioral profile.

For example, Raine (Raine, Venables, & Williams, 1990) collected heart rate, skin conductance, and EEG measures from a group of British adolescents ages 14 to 16. Ten years later, Raine and colleagues returned to see that 17 of the original 101 children now had criminal records. When comparing these two groups, Raine and colleagues found that the adolescents who went on to have a criminal record had lower heart rates as well as dampened electrodermal and EEG arousal. Although the individual findings do not point to any gross deviance, disorder, or, to use a nineteenth-century term, degeneracy, they do point to an interconnected physiological system that may create a profile that is vulnerable to antisocial behavior.

Understanding Dissociations between Physiology and Behavior

It is of obvious interest to examine physiological change, concurrent with behavioral change, in response to a specific psychological challenge. Such associations provide another level of analysis around which one may interpret behavior, understanding the significance of the physiological change as it affects or supports a behavioral response. However, disassociations between overt behavior and physiology may also be of interest for understanding the individual’s response to psychological challenge. In this instance, measurement of physiological change may provide important information that may not be readily apparent to the observer. An example of this may be found in the work of James Gross (Rottenberg, Kasch, Gross, & Gotlib, 2002) on emotion regulation. Gross and colleagues asked subjects who were watching videos designed to elicit different emotions to either freely respond or to inhibit their affective responses, measuring both overt behavior and autonomic responses. During the period in which subjects were inhibiting their affective responses, there was a noticeable decrease in observable behavior. However, these same subjects displayed a significant increase in autonomic activity (e.g., heart rate, blood pressure). This dissociation between behavior and psychophysiology was linked to more extreme concurrent depression and a decreased likelihood for satisfactory recovery. Dissociations between overt behavior and physiology may provide important information about psychological processes, in this case, inhibition of emotional behavior.

The issue of dissociation between physiology and behavior is complex, however. In the case of Gross’s studies, subjects were given specific instructions and acknowledged complying with such instructions via self-report. However, in the absence of such task specificity and instruction, it is often difficult to interpret physiological change without a concurrent behavioral response. This dilemma underlies the first of two cardinal rules regarding psychophysiological research: Whenever possible, physiological responses should be anchored to behavior. Practically, this means that one should usually not interpret physiological change in the absence of concurrent behavioral change. There are, however, multiple exceptions to this rule. First, as described
earlier, if subjects are asked to inhibit behavior, then their physiological response becomes of interest independent of behavioral response. Second, tasks assessing sensory processing may not require a behavioral response. For example, examining brain stem auditory evoked responses or even mismatch negativity (i.e., an early ERP component that reflects a discrepancy between a stimulus and the traces in short-term memory produced by the immediately preceding stimulus) to auditory tones does not require active response from the subject. In these instances, it is not necessary to link behavioral response to physiology. It is in cases of complex cognitive or affective challenges that the interpretation of a physiological response without a behavioral anchor is problematic. Due to the complexity of the systems involved and the multidetermined processes influencing these responses, it is often difficult in such instances to specify the source of the physiological change and its contribution to a discrete psychological state.

Providing Insight into the Behavior of Preverbal and Young Children

An additional strength of the psychophysiological approach lies in its ability to provide insight into the behavior of preverbal infants and young children who cannot self-report or participate in interviews. In such cases, the psychophysiological approach provides a window onto reactivity and processing of stimuli that, together with behavioral analysis, offer a reasonable basis for judging an infant’s or young child’s response to psychological challenge. This is of particular importance when examining developmental psychopathology because researchers are often faced with the task of distinguishing between overlapping and nondistinct symptomatology due to children’s limited behavioral repertoires.

The utility of these methods with infant and young child populations comes with several important caveats. It should come as little surprise that accompanying physical and psychological development is the development and change in underlying physiological systems, which support both of these areas. In some instances, the maturation of the system is rapid, over the 1st year of life, whereas for other systems there is consistent change through adolescence. For example, autonomic control systems change rapidly over the 1st year, and although mean heart rate levels change with development, the physiological system of vagal and sympathetic innervations, the links to respiratory control and blood pressure exist at birth and are stably in place by the end of the 1st year of life. On the other hand, concomitant with maturation of brain regions, particularly in cortical areas, there are significant changes in frequency and amplitude of the EEG through adolescence. There are also major changes in the morphology of the components that are evoked by exogenous stimuli and that form the ERP. These changes in the physiology of the system directly affect the measurement of the system.

QUESTIONS ADDRESSED BY THE PSYCHOPHYSIOLOGICAL APPROACH

There are three broad areas in which psychophysiological methods are meaningfully applied: (1) examination of basic cognitive processes, (2) measurement of variations in physiological arousal and reactivity, and (3) examination of the processes surrounding motivation and emotion. In each of these areas, psychophysiology has a long history of research with both “normal” and clinical populations. In general, certain methods are more applicable for specific areas as opposed to others. Thus, for example, when examining basic cognitive processes such as attention, sensory processing, perceptual sensitivity, or memory, most of the work has entailed the use of ERP methods. Such methods require precision in stimulus definition and the timing of stimulus presentation and provide information about the timing and intensity of neural events involved in different aspects of cognitive processing. For studies in the preparedness of the system to react or respond to psychological challenge (e.g., arousal and reactivity), measures of the autonomic nervous system have been most commonly used. Assessments of arousal have traditionally been accomplished via measurement of sympathetic and parasympathetic activity. Such studies may examine heart rate, skin conductance, or sympathetic activity during a resting or baseline state and then during subsequent challenge and recovery to baseline. The use of psychophysiological methods to study emotion and motivation covers a wide range of methods, including those examining specific neural systems (e.g., the “fear” system) and those examining broad motivational processes (e.g., approach versus withdrawal). Included as well in this area is the work on the stress response and the physiological system involved.

The wide array of methods in part reflects the history of behavioral research in emotion, where precision in both the stimulus characteristics eliciting emotion and the approach to quantifying or identifying the presence of emotion have undergone important advances in only the past 30 years. This range of approaches has led to a range of studies, only some of which specify the nature of the stimulus and context in which it is presented. As well, among studies of
emotion or motivation only some anchor the physiological response to behavior, making interpretation of the physiological change ambiguous.

The following sections of this chapter are divided along these three broad domains. We first cover those methods useful for examining cognitive processes such as attention and review the empirical findings that are relevant for understanding both normative and clinical patterns of behavior in development. We then provide an overview of the methods used to examine the physiological organization of arousal and reactivity. The third section provides a review of those methods that may be useful for examining motivation, emotion, and emotion regulation in children. The literature discussed in each of the three broad domains illustrates how the application of psychophysiological methods has contributed to our current understandings of individual differences in developmental trajectories generally and developmental psychopathology in particular.

**PHYSIOLOGICAL MEASURES OF COGNITIVE PROCESSING**

In the psychophysiological literature there is often the implicit assumption of a dichotomy between cognition and emotion such that central nervous system measures are appropriate for the study of cognition and peripheral nervous system measures are suitable for studies of emotion (Keller, Hicks, & Miller, 2000). However, over the past 2 decades there has been a growing understanding of the interconnections between cognition and emotion in shaping both normative and disordered functioning and development. For example, recent research has suggested that individual biases to process or attend to negative threat information may play an important role in the development and maintenance of anxiety disorders in both children and adults (E. Fox, Russo, Bowles, & Dutton, 2001). In psychophysiology research, much of the work examining the relationship between cognition and emotion has relied on the ERP as a central methodological tool. This is due to the fact that these measures are very well suited to address questions of speed and efficiency of processing as well as perceptual sensitivity to variations in stimulus complexity. In addition, prepulse inhibition has been used to tap into basic cognitive processes and is therefore also explored in this section.

**Event-Related Potentials**

ERPs are currently the best noninvasive method for measuring the physiological manifestations of psychological processes within a small temporal window (Deldin, Shestyuk, & Chiu, 2003; Fabiani, Gratton, & Coles, 2000). ERPs are able to supplement the broad neuropsychological and neuroanatomical correlates of psychopathology assessed through the use of EEG, positron emission tomography (PET), and magnetic resonance imaging (MRI) by providing a more direct link between physiology and discrete instances of information processing.

There are four basic questions that can be asked with ERP data (Rugg & Coles, 1995). First, do the waveforms differ across experimental groups as a function of stimuli characteristics? Second, when do these differences appear? This question can be answered by looking at the timing of the divergence point. Presumably, divergences in the waveform indicate when processing begins to differ across stimuli or conditions. Third, are the processes underlying performance evoked to a different degree? This question is answered by measuring any differences in amplitude across the waveform. Fourth, do the ERPs fit any standard pattern? Psychophysiologists look for standard components, and deviations from the standard waveform are often taken as signs of deviance, delay, or immaturity. For example, individuals normally produce a smaller P50 ERP component to the second of a pair of identical stimuli. Schizophrenic individuals do not show a reduced P50 to the second stimulus, suggesting poor sensory filtering (Light & Braff, 1998; D. A. Smith, Boutros, & Schwarzkopf, 1994). These data suggest that poor sensory gating may lead to the perceptual and attentional deficits seen in schizophrenia by allowing irrelevant or distracting information to interfere with normal functioning (Braff & Geyer, 1990).

Aside from marking the general processing of a particular stimulus, ERPs are also sensitive to the particular meaning the stimulus holds for the individual. For example, given a presentation of positive, negative, and emotionally neutral stimuli, researchers can use the neutral stimuli as a baseline against which to compare the processing of the affectively charged stimuli. One could then see if an individual’s pheno-

typic presentation of, for example, depression is linked to an overresponse to the presentation of negative stimuli or an underresponse when presented with positive stimuli. The temporal resolution of the ERP also makes it a useful tool in the study of psychopathology because the core phenomena of emotion and attention are brief and require fast resolution to accurately reflect timing and intensity (Davidson, 1994). It is this sensitivity that makes ERP-based research attractive to researchers interested in the psychological, as well as biological, components of psychopathology.

**Methodology for Event-Related Potentials**

ERPs are time-locked electrophysiological recordings timed to the presentation of a specific stimulus or class of
stimuli (Coles & Rugg, 1995). The ERP for a particular condition or subset of the data is calculated by averaging over the EEG signals collected for each individual trial. The waveform produced is characterized by the size (amplitude) and timing (latency) of deflections in the wave. Increases in component amplitude and/or decreases in latency are taken as evidence that individuals are investing greater cognitive resources in processing the stimuli presented to them. Specific deflections or components are designated by their polarity (P = Positive; N = Negative) and either their order of appearance (e.g., N1, P1, N2) or their specific latency (e.g., N170, P360). For example, the P300 is a positive wave that occurs approximately 300 to 600 msec after stimulus onset and is maximal over central-parietal sites. The amplitude of the P300 is thought to vary with the task relevance and probability of a stimulus (R. Johnson, 1993) and marks the evaluation of stimulus significance. A detailed discussion of the methodology underlying ERP research can be found in Picton et al. (2000) and M. J. Taylor and Baldeweg (2002).

Although derived from a common electrocortical substrate, EEG and ERP measures appear to comment on different aspects of a particular behavior or process. For example, in their study of verbal and spatial working memory in adults, Gevins, Smith, McEvoy, and Yu (1997) found that changes in EEG were more likely tied to changes in the functional networks underlying task performance, whereas their ERP data were indexing the specific “operations being performed on internal representations” (p. 383). Along the same lines, Sobotka, Davidson, and Senulis (1992) found that EEG measures were more sensitive to incentive variations than were ERP measures.

There are a number of developmental changes that occur in the ERP through infancy and childhood (Cheour, Leppänen, & Kraus, 2000). First, the waveform becomes more complex and new components appear. For example, the Nc (negative component) generated by infants to stimuli will differentiate over time into an adult component (Richards, 2003). Second, ERP amplitudes appear to follow an inverted U shape as a function of age, perhaps reflecting greater processing demands and inefficiency during task performance (Ridderinkhof & van der Stelt, 2000). Third, ERP latencies grow progressively shorter, indicating an increase in processing speed (Thomas & Crow, 1994), perhaps due to more extensive myelination. Fourth, there are on occasion indications of a polarity shift in components over time (Novak, Ritter, Vaughan, & Wiznitzer, 1990). Finally, the localization of the component generator becomes more differentiated (M. J. Taylor & Baldeweg, 2002).

By far the most common use of the ERP has been to examine the physiological correlates of attentional processes. This is true for both children and adults in healthy and clinical populations. Hillyard and Hansen (1986, p. 227) have suggested that the term attention “has become more of a chapter-heading word, encompassing a diverse set of processes and paradigms, than a precisely defined theoretical construct,” but one cannot deny the central role attentional processes play in development. From birth, adaptive functioning is often dependent on the individual’s ability to appropriately select those aspects of the environment that are of interest from among the constant and simultaneous presentation of competing stimuli. Ridderinkhof and van der Stelt (2000) argue that age-related improvements in this ability, particularly when under strong voluntary control, are one of the most profound advances in information processing that takes place in childhood. The advantage of the ERP paradigm is that it often forces the researcher to break down the larger construct of attention into its constituent parts in order to collect quantifiable data.

Traditionally, performance in attentional selection tasks is monitored via the speed and/or accuracy of an overt behavior in response to the information (e.g., stimulus identity or location) presented. For example, reaction times in response to cued and noncued visual targets have been compared as an indicator of the individual’s ability to disengage and reorient attention (Posner & Cohen, 1984). As the various components in the standard ERP wave are thought to reflect different stages of processing, these data may help verify the mechanisms that shape overt behavior.

There are a number of standard paradigms in use for studying attention in both children and adults. Ridderinkhof and van der Stelt (2000) provide a very extensive review of attentional studies in developmental psychophysiology. As a result, the following discussion highlights only three types of tasks used in the field and the findings generated so far. Each discussion briefly notes the normative data in adults and children and then turns to findings with clinical and at-risk groups.

The first set of tasks is commonly labeled interference tasks. In this paradigm, participants are asked to overtly respond to information presented in one stimulus domain. Researchers look to see if performance is either hindered or facilitated by information in a second stimulus domain. The classic example of an interference or conflict task can be found in the Stroop (1935) paradigm. The traditional Stroop task presents individuals with a series of words and asks them to name the color in which the word is written, while disregarding the actual meaning of the word. Individuals are faster to respond when presented with congruent stimuli (the word RED in red ink) than when the stimuli are incongruent (the word RED in blue ink).
The earliest ERP study of the traditional Stroop task (Duncan-Johnson & Kopell, 1981) found no consistent differences across conditions. The researchers concluded that Stroop interference was related to conflicts in response selection rather than in the stimulus evaluation processes. However, more recent studies have indicated that there are detectible differences in ERPs generated by the traditional (color-word) Stroop (Ilan & Polich, 1999; Liotti, Woldroff, Perez, & Mayberg, 2000; Schack, Chen, Mescha, & Witte, 1999; West & Alain, 1999). Early in the ERP wave, studies have found a distinct N1-P2-N2 complex (e.g., West & Alain, 2000b). These components are thought to index early sensory processing and low-level attention allocation (Hillyard, Luck, & Mangun, 1994). Traditional Stroop studies for the most part have not detected differences at this early stage across their two conditions: congruent versus noncongruent color words (however, see Atkinson, Drysdale, & Fulham, 2002). Rather, these studies have focused on more endogenous components, the P3 and N4 (e.g., Ilan & Polich, 1999). The larger amplitudes noted in the incongruent condition are thought to reflect the stimulus evaluation time and attentional requirements needed to ultimately suppress the information carried in the incongruent trials (West & Alain, 2000a). This interpretation also carries over to the positive slow wave prominently seen in traditional ERP studies (West & Alain, 2000b).

In the emotional Stroop, emotion words are substituted for the color words used in the traditional task. A number of emotional Stroop studies (Pérez-Edgar, 2001; Pérez-Edgar & Fox, 2003) have found that the general morphology of early ERP components (P1-N1-P2-N2) is roughly similar to those found in the traditional Stroop studies (e.g., West & Alain, 2000b). However, the later components (P3 and N4) were either attenuated or nonexistent. Overall, they indicate that there may be early processing differences across words of varying emotional valence, in line with data from other non-Stroop studies of emotion words (Shalev & Algom, 2000). A late slow wave also appears to distinguish between word categories. In particular, words conveying negative emotions seem to require or attract greater processing resources, as indexed by larger amplitudes and shorter component latencies (Hillyard et al., 1994; Schack et al., 1999).

The second major design, deviance detection tasks, requires participants to attend to the presence of a specific stimulus (the target) during the presentation of both target and nontarget stimuli. The most common deviance detection task is the oddball task. Prototypically, participants are asked to respond as quickly as possible to the presentation of a target that is embedded in a sequence of rare targets and frequent nontargets (Ridderinkhof & van der Stelt, 2000). One can also present a passive oddball design, during which no overt response is given. In fact, researchers often present participants with a book to read or video to watch in order to guarantee that they do not pay attention to the stimuli. This variant is used to examine the individual’s bias in orienting to deviance or novelty and is quite useful to developmental researchers as no overt instructions need be given or followed.

Among adults, target detection in oddball tasks has been associated with increased P300, an enhanced N2, and a slow wave. The N2 is thought to reflect stimulus comparisons necessary for discriminating between the target and nontarget stimuli (Oades, Dittmann-Balcar, & Zerbin, 1997), and the slow wave may be associated with further elaboration of the target stimulus (Sutton & Ruchkin, 1984). Among individuals with Posttraumatic Stress Disorder (PTSD), oddball paradigms often produce attenuated P300s (Charles et al., 1995; MacFarlane, Weber, & Clark, 1993) and a delayed N200. McFarlane et al. suggested that the delayed latencies for the N200 reflect more time spent in stimulus discrimination, which allowed for fewer resources in later processing, as seen in the P300.

Subtracting the ERPs generated by the standard stimuli from the ERPs for the deviant stimuli produces a difference wave with a negative component that is maximal in frontal-central electrode sites and often peaks 200 msec poststimulus (Nääätänen, 1990). This component, the mismatch negativity (MMN), is thought to reflect the mismatch between the current stimulus and the traces in short-term memory produced by the immediately preceding stimulus (Nääätänen, 1992; for a review, see Cheour et al., 2000).

The developmental literature indicates that the MMN response can be seen very early, even in newborns (Kurtzberg, Vaughan, Kreuzer, & Flieger, 1995), although there is some controversy over the stability of amplitude (Kurtzberg et al., 1995; van der Stelt, Gunning, Snel, & Kok, 1997) and latency (A. H. Lang et al., 1995; van der Stelt et al., 1997) over time. One of the main reasons for the lack of consistency is due to the large inter- and intraindividual variability in young children (Kurtzberg et al., 1995). Studies focusing on the P3 (M. J. Taylor & Eals, 1996), N2 (Oades et al., 1997), and slow wave (Wijker, 1991) also indicate that the stimulus evaluation processes necessary for the task are present even in young children and that over time children make quantitative improvements in the efficiency of processing (i.e., shorter latencies and smaller amplitudes).

Reduced MMN amplitudes have been detected in individuals with depression (Ogura et al., 1993) and Schizo-
perceptual processing (Luck, Heinze, Mangun, & Hillyard, 1996). The degree of attenuation among schizophrenics was correlated with ratings of negative symptoms (such as social withdrawal) but not positive symptoms (e.g., hallucinations and delusions; Catts et al., 1995; Javitt, Shelley, & Ritter, 1998; O’Donnell et al., 1993). The presentation of the cue engages attention during early cued-attention tasks and addresses the timing of attentional preferential processing while the processing of alternative attention, ensuring that the target stimulus will receive ga-ee, orient, and re-engage attention. The assumption is that these shifting tasks are often referred to as Posner cued-attention tasks. And they consistently produce a “validity effect” marked by faster reaction times when responding to stimuli that appear in a previously cued location (valid trials) versus stimuli that are not cued (invalid trials).

In the third major set of tasks, attention is primed on a trial-by-trial basis by a cue stimulus that instructs the individual on the identity or location of the target stimulus to attend to. By varying the location or identity of the target and cue, the tasks require participants to repeatedly disengage, orient, and reengage attention. The assumption is that the presence of the cue will prime mechanisms of selective attention, ensuring that the target stimulus will receive preferential processing while the processing of alternative stimuli is suppressed (Posner & Cohen, 1984). Examples of these shifting tasks are often referred to as Posner cued-attention tasks, and they consistently produce a “validity effect” marked by faster reaction times when responding to stimuli that appear in a previously cued location (valid trials) versus stimuli that are not cued (invalid trials).

There are a growing number of studies using ERP measures to observe neuronal activity during the Posner cued-attention task and address the timing of attentional mechanisms triggered by the task. The data indicate that the presentation of the cue engages attention during early perceptual processing (Luck, Heinze, Mangun, & Hillyard, 1990). As such, early ERP components (e.g., P1 and N1) generated by stimuli preceded by valid cues have greater amplitudes than ERP components corresponding to stimuli that were invalidly cued. The findings are most pronounced for posterior electrode sites.

For example, Anllo-Vento (1991) presented 6- and 8-year-old children with a centrally located arrow cue. They found an enhanced negativity from 200 to 500 msec after the presentation of the cue, which was maximal in the hemisphere contralateral to the cued visual field. This “early directing attention negativity” was thought to reflect the selective recruitment of processes associated with spatial attention orienting. The presentation of the target in the validly cued location produced enhanced N1 and P1 amplitudes, reflecting the modulation of sensory areas by attention. Similar results were found in a recent study of 7-year-old children using peripheral, and presumably more exogenous, visual cues (Pérez-Edgar & Fox, 2005). These data indicate that attentional priming mechanisms are largely in place in young children.

**Event-Related Potentials in the Study of Developmental Psychopathology**

As noted in the discussion of specific tasks, affective processes have increasingly been incorporated into ERP studies (e.g., Gunnar & Nelson, 1994), expanding our understanding of the neural processing of affective behavior. This in turn is shaping the way ERP studies are incorporated into studies of risk and psychopathology.

For example, recent work suggests that late components of the ERP may reflect the discrepant nature of stimuli undergoing cognitive or affective processing (Pauli et al., 1997). In particular, affective stimuli elicit larger P300s and late positive slow waves than neutral stimuli (Kostandov & Azumanov, 1977; Williamson, Harpur, & Hare, 1991). This effect is even more pronounced when the stimuli are tailored to individual subject concerns. For example, Pauli and colleagues found that panic patients showed larger P300s and positive slow waves to somatic words versus nonsomatic stimuli.

Similar effects have been found when generally content-neutral stimuli are given affective significance. For example, introverted subjects performing a lexical decision task (De Pascalis, Fiore, & Sparita, 1996), a stimulus detection task (De Pascalis, 1994), and a stimulus prediction task (Bartussek, Diedrich, Naumann, & Collet, 1993) did not differ from extraverted subjects when the task was affect-neutral. However, when the experimenter introduced competition, providing win/loss feedback after each trial or set of trials, differences emerged. More specifically, introverts showed larger peak amplitudes (particularly the N2, P3, and P6) to loss feedback and extraverts showed larger peak amplitudes to win feedback.

In the adult literature, ERPs have been used with greater frequency to explore the information-processing mechanisms thought to underlie various disorders. In the case of Major Depression, for example, ERPs have been used to study negative biases in attention and memory...
cognitive style has been implicated in both the etiology and recall more negative information, relative to nondepressed depressed individuals are more likely to attend to and later
were stronger in the left posterior region, an area associated with face processing in working memory. Taken together, the psychophysiological measure helps test and refine our understanding of previously collected behavioral data.

A representative example of recent work in the developmental psychopathology literature can be found in Pollak's work with maltreated children (Pollak, Cicchetti, Klorman, & Brumaghim, 1997; Pollak, Klorman, Thatcher, & Cicchetti, 2001). Maltreatment and abuse place children at an extremely high risk for psychopathology (Cicchetti & Toth, 1995), and one area of particular concern is emotional functioning. For example, maltreated children appear to have a bias toward negative emotions. In infancy they manifest negative emotional expressions earlier and more often than nonabused peers (Gaensbauer & Hiatt, 1984). Over time, they are primed to detect negative affect in the environment (Weiss, Dodge, Bates, & Pettit, 1992) and have difficulty interpreting and responding to potentially hostile gestures in others (Klimes-Dougan & Kistner, 1990). Maltreatment and abuse may selectively increase children's psychological sensibilities to specific emotional cues, such as an angry face (Pollak et al., 2001).

Pollak and colleagues (1997) found that the ERP responses of maltreated children when processing emotion faces were sensitive to the context and attentional demands of the task at hand. Children ages 7 to 11 were presented with photographs of a single individual posing with either a happy, angry, or neutral facial expression. In this study, maltreated children had smaller component amplitudes and slower reaction times than their nonmaltreated counterparts when responding to the emotion faces. When asked to specifically attend to the angry faces, the maltreated children showed an increase in amplitude over the happy face condition, whereas the other children showed an equivalent response. These data indicate that the emotion processing need not be completely stimulus-driven, but may depend on the contextual importance of the stimulus and task at hand. Indeed, a follow-up study (Pollak et al., 2001) indicated that the effect was specific to angry faces, suggesting that maltreated children do not exhibit a global deficit in emotional information processing.

Future Directions in the Use of Event-Related Potentials

ERP measures have allowed researchers to examine the processing mechanisms that bridge the presentation of a stimulus with the observation of overt behavior. Indeed, the technology opens a window onto cognition even in the absence of behavior. In general, it appears that affective information can influence the topography of ERP components if the affective loading of the stimulus is high and the individual attends to stimulus meaning (Johnston & Wang, 1991; Williamson, Harpur, & Hare, 1991). The ERP has proven to be a robust, noninvasive measure amenable across a wide age range of uses, yet there are a number of considerations that should be kept in mind when collecting and interpreting such data.

First, a better understanding of the development of the ERP, independent of our interest in psychopathology, will be needed to make the best use of the methodology. One cannot presume that measures from children and adults are equivalent in structure or function. For example, many of the studies incorporating ERP measures into the study of emotion and emotional processing have used pictures of facial affect as the central stimulus (e.g., M. H. Johnson & Morton, 1991; Nelson, 1987; Pollak et al., 1997). These stimuli are relatively easy to produce, can be standardized and incorporated across a set of studies, and are in most cases appropriate for use across a wide developmental range. Indeed, ERP measures have been successfully used in studies with participants as young as 6 months (e.g., Nelson, 1994). Although the technology allows researchers to compare children and adults on identical measures generated via identical stimuli presented in the context of the same task, there are important developmental differences involving both the psychophysiological measures of interest themselves and the processing mechanisms they are thought to reflect.

The ERPs generated in children by the task at hand often do not correspond to those of adults. These age-related differences are more pronounced the younger the child. For example, as noted earlier, adults participating in an oddball paradigm display an enhanced N2 component to the presentation of the target stimulus approximately 200 msec after onset (Oades et al., 1997). Infants participating in similar procedures display a large nega-
tive component (morphologically similar to an adult slow wave) occurring approximately 400 to 800 msec after the stimulus. This component is known as the Nc because it is negative in polarity and maximal in central sites (Richards, 2003).

Even when dealing with older children, who often generate ERP waves that are morphologically comparable to those of adults, one cannot assume that visual similarity reflects an equal similarity in the psychological processes involved. This becomes evident when trying to compare the performance of children and adults across conditions of the same task. For example, Kestenbaum and Nelson (1992) presented 7-year-old children and adults with pictures of angry, happy, fearful, and surprised faces and asked them, across two conditions, to respond to either the happy or angry face. Adults in this study showed greater ERP (e.g., P300) amplitudes to the happy faces. The children, however, showed larger amplitudes for the angry faces. In addition, this finding held only when calculating the area scores for the component. When peak values were calculated there was no differentiation across valence. The method of analysis made no difference in the adult data.

Because ERPs are derived from raw EEG signals, the issues and concerns discussed in that section are also applicable here. For example, ERP component amplitude is sensitive to the overall power of the EEG signal. As a result, age-related changes in ERP amplitude to the presentation of a particular stimulus need not solely reflect developmental changes in the ability to process or derive meaning from that stimulus. Rather, it may be largely driven by maturational changes in the overall strength of the EEG signal. Group differences observed in the ERP may also similarly be rooted in variations in the underlying EEG substrate. For example, Lazzaro and colleagues (Lazzaro, Gordon, Whitmont, Meares, & Clarke, 2001) found that amplitude reductions in the P3 component of children with ADHD could be linked to prestimulus increases in theta wave activity.

As such, it is important that any age-related changes in the ERP can be traced to manipulations of the task or conditions at hand. If not, it is difficult to disentangle results from the general effects of brain maturation. For example, after reviewing a variety of deviance detection (oddball) studies focusing on the P300 and finding that age-related changes in topography were invariant across myriad stimulus and task demands, M. J. Taylor (1988) came to the somewhat controversial conclusion that the findings were due to the expression of brain maturation, not developmental changes in specific cognitive abilities.

Prepulse Inhibition

It has long been surmised that seemingly simple human reflexes do not function in isolation in the intact nervous system (Fearing, 1930). For instance, at the turn of the previous century, Bowditch and Warren (1890) documented that the human patellar (i.e., knee-jerk) reflex was substantially suppressed when subjects clench their hands in response to a bell milliseconds before the knee was stimulated. Years later, Hilgard (1933) documented changes in the amplitude of the eyeblink (i.e., startle) reflex in response to the presentation of a loud, startle-evoking noise when a visual stimulus (i.e., flashing light) was presented prior to the auditory stimulus. Further, Hilgard found that temporal variation in the presentation of the visual stimuli served to differentially modify the acoustic startle response. These early studies mark the first evidence to suggest that reflexes, previously thought to be isolated functions of the central nervous system, are in fact modulated by psychophysiological processes (M. E. Dawson, Schell, & BöhmeU, 1999). Hence, measurement of the degree of modulation in the startle response permits exploration of psychological states on physiological responding.

Graham, Putnam, and Leavitt (1975) showed that the presentation of a nonstartling, neutral, “lead” probe (e.g., a series of tones) immediately prior to the startle probe yields an attenuation of the blink amplitude, a phenomenon referred to as prepulse inhibition, defined formally as “the normal suppression of the startle reflex when the intense startling stimulus is preceded 30 to 500 msec by a weak lead stimulus” (Swerdlow & Geyer, 1999, p. 115). The opposite pattern was documented for lead stimuli that were presented at longer (>1,400 msec) intervals, describing a phenomenon referred to as long-lead facilitation. Graham’s findings regarding the inhibition or facilitation of startle relative to temporal variation in the presentation of lead stimuli has been well replicated and is a robust phenomenon in adults (Ornitz, 1999).

The neural circuitry involved in prepulse inhibition is regulated by forebrain and limbic structures that descend on the pallidum and pontine tegmentum. This top-down pathway is not direct and involves inputs to the striatum from the limbic cortex, striatal connections to the pallidum from the striatum, and inputs to the pontine tegmentum from the pallidum. Such top-down effects of higher-level processes on brain stem modulation of startle are related to early attention and sensory processing of input. The temporal variation in the presentation of the lead stimuli, relative to the experimental stimuli (i.e., affective; see discussion of affective modulation of startle later in chapter) and the
startle probe, has been investigated and findings here mark an important contribution to understanding the role of attention and affect in startle modulation. In their review of this literature, M. M. Bradley, Cuthbert, and Lang (1999, pp. 167-169) have summarized these findings into six general conclusions:

First, strong inhibitory effects are obtained when blink reflexes are elicited immediately after picture onset. Second, reflex inhibition is maximal 300 msec after picture onset, which is somewhat later than is typically found for simpler foreground stimuli. Third, at the point of maximum inhibition (300 msec), reflex inhibition is significantly larger for emotional pictures (pleasant or unpleasant), compared with neutral materials. Fourth, reflexes continued to be relatively inhibited, compared with responses elicited in the interpicture interval, for up to 3 s after picture presentation, at which time reflex magnitude appears to asymptote for all picture contents. Fifth, by 500 msec after picture onset, reflexes are significantly augmented for unpleasant, compared with pleasant materials, suggesting that affective modulation has been initiated by this time. Affective modulation then continues throughout the picture-viewing interval. Sixth, no significant effects of affective valence are found for reflexes elicited after picture offset.

Bradley and her colleagues interpret such effects as the result of attentional mechanisms involved in the initial processing of the foreground stimulus. Essentially, the more interesting the prepulse stimulus is, the more resources are involved in the encoding of it. However, at the point at which encoding of the stimulus is complete (at approximately 500 msec), the affective quality of the stimulus has been perceived and the startle reflex will henceforth be modulated by the affective nature of that stimulus until the time when the stimulus is no longer presented.

According to Graham and colleagues (1975), prepulse inhibition is due to a "transient detecting reaction" that serves to suppress startle reactions temporarily to ensure that perceptual processing of the lead stimulus is complete. In this way, prepulse inhibition serves a protective function, inasmuch as attenuated startle reactions allow for increased allocation of cognitive resources to the stimulus encoding process. Thus, the individual differences in prepulse inhibition are of scientific interest in their own right, as variation in the degree to which the startle response of participants is modulated following the presentation of simple lead stimuli is thought to be an indicator of individual differences in attention and sensory processing as relevant to initial perceptual encoding of information at lower brain stem levels (Ornitz, Hanna, & Traversay, 1992).

**Startle Methodology**

The startle reflex is thought to be a primitive defensive response that may serve at least two purposes: (1) to avoid bodily injury, as in the function of the eyelid; and (2) to halt ongoing activity and prepare the organism for flight or flight in the face of looming threat (P. J. Lang, 1995). Landis and Hunt (1939) were the first to provide a detailed depiction of the startle response in humans. These researchers used slow-motion video documentation to characterize the response that followed the presentation of a pistol shot. They reported that the startle response consists of a forward head thrust, descending flexor wave reaction, and the sudden closure of the eyes. It is the last of these responses that is used as the index of startle amplitude, as it has been shown to be the earliest, fastest, and most stable process involved in the startle response (P. J. Lang, Bradley, & Cuthbert, 1992).

There is considerable variability in the degree of amplitude of the startle reflex related to attention and affective processes. This variability in amplitude is used as an index of an organism's underlying emotional state. Researchers interested in the affective modulation of the startle reflex tend to rely also on additional psychophysiological indices of emotional reactivity and attention, including heart rate, blood pressure, skin conductance, ERPs, and facial electromyographic responses. These are also incorporated into the protocol to confirm that the appropriate/desired level of affective arousal has been achieved by the emotional stimulus (M. M. Bradley et al., 1999).

The eyelid startle reflex is measured with electromyogram (EMG) by placing two electrodes under one eye. The EMG waveforms are rectified and integrated (see van Boxtel, Boelhouwer, & Bos, 1998, for a full review) and scored for degree of amplitude in the EMG response. Onset of the eyelid reflex is triggered most often with the presentation of brief, high-intensity white noise for baseline startle and during the presentation of experimental stimuli. Experimental stimuli have ranged from visual stimuli such as pleasant or unpleasant pictures or videos (M. M. Bradley & Lang, 2000; Cuthbert, Bradley, & Lang, 1996; P. J. Lang, Bradley, & Cuthbert, 1990), administration of shocks (Hamn & Stark, 1993), use of air blasts administered to the neck (Grillon & Ameli, 1998), and manipulation of levels of light and darkness (Grillon, Morgan, Davis, & Southwick, 1998; Walker & Davis, 1997). According to Grillon and Baas (2003), the method used to assess the degree of change in startle amplitude between the control and experimental conditions has major implications for the results of a study and should be based on knowledge of the particular underlying system being as-
sessed. The startle paradigm is ideal for use with infants and young children as well as adults and the elderly. However, choice of emotional stimuli used for experimental conditions must be appropriate for the particular age group targeted in the study (Grillon & Baas, 2003).

**Prepulse Inhibition and the Study of Developmental Psychopathology**

The literature exploring the role of attention in the modulation of the startle reflex in infants and children provides preliminary evidence for a meaningful developmental trend in the degree to which variable lead intervals affect startle responses. In his review of this literature, Ornitz (1999) concludes that there is little evidence for the presence of prepulse inhibition prior to the age of 8 years. For instance, there is a 25% response inhibition in 2- to 6-month-olds, 23% inhibition in 3-year-olds, and 30% inhibition in 5-year-old boys (Ornitz, Guthrie, Kaplan, Lane, & Norman, 1986). After age 8, however, adult-like levels of prepulse inhibition are evident. This effect is consistent with the notion that prior to the middle of childhood, young children lack impressive degrees of inhibitory control. This notion regarding inhibitory control is further supported by data that have revealed peaks in the degree of long lead stimulus startle facilitation in 3-year-olds relative to adults and children older than 8 (Ornitz et al., 1986). Ornitz suggests that these findings provide preliminary evidence that the brain stem mechanisms that mediate startle response modulation are developing during childhood and are not fully mature until approximately age 8. Such a conclusion is indeed tentative at best, as no replication of Ornitz’s developmental findings yet exists. The notion that these patterns of findings are due to the increase in the development of inhibitory control across the preoperational to concrete operational years is certainly plausible. One important contribution to this area will be the examination of attentional modulation of startle in children between ages 3 and 8, during the transition from preschool to middle childhood.

To date, there are only a few published studies that have examined the role of startle modulation in childhood psychopathology. Two are investigations of attentional modulation of startle undertaken by Ornitz and his colleagues. In the earliest of these works, Ornitz and Pynoos (1989) examined startle modulation based on variable lead intervals, on the premise that the exaggerated startle pattern manifested by individuals with PTSD would yield atypical patterns in attentional modulation of startle assessed in the laboratory. They anticipated that children with PTSD would show a reduction in prepulse inhibition and enhanced startle facilitation due to longer lead intervals. Ornitz and Pynoos assessed their small sample of children with PTSD and a normative sample of nonmatched controls multiple times across 2 years (six of the children in the study had onset of PTSD following a sniper attack at their school playground and a seventh child in the study witnessed the murder of his father). The children with PTSD showed less startle inhibition with prestimulation relative to controls. Close examination of the case that witnessed murder revealed that the reduced prepulse inhibition was quite variable across the 2 years following the incident, with the most pronounced effects emerging at assessments closest temporally to the traumatic event. The authors concluded that the lack of prepulse inhibition of the PTSD group relative to normal controls might indicate a slowing in the normal development of the brain stem mediated function due to severe stress. Additionally, although marked by many limitations, including the lack of a matched control sample and a small sample size, this study provides preliminary evidence to suggest that the deviant startle pattern in children with PTSD is most pronounced at temporal points closest to the traumatic incident and may ameliorate over time.

In another study of childhood psychopathology and startle modulation, Ornitz and his group (Ornitz et al., 1992) examined differences in prepulse inhibition and long-lead facilitation of startle in boys ages 6 to 11 diagnosed with ADHD, primary nocturnal enuresis, and the comorbid condition (i.e., both ADHD and enuresis) relative to normal peers. In their clinical sample, a high degree of comorbidity between nocturnal enuresis and ADHD was found (with enuresis occurring in some 30% of boys with ADHD). Hence, Ornitz and his colleagues explored the extent to which previously documented (Anthony, 1990) startle abnormalities in children with ADHD are more closely related to the attention deficit primary to their condition or to the physiological immaturity associated with nocturnal enuresis. The findings of this study are indeed quite telling, for although no ADHD effects were noted, all enuretic boys (i.e., children with both primary and secondary nocturnal enuresis) showed immature patterns of prepulse inhibition and long-lead facilitation that were comparable to levels found in 5-year-old children. The authors interpreted these findings as providing evidence for underdeveloped mesopontine reticular mechanisms, which serve to mitigate the lower-level processing of the signals associated with urinary continence. During sleep, appropriate functioning of the inhibitory functions involved in urinary continence are dependent on the modulation of sensory input to indicate bladder fullness by the spinal reflex activity of the...
pontine micturition center. This pathway may be anatomically and functionally related to the pathways involved in startle modulation, inasmuch as the processing of sensory information relevant to startle is modulated by an inhibitory pathway that parallels the inhibitory pathway in the mesopontine lateral tegmental area associated with the processing of sensory signals from the bladder. Hence, "primary nocturnal enuresis can be considered a disorder of early sensory processing, that is, a dysfunction of subcortical preattentive mechanisms" (p. 447).

Such a finding marks an important contribution to current understandings of developmental psychophysiology on several grounds. First, a good deal of research has sought to understand the neurophysiological nature of nocturnal enuresis with little resolution. For instance, as Ornitz and his colleagues indicate, deviant sleep patterns, arousal mechanisms, and bladder functions have been implicated as the source of nocturnal enuresis, and each of these literatures has been met with mixed results. The findings involving startle modulation offer new and exciting directions for understanding the nature of primary nocturnal enuresis as a deficit in early sensory processing. The lack of effect for the boys with ADHD suggests that ADHD is perhaps less related to lower-level preattentive mechanisms than it is to higher-level processing, such as executive functions located in the prefrontal cortex.

**Future Directions in the Use of Prepulse Inhibition**

The use of the startle methodology to the field of developmental psychopathology, although still very much in its infancy, holds promise. Studies of the temporal variation of lead intervals provide windows onto the role of the most basic processes, including that of early preattentive sensory processing, on pathological development. Ornitz's work (Ornitz et al., 1992; Ornitz & Pynoos, 1989) has demonstrated that central nervous system immaturity associated with basic processing is associated with childhood-onset PTSD and primary nocturnal enuresis, and not ADHD. Indeed, issues of sensory gating are relevant to many psychopathological conditions, particularly Schizophrenia and conditions of anxiety, learning disabilities, mental retardation, and Pervasive Developmental Disorders. It is especially important to note that the prepulse inhibition paradigm is ideal for use with such compromised populations, as the laboratory paradigm places no burden on the participant to read or socially interact with an experimenter. As such, the prepulse inhibition methodology can meaningfully be applied to special populations of children, and its use should yield great strides in uncovering the aberrant sensory processing associated with a diversity of psychopathological conditions.

**MEASURES OF PHYSIOLOGICAL AROUSAL**

Although variations in psychopathology differ in etiology, developmental course, disruptiveness, and amenability to treatment, they are thought to share some core characteristics. Chief among these is the notion that children diagnosed with or at risk for psychopathology have a difficult time adjusting and adapting to the shifting demands of their environment. A good deal of work in developmental psychopathology has focused on individual differences in the preparedness of the system to react or respond to psychological challenge. Related to this are differences in level of reactivity to threatening stimuli and in the subsequent regulation of fight/flight responses. Measures covered in this section include measures of autonomic arousal, including heart rate, preejection period, electrodermal activity, and vagal tone, as well as additional measures of physiological arousal, namely, cortisol and EEG power.

Walter Cannon (1915) offered the earliest account of the functional significance of the autonomic nervous system (ANS). According to Cannon, the ANS served to keep the organism in a state of homeostasis, with two separate branches of the ANS (sympathetic and parasympathetic) serving in reciprocal harmony. The ANS is of interest to psychopathological processes because it plays a central role in mitigating somatic responses that are associated with perceived environmental threat (Boyce et al., 2001).

In a classic paper on the relationship between somatic and psychological processes, Cannon (1928) reported associations between negative affect and heart rate, hypertension, the digestive system, the menstrual cycle, thyroid function, and the immune system. ANS reactivity has been found to correlate with behavioral inhibition in infants and young children (N. A. Fox, 1989), internalizing and externalizing psychopathology in middle childhood (Raine, 2002), and ADHD and Conduct Disorder in adolescents (Beauchaine, Katkin, Strassburg, & Snarr, 2001).

This portion of the chapter first discusses the measurement of sympathetic activation and includes discussion of measures of heart rate via electrocardiogram (ECG), preejection period, and electrodermal activity. Measurement of the activation of the parasympathetic branch of the ANS is discussed next, followed by a review of the findings regarding autonomic reactivity and the development of psychopathology.
Measures of Sympathetic Activity and Reactivity

The sympathetic branch of the ANS prepares the body for the release of energy and is activated during fear-eliciting situations. Activation of this branch yields an increase in blood circulation to the muscles vis-à-vis increases in heart rate and force of heartbeats (Ohman, Hamm, & Hugdahl, 2000). Sweat glands also respond during activation of the sympathetic branch, such that increases in perceived threat result in filling of eccrine sweat glands. Psychologically, sympathetic autonomic reactivity is of interest to psychophysicists because of its relationship to the activation of the approach-avoidance system, the motivational system implicated in individual differences in arousal (Fowles, 1980).

Heart Rate

According to Fowles (1980), heart rate is a sympathetic manifestation of Gray’s (1975) behavioral activation system (BAS). In his landmark theoretical paper, Fowles points to the abundant body of early empirical evidence that found associations between heart rate acceleration and behavioral activation when level of somatic activity is controlled (e.g., Belanger & Feldman, 1962; Ehrlich & Malmo, 1967). According to Gray, the BAS also mitigates behavioral response patterns of active avoidance. Fowles cites additional work, such as that of Obrist (1976, as cited by Fowles, 1980), that found heart rate accelerations during conditions in which participants were able to actively avoid shocks based on successful task performance. In Fowles’ own words, “The BAS represents a central control system which responds to incentives and whose activity is reflected in increased HR [heart rate]” (p. 92). It is important to note, however, that simple estimates of heart rate are by no means uncontaminated estimates of sympathetic functioning, as patterns of heart rate acceleration and deceleration are associated with both somatic activity (Fowles, 1980) and respiration (Porges, McCabe, & Yongue, 1982). Hence, heart rate is an index of activation of the BAS (either in the form of reward seeking or active avoidance of punishment) when degree of somatic activity and respiration are controlled.

ECG is a psychophysiological measure that involves recording the electrical potentials of the heart during each cardiac cycle (Papillo & Shapiro, 1990). Heart rate is perhaps the most salient and easily observable manifestation of sympathetic ANS arousal. The large bioelectrical signals generated by the heart are recorded from placement of electrodes on the body’s surface. Although as many as 12 leads can be tactically placed on the limbs and chest to diagnose irregularities of the heart, psychophysicists are typically interested in heart rate alone, which can be reliably recorded from as few as two electrode sites. Positioning of the ECG electrodes is not a critical consideration in ECG setup, as the large electrical signals can be recorded from almost any site in the general region of the heart. Although it is not within the scope of this chapter to provide a depth of knowledge about ECG indices (see Papillo & Shapiro, 1990), guidelines for those interested in psychophysiological research can be found in Jennings (1981).

There are two indices determined by ECG that warrant mention. The first is simple heart rate, which is determined by the number of beats per some prespecified unit of time, typically 1 minute. Heart period, or the interbeat interval, is the elapsed time between two successive heart cycles and is usually determined online by a computer. The decision of which index is most appropriate depends on a number of considerations, including whether the research questions involve analysis of individual or group differences, if the participants are infants or adults, and whether raw scores or change scores are desired (Graham, 1978; Graham & Jackson, 1970; Jennings, Stringfellow, & Graham, 1974).

Systolic Time Intervals

More recent work in autonomic reactivity has relied on the use of measurement of the systolic time interval as an estimate of autonomic reactivity. Measurement of the preejection period (PEP) is one such estimate and is defined operationally as the temporal latency between the onset of isovolumetric contraction (i.e., ventricular depolarization) and the onset of left ventricular ejection (Sherwood, 1993; Uchino, Cacioppo, Malarkey, & Glaser, 1995). The PEP is obtained by collecting both ECG and an impedance signal of thoracic blood flow, such that PEP equals the temporal interval from the Q wave on ECG to the B point on the dZ/dt signal. Shorter intervals indicate greater sympathetic activation. The PEP of the cardiac cycle is a sensitive measure of sympathetic tone that is free of parasymptomatic influence inasmuch as the ventricular myocardium is innervated almost exclusively by the sympathetic nervous system (Cacioppo, Uchino, & Bernston, 1994).

Electrodermal Activity

Another method for gauging activation of the sympathetic ANS involves the measurement of electrodermal activity (EDA). Before the turn of the previous century, Vigouroux (1879, as cited by M. E. Dawson, Schell, & Filion, 2000) began using degree of tonic skin resistance as a clinical diagnostic tool. Fere (1888, as cited by M. E. Dawson et al.,
energy-restoring function (Ohman et al., 2000). Activities supported by the parasympathetic branch include gastric

The parasympathetic branch of the ANS serves a catabolic, and Reactivity

Measures of Parasympathetic Activity

EDA is the result of activity of eccrine sweat glands found on the surface of the body and largely concentrated in the hands and feet. The eccrine glands are responsible for regulation of skin temperature, although the glands located on the hands and feet are also thought to play a role in grasping and are more reactive to emotional versus thermal stimuli than are eccrine glands located on other skin surfaces. The relationship between sweat gland and electrical activity is such that, as the sympathetic ANS is activated, sweat fills sweat ducts on the surface of the skin and electrical conduction is increased (M. E. Dawson et al., 2000). Eccrine sweat gland activity is controlled by cholinergic innervation from fibers that originate in the sympathetic system. Hence, unlike cardiac functioning, EDA receives no parasympathetic input (Fowles, 1980).

Functionally, EDA is thought to reflect activation of the behavioral inhibition system (BIS; Fowles, 1980; Gray, 1975). In his synthesis of the EDA literature, Fowles called on studies such as Elliott’s (1969) study of autonomic arousal and Stroop performance and Haywood’s (1963) work in autonomic reactivity and delay of auditory feedback to illustrate the utility of EDA as a measure of the BIS, as these studies revealed that autonomic reactivity was manifest by EDA (but not heart rate) during conditions of nonreward. Fowles cautioned, however, that EDA’s index of activation of the BIS is confounded by degree of cognitive activity (e.g., orienting, itself mediated by the BIS) involved in the laboratory paradigm (Szpiler & Epstein, 1976), frequency of response required by a task (with frequent responding yielding nonspecific EDA patterns; Schneider & Fowles, 1978), and degree of hydration of the skin (Bundy & Mangan, 1979). However, with careful experimental control, Fowles has suggested that EDA can be used to assess degree of emotional arousal stemming from activation of the BIS.

Measures of Parasympathetic Activity

The parasympathetic branch of the ANS serves a catabolic, energy-restoring function (Ohman et al., 2000). Activities supported by the parasympathetic branch include gastric and intestinal motility, secretion of digestive juices, salivation, and increased blood flow to the gastrointestinal tract. Cells of the parasympathetic branch are located in the nuclei of the cranial nerves (3, 7, 9, and 10) and in the sacral region of the spinal cord. Focus on this division of the ANS has been centered on the role of the vagus, the cranial nerve that regulates deceleratory parasympathetic activity (Beauchaine, 2001) and hence mediates patterns of cardiac reactivity during periods of orienting and fight/flight responding. Historically, interest in the parasympathetic branch of the ANS was based on the notion that it worked with the sympathetic branch in a symbiotic fashion such that each were separate, antagonistically related components of one unitary system. However, evidence offered by Porges (1995) indicates that the parasympathetic system is more complex than previously thought.

Heart Rate Variability (Vagal Tone)

Quantification of heart rate variability is used as an index of parasympathetic functioning, or vagal tone. The vagus itself contains both afferent and efferent fibers that play a role in cardiac functioning. Efferent vagal fibers from the brain stem extend to the sinoatrial (SA) node. Activation of these inhibitory fibers yields a decrease in SA firing, which yields a general attenuation in heart rate. Afferent fibers, originating in the heart, extend to the nucleus solitarius and provide feedback to the brain that ultimately serves to regulate generalized cardiac functioning. Vagal tone, or RSA, is the result of vagal efference occurring during exhalation (slowing the heart) and of vagal efference during inhalation (increasing heart rate). Because the sympathetic regulation of the heart via acceleratory sympathetic projections to the SA node confound simple estimates of heart rate, neither heart rate nor heart period alone can serve as an uncontaminated index of RSA.

The simplest methods for gauging RSA rely on the range, variance, or standard deviation of the cardiac interbeat interval. The peak-to-trough method proposed by Fouda, Tarazi, Ferrario, Fighaly, and Alicandri (1984) involves the monitoring of both interbeat interval and respiration and is the mathematical difference between the longest interbeat interval corresponding to expiration and the shortest interbeat interval corresponding to inspiration. Porges (1986) recommended using spectral analysis to isolate the portion of variance within the interbeat interval that is due to RSA from that which is due to heart rate.

The functional significance of the RSA is provided by Porges’s (1995) polyvagal theory. Porges argued that the vagal system is controlled by two very distinct motor systems, each of which has different evolutionary origins and
locations. One system originates in the dorsal motor nucleus, is phylogenetically older, and is termed the vegetative vagus. This system is associated with reflexive regulation of primitive functions, including the deceleration of heart rate during states of attentiveness and primitive behavioral freezing in the face of perceived threat. The other motor system is purely mammalian, originates in the nucleus ambiguous, and is called the smart vagus because it is associated with attention and orienting responses. In the face of impending threat, higher-order mammals must first orient and then either become engaged or enter into a fight-or-flight behavioral pattern. Engagement is associated with vagal withdrawal, and the emotional reaction triggered by a fight/flight response system is associated with a nearly complete vagal suppression, or “vagal break,” which is accompanied by sympathetic heart rate acceleration. As such, cardiac reactivity postorienation, during engagement of the fight/flight system, is mediated by the activation of the smart vagus. The vegetative vagus, in contrast, mediates heart rate deceleration during orienting behavior (Porges, 1995).

As Beauchaine cautions (2001), the functional significance of RSA is by no means clear-cut and is largely dependent on the context in which RSA data are collected. According to his review, RSA reflects generalized temperamental reactivity and emotionality when it is obtained during quiescent states, such that high-RSA infants are more likely to be extremely emotionally reactive (i.e., either affectively negative or positive in response) than infants who have lower levels of RSA (N. A. Fox, 1989; Stifter & Fox, 1990; Stifter, Fox, & Porges, 1986). In contrast, when RSA is obtained during specific environmental demands, the measure will reflect the manifestation of either attentional focus or emotion regulation. For example, in a sample of boys ages 5 to 9 years, Weber, van der Molen, and Molenaar (1994) found that RSA decreased significantly from baseline during an attention-demanding task. Indeed, Beauchaine argues that there is ample consistency in the infant, childhood, and adult literature to conclude that periods of cognitive engagement result in partial vagal withdrawal.

The literature exploring emotional reactivity to specific emotionally charged events is less clear. Calkins and Fox (1997) reported RSA reduction from baseline in preschoolers during the presentation of both affectively positive and negative events. Beauchaine (2001) suggests that although moderate degrees of vagal withdrawal are associated with adaptive responses to danger, excessive vagal withdrawal is associated with emotional lability, or dysregulation, and is therefore an important index of psychopathology, particularly when parasympathetic reactivity is supplemented with measures of sympathetic reactivity such as EDA and heart rate, which can then serve to help specify whether or not activation involves Gray’s (1975) BAS or BIS.

**Autonomic Reactivity and Developmental Psychopathology**

Most substantive work in the area of autonomic reactivity and childhood psychopathology has emphasized the role of the BIS, BAS, and, more recently, the parasympathetic regulatory system in the childhood onset of aggression and impulsivity (Beauchaine et al., 2001; Boyce et al., 2001; Harden & Pihl, 1995; Herpertz et al., 2003; Raine, 2002). For instance, the application of both sympathetic and parasympathetic measures of reactivity to childhood externalizing disorders has yielded great strides in the disentanglement of the distinctive etiological underpinnings of ADHD and Conduct Disorder (Beauchaine et al., 2001). More general studies of childhood psychopathology have revealed distinctive patterns of autonomic reactivity associated with internalizing versus externalizing conditions.

Boyce and his colleagues (2001) conducted a cross-sectional investigation of autonomic reactivity, including measures of sympathetic and parasympathetic responding and psychopathology, in a sample of 6- and 7-year-olds. Included in their reactivity protocol were indices of heart rate, RSA, and PEP. Autonomic reactivity measures were obtained at baseline and across various challenging contexts, including a structured interview, a digit span task, placement of lemon juice on the tongue, and during the showing of two emotion videos designed to evoke fear and sadness. Children were divided into four symptom groups: children with low symptoms on both internalizing and externalizing, high internalizing children, high externalizing children, and children who scored high on both externalizing and internalizing disorders.

Results revealed that children who scored high on internalizing problems showed significantly more parasympathetic reactivity (low RSA). Children who scored high on externalizing manifested lower degrees of parasympathetic and sympathetic reactivity than children in the low symptom group. Subsequent analyses examining the discriminant validity of the autonomic profiles of the sample revealed that children with high internalizing problems could be significantly discriminated from children in the low symptoms group based on a profile of high parasympathetic reactivity during challenge tasks and recovery from those tasks. Externalizing children, in contrast, were significantly discriminated from the other three groups based on a profile that reflected a generalized (i.e., non-task-specific) pattern of
low sympathetic and parasympathetic reactivity. Children in the high internalizing/externalizing group showed lower generalized sympathetic reactivity only. Child gender and patterns of autonomic reactivity were also explored in this study, and no evidence of main or moderating effects were found. Hence, results of this study are indicative of differential degrees of reactivity that are specific to each of the broadband classifications of childhood pathology. High internalizers in Boyce’s study showed dysregulation in fight/flight responding during and after challenging paradigms, providing evidence that the underlying substrate of childhood anxiety and depression is related to the perception of environmental threat. In contrast are externalizers, who manifest a generalized pattern of autonomic underarousal that does not seem to be linked to any specific event. Such children manifested global dysregulation in the fight/flight system and abnormal levels of reactivity related to BAS functioning.

In a similar study, Harden and Pihl (1995) found that boys who were classified as high on internalizing and externalizing behavior problems evidenced an ANS profile of hyperreactivity when compared to children with no behavior problems or problems of only the externalizing variety. In their sample of 51 10-year-old boys, ANS reactivity was gauged with EMG, finger pulse amplitude, and interbeat interval of the cardiac cycle during a laboratory paradigm in which the children were rewarded for correct responses to a series of challenging arithmetic questions (the Arithmetic Stress Task, adapted from Carroll, Turner, & Hellawell, 1986). Results of the test of group differences across the psychophysiological indices revealed that boys who were both disruptive and anxious manifested significantly higher degrees of sympathetic reactivity than either the disruptive group or the controls, and the group of boys who had histories of disruptive behavior without anxiety manifested sympathetic underarousal as indexed by low levels of EDA during the cognitive stress task.

Indeed, there is an ample body of evidence to suggest that global ANS underarousal may constitute an early marker for subsequent antisocial behavior in adulthood. In a recent review, Raine (2002, p. 417) suggests that low resting heart rate “is the best-replicated biological correlate of antisocial and aggressive behavior in children.” In his meta-analysis of 29 studies that examined resting heart rate and antisocial behavior in children and adolescents, the combined effect size was robust ($r = .56$), was equal in strength for both males and females, and was found across various types of measurement and in data collected across multiple countries (Raine, 1996). Raine (2002) also suggests that heart rate findings are particularly diagnostically significant (when compared to other ANS measures), inasmuch as no other psychopathological condition is associated with low heart rate. ANS underarousal when assessed by heart rate also appears to be a strong biological marker for the condition, as it has been found to contribute unique variance to childhood violence beyond the effects of contextual factors such as family risk and interacts with psychosocial risk factors. For instance, Farrington (1997) showed that the joint effect of low resting heart rate and a poor parent-child relationship placed boys at the most risk for becoming violent offenders in adulthood. According to Raine (2002), the heart rate findings in children at risk for the development of antisocial behavior holds much promise for the advancement of current understandings regarding etiological contributions to the disorder as well as psychopharmacological treatment of violent behavior in childhood.

Recent work to uncover the ANS correlates of childhood externalizing behaviors has turned to the role of the parasympathetic branch (Beauchaine et al., 2001; Herpetz et al., 2003; Pine, Wasserman, & Coplan, 1996). In their study of aggressive behavior in children, Pine and his colleagues showed that childhood aggression was associated with increased parasympathetic reactivity, as manifest by reduced levels of vagal tone. Beauchaine and his colleagues have extended the literature in ANS reactivity and conditions of externalizing by examining the sympathetic and parasympathetic reactivity profiles of adolescent boys with ADHD with and without the comorbid condition of Conduct Disorder (CD) and normal controls. Differentiation between these two conditions is of particular relevance to understanding the ANS underpinnings of childhood aggression, as both groups are characterized by disinhibition, with aggression and antisocial behavior unique to only one group. Results of this study revealed that both clinical groups manifested less BIS activity (i.e., lower levels of EDA) relative to normal controls. Further, children with CD and ADHD showed reduced BAS activity (i.e., lengthened PEPs) relative to normal controls and children with only ADHD. Finally, children with comorbid ADHD/CD exhibited parasympathetic hyperreactivity, as evidenced by low vagal tone. Hence, results of this important study show that although BIS dysfunction is common among both groups of externalizers, reduced regulatory control in fight/flight responding and sympathetic underarousal is specific to the more aggressive, antisocial children with CD.

Herpetz and his colleagues (2003) conducted a similar study of externalizing disorder and ANS reactivity. Their study included children with an exclusive ADHD diagnosis, the comorbid ADHD/CD condition, and a group of children with an exclusive CD diagnosis. The inclusion of which per-
Cortisol acts to maintain physiological systems in working (Bauer et al., 2002). Cortisol fine-tunes multiple physiological systems to meet continual changes in both the external and internal environments. Its impact is wide-ranging and is not simply tied to moments of high stress, as would normally be defined for research in psychopathology. For example, exercise will increase cortisol secretion if its duration challenges metabolic and cardiovascular expenditures (Sung, Lovallo, Pincomb, & Wilson, 1990).

As a daily regulator, cortisol is marked by a stable diurnal rhythm of secretion. The diurnal cycle is marked by peak cortisol levels in the early morning hours that then bottom out in the midafternoon. The magnitude of this cycle is quite extreme, such that there is often a 10-fold difference in cortisol levels between the peak and the trough (Goodyer, Park, Netherton, & Herbert, 2001). This pattern suggests that LHPP activity is providing the “wake-up energy” needed to transition from a sleep state to the active events of the day (Erickson, Drevets, & Schulkin, 2003).

The allostatic load of an environment is tied to the frequency, intensity, and predictability of the demands placed on the individual. Prolonged functioning under high allostatic load can lead to alterations in central regulatory mechanisms in terms of both daily functioning and in response to acute stressors (Johnston-Brooks, Lewis, Evans, & Whalen, 1998). This dysregulation, which is itself a form of allostatic load, may act as a causal mechanism for both psychological disorders and their behavioral precursors (Bauer et al., 2002). The impact of this type of disturbance may be particularly high in childhood given that early exposure to stress may produce lifelong effects on neuroendocrine function that may be behaviorally transmitted to future generations (McEwen, 1999).

Cortisol Methodology

In the literature, LHPP activity in children has been assessed through the use of serum cortisol, urinary cortisol (Krues, Schmidt, Donnelly, Hibbs, & Hamburger, 1989; Tennes & Kreye, 1985), adrenocorticotropin hormone (ACTH), and, most commonly, salivary cortisol (Schmidt, Fox, Sternberg, et al., 1999; Schmidt et al., 1997). Unlike more cumulative measures of LHPP functioning, salivary cortisol is sensitive to variations in cortisol levels throughout the day (Bauer et al., 2002). It is highly correlated with cortisol levels in the blood and cerebral spinal fluid, and, unlike with serum cortisol, collecting salivary cortisol is a benign, noninvasive process that can be used with relative ease across a wide age range. Most studies have asked children to either deposit saliva directly into a small container or have had children chew on a dry piece of cotton soaked in a sugary substance. The sample is then squeezed out of the cotton into a container for assaying.
Given that collection is relatively simple, researchers have the luxury of collecting multiple samples both within and across a period of time. Depending on the exact parameters of the study, researchers are then faced with a choice of how best to summarize and quantify LHPA activity. For example, a review of the literature indicates that studies have employed a variety of measures, including basal level, median level, daily range, reactivity to stress, pulse amplitude, and frequency. These measures capture different facets of the LHPA system's dual role: regulation and reactivity.

Each particular measure provides very different views into the relationships between the LHPA axis, behavior, and affect (Gunnar & Donzella, 2002; Tout, de Haan, Kipp-Campbell, & Gunnar, 1998). For example, Schmidt et al. (1997) found a significant positive correlation between temperamental withdrawal and basal cortisol levels. However, there were no group differences when comparing the same children after a series of startle probes. Findings such as these reflect the fact that different measures are linked to different patterns of neural activity. That is, although stress-induced cortisol is produced after an acute activation of the paraventricular nucleus of the hypothalamus, basal levels of cortisol are governed by neuronal projections originating in brain nuclei associated with biological clocks (Gunnar & Donzella, 2002).

The particular cortisol measure used may also greatly affect the strength of the available data. For example, Gunnar and Donzella (2002) argue that it is relatively difficult to elicit increases in cortisol among young children through the introduction of the mild stressors normally approved for laboratory use. Given that one cannot dramatically increase the potency of the stressors, Boyce et al. (2001) suggest expanding the way reactivity is defined. Currently, reactivity is most often defined as the difference between baseline arousal and stress-induced arousal. It may be more informative to try to capture the broader pattern of response. This includes the magnitude of the physiological response, the variability of the response, recovery time, and the ability to habituate to the triggering stimulus. Boyce (Boyce et al., 2001) has speculated that reactive children have difficulty regulating their initial arousal response and that this difficulty extends from their physiological responses to their behavioral coping strategies. To examine children's ability to dampen a response after an acute stressor, one needs to have multiple measures of cortisol after the introduction of the triggering stimulus (Ramsay & Lewis, 2003).

Cortisol and Developmental Psychopathology

Not all individuals with objectively high allostatic loads exhibit psychological distress. Individual differences in vulnerability have been tied to differences in resting physiological arousal as well as reactivity to an environmental stimulus. The hippocampus, a central limbic structure, is considered a primary regulator of cortisol during both normal activity and periods of high stress (Jacobson & Sapolsky, 1991). It performs through negative feedback regulation, inhibiting secretion during normal functioning (shaping the nadir seen in the diurnal cycle) and in times of acute stress. In the hippocampus, it has been suggested that one set of receptors (mineralocorticoid; MR) regulates diurnal variations in cortisol levels and another (glucocorticoid; GR) regulates stress-related secretion (Dallman et al., 1987).

This division of labor is an important factor in shaping individual responses to environmental change. The diurnal cycle regulated by MR is sensitive to negative feedback, helping to ensure regularity (Munck, Guyre, & Holbrook, 1984). However, negative control of the acute GR response is weakened by strong activation of the amygdala (Lovallo & Thomas, 2000). Hyperarousal of the amygdala, in turn, is thought to play a central role in shaping the fear response in both animals (LeDoux, 1996) and humans (Kagan, 1984). In young children, it has been linked to individual differences in temperamentality shyness and social withdrawal (Garcia Coll, Kagan, & Reznick, 1984). The data indicate that the LHPA axis response is not governed solely by the nature of the stressor. Rather, individual differences in stress response often result from the individual's cognitive and emotional reactions to the stimulus (Lazarus & Folkman, 1984).

The LHPA axis is one actor among an interconnected system of regulators that help the individual respond to the environment. Individual differences in the way these systems interact and respond may help our understanding of phenotypic differences in behavior. Unlike the catecholamines of the sympathetic-adrenal-medullary (SAM) system, which act quickly to generate the fight-or-flight response (Henry, 1992), the glucocorticoids produced by the LHPA axis are slow-acting steroid hormones. Cortisol must be synthesized on demand and acts by affecting protein synthesis. Cortisol is released by the adrenal cortex only after a signal from the anterior pituitary, which must, in turn, be signaled by the release of corticotropin-releasing hormone (CRH) from the hypothalamus (Bauer et al., 2002). As a result, although cortisol is released within 10 to 30 minutes after a stressor, its effects on target tissues may not be evident for over an hour (Kirschbaum & Hellhammer, 1994).

Henry (1992) has argued that the SAM system acts to generate a "defense reaction," whereas the LHPA system...
activates a "defeat reaction." The SAM system is thought to mount an effortful response to a stimulus that is considered manageable or under personal control (Peters et al., 1998). For example, individuals with a Type A personality are likely to show larger SAM responses, even as early as 3 years of age (Brown & Tanner, 1988; Lundberg, 1986). In contrast, adults show a larger LHPA response to situations that are deemed uncontrollable (Peters et al., 1998) or are likely to provoke fear and frustration (Lovallo & Thomas, 2000).

For children, the response is particularly strong if it involves a situation whose outcome they view as highly important (Gunnar, Brodersen, Nachmias, Buss, & Rigatuso, 1997; Kirschbaum & Hellhammer, 1994). Lewis and Ramsay (2002) found that at age 4 children who exhibited embarrassment and shame after failure had higher levels of salivary cortisol. They argued that cortisol levels might differentially reflect stress experienced after negative evaluations. These data are also in line with the temperament literature which indicates that behaviorally inhibited children are likely to show elevated cortisol levels at baseline (Kagan, Reznick, & Snidman, 1987; Schmidt et al., 1997).

In both children and adults, the cortisol response is closely tied to individual variations in the affect-stress response. A prime example of this can be found in a growing literature indicating that the relationship between LHPA activity and behavior varies as a function of gender. To begin with, men and women appear to differ in the experiences they consider stress-inducing (A. Taylor, Fisk, & Glover, 2000). The assumption is that the stress response in women involves less sympathetic arousal, is primarily defensive, and is likely to be moderated by social context. For example, college-age women showed elevated cortisol levels after experiencing a social stressor in the form of social rejection (Stroud, Salovey, & Epel, 2002). Their male counterparts showed greater reactivity to an achievement challenge involving difficult mathematical and verbal problems. Over time, these variations in stress response may alter the relationship between basal cortisol levels and behavior.

Boys and girls also differ in how dysregulation is manifested in behavior. In general, boys are more likely to show high levels of externalizing behavior, whereas girls show more internalizing behavior (Merrell & Dobmeyer, 1996; Keiley, Bates, Dodge, & Pettit, 2000). This dichotomy suggests that the developmental role of underlying regulatory mechanisms also differs. For example, Carrion et al. (2002) found that girls with PTSD had higher basal cortisol levels than boys with equivalent levels of PTSD. Klimes-Dougan and colleagues (Klimes-Dougan, Hastings, Granger, Usher, & Zahn-Waxler, 2001) also found differing diurnal rhythms between male and female adolescents at risk for psychopathology. This is in line with data from a nonclinical sample that LHPA activity helps sustain temperamental biases from infancy to early childhood in boys, but not girls (Pérez-Edgar, Fox, Schmidt, & Schulkin, 2004).

This is not to say that the SAM response is "good" and the LHPA response is "bad." Indeed, Munc (Munc et al., 1984) argues that the LHPA response must step in to suppress the initial fight/flight response and prevent lasting damage to the individual by regulating sympathetically mediated changes in cardiovascular function, metabolism, and immune function (Sapolsky, Romero, & Munc, 2000). In addition, brief and periodic increases in cortisol may enhance focused attention on emotionally arousing stimuli and marshal cognitive forces for a response (Ericson et al., 2003). As such, it appears that the SAM and LHPA systems must work in tandem to provide the optimal level of arousal and attentional engagement that higher-order cognitive mechanisms rely on.

The growing consensus in the psychopathology literature holds that dysregulation of the LHPA system, often due to prolonged periods of high allostatic load, disrupts the individual's ability to self-regulate and adapt to shifting environmental demands. This leaves the individual vulnerable to psychological maladaptation. The data, as outlined next, indicate that this mechanism may be central to psychopathology in both children and adults, playing a role in its etiology, maintenance, and perhaps intergenerational transmission.

For example, findings from the adult literature suggest that PTSD may be linked to hippocampal attrition, as seen in reduced volume (Bremner, Krystal, Southwick, & Charney, 1995; Gurvitis, Shenton, Hokama, & Ohta, 1996), decreased blood flow (Semple et al., 1993, but not Rauch et al., 1996), and poor working memory performance (Bremner et al., 1995). Both Nadel and Jacobs (1998) and Yehuda (1997) have suggested that the damage is due to stress-related steroid exposure via dysregulation in the LHPA axis. In the glucocorticoid cascade hypothesis, the presence of cortisol in GR and MR during stress negatively impacts hippocampal neurons (Lovallo & Thomas, 2000). Damage to the hippocampus, a critical feedback site, may disrupt diurnal regulation and lead to chronically high levels of cortisol, further increasing the system's vulnerability to future stress. Along the same lines, disturbances in autobiographical memory in depressed adults have been linked to hippocampal damage due to excessive cortisol secretion (Axelson et al., 1993).

Parallel work in the developmental literature suggests that a similar mechanism may also shape behavior and
psychological adjustment in children. For example, Gunnar and Nelson (1994) found a diminished late positive component in the ERPs of 12-month-olds with high levels of cortisol, reflecting the dampening effect of cortisol on hippocampal activity and perhaps also development. Some (e.g., Goodyer, Park, Netherton, et al., 2001) have speculated that this disruption of the hippocampus will directly impact memory formation, particularly memories of an autobiographical nature, thus placing the child at risk for later difficulties (Lynch & Cicchetti, 1998; Pollak, Cicchetti, & Klorman, 1998).

Under normal circumstances, the LHPA system goes through at least two major shifts in functioning and reactivity in the 1st year of life. The first 3 months sees the emergence of the cortisol diurnal rhythm and a reduction in the cortisol response to a specific stressor. In the next 9 months, the cortisol response to nonspecific general stressors decreases again (Gunnar, Brodersen, Krueger, & Rigatuso, 1996). This buffering can be seen in the fact that routine examinations by a pediatrician will trigger a cortisol response in the young infant (Gunnar, Brodersen, Nachmias, Buss, & Rigatuso, 1996) but will not do so in the 2nd year of life. This developmental progression is sensitive to environmental characteristics. Indeed, the connection between early life events and later LHPA activity is sensitive to extremely subtle environmental differences. For example, 8-week-old infants who underwent an assisted delivery (e.g., forceps) show a larger cortisol response to inoculation than do infants who had vaginal or cesarean deliveries (A. Taylor et al., 2000).

Similar mechanisms may be at play for children of highly stressed or depressed mothers, shaping behavior through both biological and environmental channels. Stress during pregnancy, as measured by morning cortisol levels, has been associated with delays in motor and mental development at 8 months of age (Huizink, Robles de Medina, Mulder, Visser, & Buitelaar, 2003). Depressed mothers often provide detached and inconsistent care to their children (Ashman, Dawson, Panagiotides, Yamada, & Wilkinson, 2002; G. Dawson & Ashman, 2000). Unpredictability in the environment has, in turn, been suggested as a possible factor in LHPA dysfunction. In fact, depressed mothers have higher salivary cortisol levels than nondepressed mothers, and these elevations are associated with more depressed behaviors in the infants (Field et al., 1988). At age 3, children of depressed mothers displayed higher baseline cortisol levels than children of nondepressed mothers (Hessl et al., 1996). Recently, Ashman et al. examined the effect of maternal depression on offspring LHPA activity as a function of the timing of depressive episodes and found that the presence of depression in the first 2 years of life was the best predictor of cortisol production at age 7.

Given these data, it is not hard to imagine that a prolonged disruption in a child's environment could have profound effects on allostatic load and the body's ability to self-regulate. As a relatively benign example, infants with colic show a flattening of the normal daily cortisol cycle (Finsterwald, Selig, Schieche, Wurmser, & Papousek, 2000; B. P. White, Gunnar, Larson, Donzella, & Barr, 2000), which may reflect the toll of persistent crying and the disruption to normal daily events (e.g., colicky babies tend to have bouts of interrupted sleep).

In general, the literature indicates that children with severe difficulties in their caretaking environment have either chronically high cortisol levels or unusually low basal cortisol levels with occasional spikes (Flinn & England, 1995). Chaotic or unpredictable schedules also contribute to the blunting of the normal diurnal rhythm (Gunnar & Vazquez, 2001). For example, maltreatment and abuse may produce chronic disruptions of the LHPA axis and play a central role in the development of psychopathology. DeBellis et al. (1999) found that cortisol concentrations in abused children were positively correlated with the duration of trauma and the intensity of symptoms in children subsequently diagnosed with PTSD. Indeed, Cicchetti and Rogosch (2001) found that cortisol patterns also reflected the form of the abuse experienced by the child. Carrion et al. (2002) found that young children with PTSD exhibited elevated basal cortisol levels and a flattening of the diurnal cycle.

To date, most studies have assessed outcomes in two broad categories: internalizing and externalizing behavior. Studies generally look at either one form of behavior or the other. When included in a single study, internalizing and externalizing behaviors are often treated as orthogonal to each other, despite the fact that these behaviors are often highly related (e.g., Granger, Weisz, & Kauneckis, 1994).

In general, the data indicate that low LHPA activation is associated with externalizing, aggressive, or disruptive behavior in children (McBurnett et al., 1991; Tout et al., 1998). For example, Van Goozen et al. (1998) had boys ages 8 to 11 diagnosed with Oppositional Defiant Disorder (ODD) or CD participate in a competitive stressor. Compared to the control children, the boys with ODD/CD had lower baseline levels of cortisol. However, there were no differences in stress-induced cortisol across groups. Pajer and colleagues (Pajer, Gardner, Rubin, Perel, & Neal, 2001) found a similar relationship between low resting cortisol and externalizing behavior in a group of 15- to 17-year-old girls diagnosed with CD.
Indeed, the most dramatic example of hypocortisolism can be found in environments marked by maltreatment, neglect, and natural or sociopolitical disaster, including children reared in orphanages (Carlson & Earls, 1997), cloth-reared monkeys (Boyce, Champoux, Suomi, & Gunnar, 1995), and adolescent survivors of earthquake with subsequent symptoms of PTSD (Goenjian et al., 1996). Yehuda (Yehuda, Boisneaux, Mason, & Giller, 1993; Yehuda, Southwick, et al., 1993) has argued that hypocortisolism may be due to early life stresses that result in a negative regulation of the LHPA axis, which may in turn create an inability to effectively deal with subsequent stressors.

The studies reviewed so far indicate that disruptions in the child's environment may disrupt LHPA functioning and place the child at higher risk for psychopathology. Studies focused on childhood depression illustrate the consequences of LHPA dysfunction on subsequent development. Goodyer and colleagues (Goodyer, Herbert, Tamplin, & Altham, 2000a, 2000b) have found that among healthy adolescents at high risk for depression there is a high correlation between cortisol levels and subsequent diagnoses of Major Depression. In addition, approximately one-quarter of children and adolescents with depression show elevated cortisol levels (Rao et al., 1996). For example, Goodyer and colleagues (Goodyer, Park, & Herbert, 2001) followed a group of clinically depressed 8- to 16-year-olds across a 72-week period, collecting morning and evening cortisol samples for two consecutive days at three points in the study: inception, 36 weeks, and 72 weeks. Those children whose symptoms had not diminished were classified as chronically depressed. The other children were placed in the recovery group. At each of the collection points, the children in the chronically depressed group had higher evening cortisol levels than the children in the recovered group.

In addition, Goodyer, Park, and Herbert (2001) found that adverse life events over the course of the study were associated with elevated cortisol levels at inception. They speculated that cortisol hypersecretion might affect cognitive processes that influence risk for adverse events. Indeed, there are initial indications (E. P. Davis, Bruce, & Gunnar, 2002; Vedhara, Hyde, Gilchrist, Tytherleigh, & Plummer, 2000) that LHPA activity may be related to both the development and current functioning of the prefrontal cortex, specifically the anterior cingulate cortex (ACC). Poor prefrontal functioning has, in turn, been linked to the appearance of behavioral maladjustment (Bush et al., 1999; E. P. Davis et al., 2002) and poor or risky decision making. Given that the ACC is undergoing significant maturation during childhood (Janowsky & Carper, 1996; Rothbart, Posner, & Hershey, 1995), one may speculate...
that this process may impact the observed relationship between cortisol and behavior. Unfortunately, the extant literature cannot at this time address basic questions concerning the direction of the effect and the potential causal bases.

**Future Directions in the Use of Cortisol**

For the most part, studies examining the relationship between cortisol and psychopathology have relied on two basic measures: baseline cortisol and acute cortisol after the introduction of a stressor. These measures have added to our understanding of the impact of the LHPA system on affect and behavior. However, recent work suggests that an additional quantification of LHPA functioning may greatly help. That is, an examination of variations in the diurnal cycle may allow researchers to examine the shape of the cortisol cycle in response to environmental challenges (Gunnar & Vazquez, 2001). An example of this research strategy can be found in the child care studies overseen by Gunnar and her colleagues.

A number of studies have now noted that children in full-time center-based child care often show an increase in cortisol levels throughout the day (Tout et al., 1998; Watamura, Sebanc, & Gunnar, 2002), rather than the expected dip in cortisol seen in children tested in the home setting (Watanura, Donzella, Alwin, & Gunnar, 2003). Watamura et al. (2003) note that cortisol increases appear to emerge in infancy, peak in the toddler years, and disappear by the early school years. The available data suggest that the increase in cortisol is linked to the increasing social demands and complexity of the child’s environment as he or she moves from infancy into toddlerhood (Dettling, Gunnar, & Donzella, 1999; Tout et al., 1998; Watamura et al., 2003). The subsequent downturn in the trend is presumably due to the child’s increasing ease when engaged in social interactions.

The data also suggest that the developmental trends in cortisol production are context-specific. That is, children appear to revert to the “normal” cortisol rhythm when not in the child care setting (Watamura et al., 2003). Because older children in full-day child care also show the expected dips in afternoon cortisol levels, it does not appear that mild environmental challenges, even if relatively frequent, permanently alter the diurnal cortisol pattern. This is in contrast to the abuse and maltreatment literature, which finds that prolonged adversity can flatten the diurnal cycle (Carrion et al., 2002). As such, these data point to the importance of noting individual differences in both context and developmental state when examining cortisol production throughout the day. In this way, research may be better able to capture both the regulatory and reactive functions of the LHPA axis.

**Electroencephalogram**

The use of EEG to assess human behavior and development began quite early with the work of Berger (1929, 1932). Although the first reports were met with skepticism, the measure was soon widely accepted in the biomedical research community, particularly after a live demonstration at a 1935 meeting of the Physiological Society in London convinced people of its usefulness (Davidson, Jackson, & Larson, 2000). Much of the early work was hampered by the fact that reports were largely descriptive, used adult indices of behavior (e.g., alertness) even when dealing with children and infants, and were reliant on cumbersome, and perhaps inaccurate, manual analyses of the EEG data (e.g., J. R. Smith, 1938a, 1938b, 1938c).

Many of the methodological issues limiting the early research were beginning to subside by the 1960s, when Hagne and colleagues (Hagne, 1968, 1972; Hagne, Persson, Magnusson, & Petersén, 1973) began their longitudinal studies of EEG development. The introduction of quantitative EEG analysis through the use of computers and the fast Fourier transform greatly increased the scope of data available to the researcher. These include waveform amplitude (Matousek & Petersén, 1973), absolute and relative power (Clarke, Barry, McCarthy, & Selikowitz, 2001c), dominant and subordinate frequency analysis (Katada & Koike, 1990), mean frequency (Chabot & Serfontein, 1996), the wave percentage time (Matouura et al., 1985), EEG asymmetry (Davidson, 1995), and the coherence of the EEG signal across regions (Chabot & Serfontein, 1996; Thatcher, 1992).

Taking advantage of these technological advances, Hagne was able to emphasize the importance of changes in relative power and peak frequency. For example, she found that the ratio between delta (1.5 to 3.5 Hz) and theta (3.5 to 7.5 Hz) frequency changes between 8 and 12 months of age due to an increase in theta and a decrease in delta (Hagne, 1968, 1972). These shifts in relative power were then linked to patterns of change in behavior.

In addition to examining normal functioning and development, the use of EEG measures to examine psychopathology in adults and children began fairly early. P. A. Davis and Davis (1939), for example, collected resting EEG from a large sample of psychotic adults and found that the patients demonstrated significantly less alpha activity than did control subjects. Later studies also found a similar pattern in
anxious adults (Duffy, 1962). Investigations of ADHD, then known as minimal brain dysfunction syndrome, began in the 1930s (Jasper, Solomon, & Bradley, 1938).

Linked to a relatively long history of EEG experimentation, the past 3 decades have seen exponential growth in the use of EEG measures in psychological research. This section reviews the collection and interpretation of the EEG signal, our current understanding of the normal developmental progression, and its application to the study of developmental psychopathologies.

**Electroencephalogram Methodology**

EEG is collected via electrodes placed on the scalp either singly or by group as part of a net or cap system. Distributed in a standard placement design (Jasper, 1958), the electrodes are referred to by the cerebral lobe their scalp locations are closest to (e.g., F = Frontal, P = Parietal) and their relative location on the scalp (Odd numbers = Left hemisphere, Even numbers = Right hemisphere, z = Midline). The electrical activity recorded via the electrodes is referenced to relatively inactive electrode site(s), and the signal is then saved offline for further processing and analysis. The collected signal is thought to be derived from the summation of postsynaptic potentials. This rhythmic electrocortical activity is regulated by the thalamus (Larson, White, Cochran, Donzella, & Gunnar, 1998), particularly through the nucleus reticularis (Steriade, Deschenes, Domicl, & Mulle, 1985).

Before statistical analyses begin, EEG power is normally aggregated across frequency bins to form measures of band power. Different epochs of the same condition are then averaged to provide more reliable estimates of spectral power, in much the same way as behavioral reaction time data. A more detailed discussion of the steps involved in EEG collection and processing can be found in Davidson, Jackson, et al. (2000) and Pivik et al. (1993).

EEG data are primarily characterized along the dimensions of amplitude and frequency, which are often used to describe the differences across major behavioral states (Pilgreen, 1995). In adults, deep sleep is associated with large and very slow waves in the delta frequency range (1 to 4 Hz). Drowsiness is characterized by reduced amplitude theta activity (5 to 7 Hz), although delta activity is also common. Alpha activity (8 to 13 Hz) is often linked to a state of "relaxed wakefulness," and points of high alert and attention are marked by low-amplitude fast activity (>13 Hz). Much of the literature has focused on quantifying alpha activity in response to experimental task manipulations.

EEG measures have proven particularly attractive in the laboratory because the signal derived has good temporal resolution, in the realm of milliseconds. Indeed, EEG can detect neuronal changes in activity almost instantaneously (Davidson, Jackson, et al., 2000). This is particularly important when dealing with processes that are fast-acting, irregular, and spontaneous, such as emotion. Behaviors that are fleeting (lasting only a second) can be easily detected given that EEG is often sampled 200 times per second. This compares favorably with the long lag times found with functional MRI (fMRI) and PET, compensating for the relatively poor spatial resolution seen in the EEG signal.

On this point, Davidson, Jackson, et al. (2000) argue that even when using high-density electrode arrays, which can collect data from up to 256 sites (compared to traditional 16- and 32-channel collection protocols), EEG recording will always lag behind metabolic and hemodynamic imaging. This is due in part to spatial resolution a full order of magnitude coarser than that found with fMRI, the distortion produced via transmission through the skull, and the fact that a particular distribution of scalp potentials can be produced by different combinations of neuronal generators.

In addition, there are some methodological concerns in collecting EEG that are common when dealing with children. First, the validity of EEG data is dependent on the analysis of a clean signal that is free of motor or movement artifact and was generated under the specific mental states of interest (e.g., at rest or alert attention). However, one cannot instruct infants and young children to either sit still or focus attention solely on the stimuli of interest. As such, researchers rely on both methodological creativity and analytical skill in circumventing these difficulties. For example, Fox (e.g., N. A. Fox, Henderson, Rubin, Calkins, & Schmidt, 2001; N. A. Fox et al., 1995) presents infants with a spinning bingo wheel filled with colorful balls to capture the infant’s attention and minimize extraneous movement. For analysis, these data are then processed to remove any movement artifacts. Even when the difficulties with artifact and attention are minimized, however, there remain concerns over the meaningfulness of the underlying data.

N. A. Fox, Schmidt, and Henderson (2000) point out that electrode placement protocol agreed on for adults (Jasper, 1958) is not necessarily appropriate for use with young children. First, it is not clear if the ratio of distances across electrode sites is stable across development, indicating that our measures may not correspond to the actual geometry or topography of the brain. Second, morphological changes in the brain throughout development may shift the location from which electrical activity is emanating. This would greatly complicate the already thorny issue of localizing the source of the EEG signal.
In documenting the change in EEG functioning over time, a number of researchers caution against using absolute power (Benninger, Matthis, & Scheffner, 1984). In particular, changes in bone thickness, skull resistance, and impedance may distort absolute power values. Instead, relative power may have better test-retest reliability (John et al., 1980) and may be more sensitive to changes in the frequency composition of the EEG with age (Clarke, Barry, McCarthy, & Selikowitz, 2001a). Relative power is expressed as the percentage of power in a specific frequency bin at each electrode site relative to total power (in all frequency bins) at the same electrode site (Marshall, Bar-Haim, & Fox, 2002).

Despite these limitations, the ease of assembling and using the equipment necessary for EEG collection, and its noninvasiveness, has made it a common tool for psychophysiological research with individuals of all ages. This has allowed researchers to document the major developmental changes that take place between the burst-suppression non-state-dependent EEG patterns seen in premature infants (less than 28 weeks conceptual age) and the organized and coherent patterns seen in normal adults. An example can be seen in Marshall et al.'s (2002) study of changes in relative power and peak frequency in children from ages 4 months to 4 years (see Figures 9.1 and 9.2).

In the 1st year of life, activity in the lower frequencies (delta and theta) decreases, whereas alpha activity increases into early adolescence and beta continues to mature into adulthood (M. J. Taylor & Baldeweg, 2002). Indeed, the normal adult EEG pattern is usually not established until 25 to 30 years of age, a point in time that corresponds to the final state of myelination (Pilgreen, 1995). The alpha band, central to many studies, migrates from the 3 to 5 Hz band in the 1st year to 6 to 9 Hz in early childhood and later settles into the 8 to 13 Hz band in adulthood (Marshall et al., 2002). Throughout the process, the rate of maturation is at its most rapid in the posterior cites and its slowest in anterior locations (Benninger et al., 1984; Gasser, Jennen-Steinmetz, Stoka, Verleger, & Mocks, 1988).

Electroencephalogram in the Study of Developmental Psychopathology

Building on these developmental data, quantitative measures of EEG have been used to examine a number of core cognitive (Bell & Fox, 1994) and emotional (G. Dawson, Patagiotides, Grofer Klünger, & Hill, 1992) processes. In both domains, the strategy has been to create a functional link between changes in behavioral performance and the purported underlying neural mechanisms by noting changes in electrocortical signals thought to reflect activity in these same neural mechanisms.

Early on, this work was hindered by the belief that many of the brain regions of interest were not well developed in childhood. The frontal cortex is directly involved in a number of the components underlying higher-order cognition and emotion, including the facilitation of emotional expression, the organization of cognitive processes associated with emotion, and the ability to regulate emotion (G. Dawson, 1994; N. A. Fox et al., 2000). However, the general consensus had long been that there was minimal frontal lobe development until middle childhood (Bell & Fox, 1992). As a result, much of our understanding of the relationship between EEG and development was limited to posterior sites. However, a number of studies have demonstrated that changes in frontal lobe activity occur as early as the 1st year of life (Chugani & Phelps, 1986; N. A. Fox & Bell, 1990), although frontal lobe development does lag behind growth in other brain regions. These studies further emboldened researchers to incorporate these tools in their studying of development.
Figure 9.2  The distribution of the peak frequency of relative power within the 3 to 10 Hz range in the first 4 years of life. The bars indicate the number of participants whose peak frequency fell in each 1 Hz bin. Modal frequencies are indicated for each site and age. Adapted from "Development of the EEG from 5 Months to 4 Years of Age," by P. J. Marshall, Y. Bar-Haim, and N. A. Fox, 2002. Clinical Neurophysiology, 113, pp. 1199-1208.
work. For example, Bell and Fox observed infants performing the A-not-B task monthly from ages 6 to 12 months. Their data provided added support to the notion that A-not-B performance is linked to dorsolateral prefrontal cortex development by showing a significant correlation between EEG power recorded from the frontal sites and performance on the task.

In addition to power and frequency, EEG coherence has proven to be an important tool in assessing early brain development. Coherence quantifies the phase relationship between two processes at a specific frequency band. Coherence can range from 0 (there is no phase relationship) to 1 (the two signals are either completely in or out of phase with each other). Coherence measures will shift over time depending on age and the processes of interest. For example, Thatcher (1992; Thatcher, Walker, & Giudice, 1987) has found that over time there is increased communication between anatomically distant locations, coupled with an increased differentiation across the cortex. These changes may be due to either the activity level of axonal connections across two regions (Nunez, 1981) or the activity of short- and long-fiber networks or the axons (Thatcher, Krause, & Hrybyk, 1986; Thatcher et al., 1987).

Thatcher (Thatcher et al., 1987) has argued that changing patterns of EEG coherence coincide with major points of transition in cognitive growth, providing neural mechanisms by which to explain observed behavioral differences. For example, Bell and Fox (1996) found that EEG coherence in infants who had moderate amounts of experience crawling was higher than in infants with either no crawling experience or who were proficient crawlers. It appears that the increase in coherence coincided with a period of time during which a new, core skill was being consolidated, requiring the coordination of multiple systems. Once mastered, the newly efficient process no longer required as complex a neural substrate for performance.

Beyond EEG findings in normative development, a number of studies have examined the EEG correlates of psychopathology in children and adults. For example, studies in depression indicate that the thalamocortical regulation of EEG rhythm (particularly alpha power) normally seen in adults is disrupted in individuals with depression (Lindgren et al., 1999). This is evident during sleep, which is marked by elevated levels of fast-frequency EEG (>16 Hz) and a reduction of low-frequency activity (Armitage, Hudson, Trivedi, & Rush, 1995) in depressed adults. These findings are of particular interest because sleep disturbances and abnormalities are linked to increased risk for relapse (Giles, Jarrett, Biggs, Guzick, & Rush, 1989) and suicide (Fawcett et al., 1989).

In the developmental literature, the most extensive empirical work has been done with children diagnosed with ADHD. Typically, studies find that children with ADHD have decreased alpha and beta activity most apparent in posterior sites (Chabot & Serfontein, 1996; Clarke et al., 2001c; Lazzaro et al., 1998). In contrast, there is often increased frontal theta (Clarke et al., 2001c; Lazzaro et al., 1998) and posterior delta (Clarke et al., 2001c) activity. The findings are most acute in children who show signs of hyperactivity, as opposed to inattentiveness (Clarke et al., 2003). These data have been interpreted as indicating that children with ADHD are cortically hypoaroused (Lubar, 1991) or have a maturational lag in central nervous system development (Clarke, Barry, McCarthy, & Selikowitz, 1998). The latter interpretation is bolstered by coherence data indicating that children with ADHD show less cortical differentiation than their non-ADHD peers (Barry, Clarke, McCarthy, & Selikowitz, 2002; Chabot & Serfontein, 1996). A thorough review of the EEG literature with ADHD can be found in Barry, Clarke, and Johnstone (2003).

**Future Directions in the Use of Electroencephalogram**

EEG studies in young populations have focused on children with learning or attention disorders (Barry et al., 2003; Marshall, Fox, & BEIP Core Group, 2004). These studies have generally found increases in low-frequency spectral power (e.g., delta and theta) and decreases in high-frequency spectral bands (e.g., alpha or beta). Until recently, very few studies have examined the effects of environment or sociocultural risk on EEG functioning. Among these studies, it appears that environmental deprivation may keep theta and delta power levels elevated beyond the normal developmental period (Harmony et al., 1988; Harmony, Marosi, Diaz de Leon, Becker, & Fernandez, 1990), whereas enrichment may depress theta and delta power (Raine et al., 2001). Given the extensive behavioral data indicating the effects of adverse environments, such as maternal depression (Field et al., 1998; G. Dawson & Ashman, 2000), institutionalization (Carlson & Earls, 1997), and abuse (Cicchetti & Toth, 1995), on socioemotional development, this appears to be an important avenue of study that could benefit from the introduction of EEG measures.

For example, Marshall et al. (2004) compared resting EEG in a group of institutionalized infants in Bucharest, Romania, to age-matched children living with their families in the greater Bucharest area. They found that the children in the institution showed more relative power in the lower-frequency bands and less relative alpha power than their community-based counterparts. In light of similar
data from children with ADHD (Barry et al., 2003) and Autism (G. Dawson, Klinger, Panagiotides, Lewy, & Castellow, 1995), it may be that EEG activity across power bands may serve as a marker for deviations or lags in development that are common to a variety of disorders or contexts (Marshall et al., 2004). This is in line with Keller et al.’s (2000) note that EEG power is multidetermined and driven by a number of summing and overlapping mechanisms. Comparisons across groups and contexts, such as those noted here, may allow us to better delineate the functional significance of resting EEG activity.

MEASURES OF MOTIVATION AND EMOTION

The use of psychophysiological methods to study emotion and motivation are relevant to the study of developmental psychopathology, particularly for disorders of affect and disinhibition. Measures covered in this section tap into the physiological substrates of the neural fear system and of the appetitive/aversive motivational systems and include EEG asymmetry and affective modulation of the startle reflex.

Electroencephalogram Asymmetry

Like the ERP, EEG asymmetry is derived from measures of raw EEG power, and, like the ERP, measures of the relative difference in activation across sites provide an additional perspective on the links between physiology and behavior. In particular, differences in EEG asymmetry have been used to examine individual differences in motivation systems both as a stable individual trait and in response to transient environmental characteristics. Indeed, the relative difference in activation across sites may be more important in determining behavior than the absolute amount of activation in a region (Davidson, Chapman, Chapman, & Henriques, 1990). This is borne out in part by the very extensive literature linking asymmetries in EEG activity to individual differences in affect in both healthy and clinical populations.

Electroencephalogram Asymmetry Methodology

EEG asymmetry is normally calculated by comparing power in two homologous electrodes (e.g., F3 and F4). Frontal EEG asymmetry is determined by subtracting the natural log of alpha power seen in the left electrode from the natural log of the alpha power in the right electrode \((\ln F4 - \ln F3)\). Because EEG power is inversely related to activation, a negative number indicates that an individual is showing more activity in the right frontal lobe relative to the left (Davidson, Jackson, et al., 2000). It is also important to note the level of activity within each lobe as this will help to explain the pattern (e.g., hyper- or hypoactivation in a particular location across individuals or conditions) underlying a particular asymmetry finding (Schmidt, 1999).

Electroencephalogram Asymmetry and Developmental Psychopathology

Davidson (1984a, 1984b, 1995) and others have argued that resting frontal EEG activation reflects an underlying motivation bias to respond to the environment in a particular hedonic manner. Individuals with right frontal EEG asymmetry are more likely to respond to the environment with negative or withdrawal emotions and behavior. In contrast, individuals showing left frontal EEG asymmetry are more likely to exhibit positive or approach responses. For example, studies have found that adults who display a pattern of greater right frontal asymmetry at rest rate film clips more negatively (Tomarken, Davidson, & Henriques, 1990) and are less sociable in a dyadic interaction (Schmidt & Fox, 1994) than are individuals with left frontal EEG asymmetry at rest.

Schmidt (1999) found that female undergraduates who rated themselves as high in shyness were likely to show right frontal EEG asymmetry due to left frontal hypoactivation. Their sociable counterparts, on the other hand, displayed more left frontal asymmetry. Schmidt further decomposed the data to compare participants who were high in shyness but varied in their level of sociability. He found that these two groups differed in the absolute power in the left frontal lobe, suggesting that there may be different types of shyness distinguishable at the behavioral (Cheek & Buss, 1981) and psychophysiological (Schmidt & Fox, 1994) levels.

Work by Tomarken and colleagues (Tomarken, Davidson, Wheeler, & Kinney, 1992) suggests that differences in asymmetry observed across individuals are rooted in functional, not structural, differences in the brain. As such, EEG asymmetry reflects functional changes in activity as well as underlying motivational biases. For example, individuals who show a pattern of left frontal asymmetry at rest may display right frontal asymmetry when presented with aversive film clips (Jones & Fox, 1992; Tomarken et al., 1990).

Adults who exhibit a stable pattern of right frontal EEG asymmetry over the course of 3 weeks report more intense negative affect when presented with negative emotional film clips (Wheeler, Davidson, & Tomarken, 1993). Participants in the same study who displayed stable left asymmetry reported more intense positive emotion when presented with positive film clips. It appears that stable patterns of
asymmetry do not simply increase general arousal, creating more intense affective responses across the board. Rather, the motivational or processing bias appears to be limited to a particular region in the affective spectrum.

EEG asymmetry may serve as a psychophysiological marker of risk for maladaptive behaviors and psychopathology. Right frontal EEG asymmetry appears to be linked to difficulty in regulating negative arousal, a bias toward negative affect, and the display of withdrawal behaviors when confronted with threat—factors that are all related to psychopathology and maladaptation.

In the adult literature, depressed individuals display less left frontal activation (Henriques & Davidson, 1991) and greater right frontal activation (Henriques & Davidson, 1990) than nondepressed individuals. Supplementing the frontal asymmetry literature, Heller (1993) has suggested that emotional functioning may also be modulated by activity in posterior brain regions. Specifically, Heller has found that depressed individuals show less EEG activity in right parietal sites. This has been replicated in a number of studies with varying experimental tasks (e.g., Bruder et al., 1995; Keller, Deldin, Gergen, & Miller, 1995) and is thought to reflect the hyperarousal often found in depression (Heller & Nitschke, 1997).

Anxiety has also been linked to greater right frontal activity, specifically in Panic Disorder (Reiman, Raichle, Butler, Herscovitch, & Robins, 1984), Generalized Anxiety Disorder (Wu et al., 1991), social phobia (Davidson, Marshall, Tomarken, & Henriques, 2000), and nonclinical individuals self-rated as high in trait anxiety (Reivich, Gur, & Alavi, 1983). Here, the direction of the effect indicates that anxiety is marked by elevated levels of negative affect and withdrawal tendencies, coupled with increased autonomic arousal. This is borne out in data indicating increased EEG activity in parietal sites (Heller, 1993).

Paralleling the adult literature, a similar pattern of frontal EEG asymmetry has been found in the 1st year of life. Davidson and Fox (1982) found that 10-month-old infants were more likely to show left frontal asymmetry when viewing a person smiling than when presented with the same individual crying. Infants of the same age also show shifts in EEG asymmetry in response to the approach of an unfamiliar adult (N. A. Fox & Davidson, 1987) and maternal separation (N. A. Fox & Davidson, 1988).

EEG measures at baseline also predict later behavior, such that infants with right frontal asymmetry will cry sooner to maternal separation than will infants with left frontal asymmetry (Davidson & Fox, 1989). In early childhood, children with right frontal asymmetry are also more likely to be behaviorally inhibited and show difficulty with social interactions (e.g., N. A. Fox et al., 1995, 2001). Infants who displayed a stable pattern of right frontal asymmetry across time also show a stable pattern of behavioral inhibition across progressively larger time windows of 2 (N. A. Fox, Calkins, & Bell, 1994), 4 (N. A. Fox et al., 2001), and 7 years.

Henderson, Fox, and Rubin (2001) found that infant temperament predicted social wariness in early childhood only for those children who displayed a pattern of right frontal EEG asymmetry in infancy. School-age children asked to prepare a potentially embarrassing speech, a task designed to elicit social stress, showed increases in right frontal EEG asymmetry that paralleled increases in anxiety (Schmidt, Fox, Schultkin, & Gold, 1999). Baving, Laucht, and Schmidt (2002) assessed EEG asymmetry in anxious children at ages 8 or 11 relative to nonanxious control groups and found that anxious girls showed more right frontal asymmetry.

In addition, parallel data indicate that children who consistently display high levels of sociability in the first 4 years of life were more likely to exhibit left frontal EEG asymmetry (N. A. Fox et al., 2001). However, increased sociability, when coupled with right frontal EEG asymmetry, may place a child at increased risk for externalizing behavior problems (N. A. Fox, Schmidt, Calkins, Rubin, & Coplan, 1996).

Future Directions in the Use of Electroencephalogram Asymmetry

EEG asymmetry has been used to examine both individual and group differences in motivational and affective biases. The measure has provided a theoretically grounded and empirically supported mechanism by which to gauge trait- and state-based variations in a core psychological construct. Future work, while continuing on this path, will also need to examine secondary measures that may moderate the relationship between EEG asymmetry and behavior. As an example of exogenous and endogenous factors that may shape individual differences in EEG asymmetry, our discussion now briefly turns to the effects of parental characteristics (exogenous) and gender (endogenous) on the relationship of interest.

Psychopathology in children arises from multiple factors, including temperament, environmental characteristics, and parenting. As a result, developmental outcomes must be placed in the context of development to be fully understood. Based on this understanding of pathogenesis, a great deal of research has focused on the impact of maternal depression on infant physiology and behavioral outcomes. Women who are depressed display less positive
affect toward their infant, provide less stimulation (Field et al., 1988; Jones, Field, & Davlos, 2000), and often display unpredictable response patterns to their child's distress (G. Dawson & Ashman, 2000). Infants of depressed mothers, who are at a greater risk for future disorders (e.g., Murray & Cooper, 1997), display less positive affect and increased irritability (Cohn, Matias, Tronick, Connell, & Lyons-Ruth, 1986: Field, 1986; Field et al., 1985) and show greater frontal activation (Field, Fox, Pickens, & Nawrocki, 1995; G. Dawson, Grofer Klinger, Panagiotides, Hill, & Speiker, 1992) than do infants with nonsymptomatic mothers. In early childhood, these children are also more likely to show greater levels of behavioral maladaptation, particularly internalizing problems (Ashman, Dawson, Panagiotides, Yamada, & Wilkinson, 2002).

These data indicate that parental characteristics shape psychophysiology in the first years of life, although we do not have the research needed to determine the relative importance of environmental and heritable factors. However, it does appear that the effects of exposure to risk factors for later maladaptation are evident within the individual very early, perhaps within the first 3 months of age (Field et al., 1995). These effects have also been shown to carry on into early childhood, such that preschoolers with depressed mothers show greater right frontal EEG asymmetry and manifest less empathic responses to distress in others (Jones et al., 2000).

In terms of endogenous factors that may affect the link between EEG and behavior, there is growing evidence that the pattern of EEG asymmetry and its relationship to affect and behavior vary as a function of gender in both children (Baving, Laucht, & Schmidt, 1999, 2002; Henderson et al., 2001) and adults (e.g., Kline, Allen, & Schwartz, 1998; Kline, Blackhart, & Schwartz, 1999). These findings are joined by gender-linked differences in raw EEG patterns among depressed individuals (Armitage et al., 2000; Armitage, Hudson, Trivedi, & Rush, 1995). This underscores studies indicating that Major Depressive Disorder is twice as prevalent in adolescent and adult females as in their male counterparts (Angold, Erkani, Silberg, Eaves, & Costello, 2002; American Psychiatric Association, 1994) and suggests that measures of EEG asymmetry may reflect the differential mechanisms at play.

Taken together, the adult and developmental data indicate that EEG asymmetry may reflect stable individual differences in temperament and motivation that are early appearing and may endure into adulthood. Resting frontal EEG asymmetry may reflect the valence of the motivational or affective bias, and the absolute power of the EEG signal may reflect the intensity of the affective experience (Schmidt & Fox, 1999).

Measures of electrocortical activity have proven to be extremely useful in developmental psychopathology. The technology is noninvasive, relatively easy to employ, and amenable to use across a wide age spectrum. As a result, researchers have available to them a set of interrelated, but distinct, measures to address questions of trait-level differences in functioning and motivation as well as changes that occur in response to change in the environment.

Affective Modulation of the Startle Reflex

The startle reflex is a defensive response, and hence, theoretically, should be enhanced when an organism is presented with an averse or threatening stimulus. This is the basis for research that uses the startle paradigm to explore emotional reactivity. According to P. J. Lang (1995, p. 372), "Defensive reflexes, including startle, increase in amplitude when an organism is aversively motivated... and defensive reflexes are reduced in amplitude when an organism is positively motivated." It is not within the scope of the current work to provide a depth of knowledge into the nature and the neural circuitry involved in such appetitive and aversive motivational systems (see P. J. Lang, 1995, for a full review). However, there is considerable evidence to support this claim, as Davis and colleagues (M. Davis, Hitchcock, & Rosen, 1987) have documented that the neural circuitry involved in conditioned fear is the same as that involved in fear-conditioned startle potentiation. Two neural circuits are believed to be responsible for fear-potentiated startle in rats. The first is the primary brain stem pathway, which transfers auditory input to the reflex effectors vis-à-vis the reticular formation. The second path mitigates transmissions in the primary circuit, as projections from the central nucleus of the amygdala to the reticular locus of the primary pathway described earlier. Davis and his colleagues have shown that the primary neural circuit attenuates or ameliorates startle responses. Additionally, lesions of the amygdala have been found to eradicate the startle response (Boulis & Davis, 1989; Hitchcock & Davis, 1986; Rosen & Davis, 1988).

According to M. M. Bradley, Cuthbert, and Lang (1999), affective modulation of the startle reflex is a robust method for measuring the activation of the underlying appetitive and aversive, or approach-withdrawal, systems, particularly because it captures the state of the organism prior to the onset of fight/flight behavior. The startle reflex itself is an index of the preparatory state of the organism...
Affective Modulation of Startle Methodology

The methods of data collection for the startle paradigm were previously discussed in this chapter (see discussion of prepulse inhibition). The setup and collection of data in studies that seek to explore affective modulation are identical in terms of lead placement and outcome measure (magnitude of the blink reflex following a startling probe). However, whereas studies of prepulse inhibition involve manipulation of the timing of the lead interval of a nonstartling, benign, prepulse stimulus, the paradigm to assess affective modulation involves manipulating the affective state of the subject prior to or during presentation of the startle probe.

Lang and his colleagues have explored the affective modulation of the startle reflex for well over a decade and have provided empirical support for the notion that the amplitude of the startle reflex varies systematically based on the ongoing emotional valence of individuals. Using a sample of undergraduates, Vrana, Spence, and Lang (1988) showed that acoustic startle probes were augmented during the presentation of negatively valenced slides, which included photographic stimuli of such unpleasant images as starving children, angry human faces, violent death scenes, and an aimed gun. In contrast, when undergraduates viewed positively valenced pictures such as those depicting happy babies, attractive nudes, and chocolate, startle responses to acoustic probes were attenuated. A later study (M. M. Bradley, Cuthbert, & Lang, 1990) extended this early work by demonstrating a linear relationship between the degree of emotional arousal participants reported while viewing foreground stimuli and startle potentiation, beyond the potential effects of startle probe modality (i.e., acoustic versus visual) and participant self-reported interest in the foreground stimuli. Another study by this research group (Cuthbert et al., 1996) showed that the affective modulation of startle potentiation is linearly related to the degree of arousal of the foreground stimuli, such that blink potentiation in the presence of negative stimuli and blink inhibition in the case of positive stimuli were most pronounced when participants reported that the corresponding stimuli elicited high degrees of arousal.

Affective Modulation of Startle and Developmental Psychopathology

The developmental literature on the role of startle modulation in both normative and abnormal processes is still in its infancy. Indeed, very few published studies have examined the role of affective modulation of startle in infants or children, and the little work that has been done has yielded mixed findings. In her study of 5-month-old infants, Balaban (1995) found early evidence for the emergence of the adult affectively modulated startle responsiveness. Specifically, infants showed startle potentiation while viewing pictures of happy faces and attenuated eyeblink magnitude while viewing photos of angry faces. In contrast are two known studies that sought to replicate this pattern in older children. McManis, Bradley, Cuthbert, and Lang (1995) examined affective startle modulation in children ages 7 to 10 and found no evidence of a generalized adult-like response pattern, although further analyses revealed that girls showed the typical affectively modulated pattern but boys did not. Similarly, Cook, Hawk, Hawk, and Hummer (1995) found no evidence of the affective modulation of startle in their school-age sample. Given only the infant evidence, it could be concluded that affective modulation of the startle reflex is salient in the early months of life. However, Cook et al. and McManis et al. show no evidence for the phenomenon in middle childhood. As pointed out by Ornitz (1999), there is much yet to be learned about the normal development of affective modulation of startle. Certainly, three studies alone do not provide sufficient resolution to this issue. For instance, one plausible explanation forwarded by Ornitz for the infant findings in light of the null findings for the same effect in older samples is that the infant pattern of responding is due to attentional focus, in that angry faces perhaps mark a more novel, and therefore interesting, set of stimuli to infants than neutral or happy faces.

Given the general scarcity of findings of affective modulation of startle in children, normal or atypical, one must turn to the adult literature to consider the contribution and relevance of the paradigm to issues related to developmental psychopathology. The degree of affective modulation in the startle response has been examined in studies of
psychopaths (Patrick, Bradley, & Lang, 1993) and fearful (Cook, Hawk, Davis, & Stevenson, 1991) and clinically depressed (Allen, Trinder, & Brennen, 1999) adults and in anxiety disorders, including PTSD (Morgan, Grillon, Southwick, Davis, & Charney, 1995) and specific phobia (Hamm, Cuthbert, Globisch, & Vaitl, 1997; Vrana, Constantine, & Westman, 1992).

Perhaps the best evidence for the contribution of the startle paradigm to the study of abnormal psychological development comes from the literature investigating the affective modulation of startle response in criminals and psychopaths (Patrick, 1994; Patrick et al., 1993). By definition, psychopathic individuals show marked abnormalities in affective responsiveness. According to Cleckley’s (1976) criteria, individuals with primary psychopathy manifest antisocial behaviors due to an underlying deficit in emotional processing. Lykken’s (1957) landmark study revealed that, relative to normal controls, psychopathic adults showed less anxiety on measures of self-report, less galvanic skin response reactivity to a conditioned shock, and less avoidance of punishment during a test of avoidance learning. This work provided the earliest evidence that the primary deficit in psychopaths involves a lack of anxiety. The predominant theory of psychopathy still contends that the central deficit in individuals who meet the criteria for true psychopathy is a lack of behavioral inhibition in response to punishment or nonreward (Fowles, 1980; Patrick, 1994).

According to Patrick (1994), the literature offering evidence for a lack of fear in psychopathic samples is limited by the use of autonomic indices, which confound assessments of the behavioral inhibition system with more generalized sympathetic arousal and higher-level processing. Further, although autonomic measures such as electrodermal activity should, theoretically, increase with activation of the behavioral inhibition system (Fowles, 1980), empirical support for this claim in normative samples does not abound (e.g., see Fowles, Kochanska, & Murray, 2000; Keltikangas-Järvinen, Kettunen, Ravaja, & Näätänen, 1999). Hence, autonomic measures fail to provide satisfactory evidence for Lykken’s (1957) and Cleckley’s (1976) notions regarding the affective deficit involved in psychopathy.

Patrick and his colleagues (1993) used startle methodology and autonomic measures to examine affective processing of psychopathic and nonpsychopathic men among a population of incarcerated sex offenders. They examined the degree of startle potentiation during the presentation of emotionally pleasant, unpleasant, or neutral pictures. Results showed that there were no statistically significant differences between incarcerated, nonpsychopathic men and a control sample of college students. In other words, for these two groups, startle responses were appropriately inhibited during presentation of positive stimuli and potentiated during presentation of negative stimuli.

In stark contrast was the psychopathic group, who not only failed to show startle potentiation during the presentation of the negatively valenced photos, but instead showed an inhibition in their blink amplitude relative to neutral slides. Hence, the psychopathic group manifested startle inhibition during presentation of both positively and negatively valenced stimuli, providing profound evidence that the nature of emotional processing between these two groups is quite discrepant. An additional subgroup of men in the study who were classified as “mixed” fell between the cutoff for clinical diagnosis of psychopathy but scored higher than average on the index of psychopathy used in this study. When this subgroup was added to the group of psychopaths, a correlation was found between degree of emotional detachment and startle potentiation to negative stimuli, such that individuals who were the most emotionally detached showed the highest levels of startle inhibition during presentation of negative stimuli (or the reversed startle potentiation effect). No between-group differences were found for autonomic response patterns: All participants showed increases in skin conductance reactions to both positive and negative stimuli and all showed normal patterns of heart rate deceleration.

**Future Directions in the Use of Affective Startle**

The application of the startle paradigm to the study of psychopathy by Patrick and his colleagues (1993) has yielded important contributions that would not have been obtained via the use of other psychophysiological measures. We suggest that startle methodology holds great promise for the early assessment of psychological risk. Methodologically, data collection is relatively clear-cut and lends itself to work with young children and infants. The ability to tap “pure” responses directly based on the neural circuitry involved in the processing of fear and pleasure (Ornitz, 1999) makes interpretation of startle data quite clean.

One logical extension of the current work in affective startle is to attempt to replicate the findings of Patrick and his colleagues (1993) in samples of children and/or adolescents. For instance, an examination of affective startle responses in a clinical sample of conduct disordered boys is currently under way in our laboratory. This work will extend the work of Patrick and his colleagues in psychopathy by establishing the degree to which the physiologically based absence of fear manifest by adult criminal samples is evident among the group of children who are at greatest risk for subsequent development of the adult condition.
One study by Schmidt and Fox (1999) also demonstrates the benefits of using the startle methodology to assess degree of risk for deviant development. Schmidt and Fox found amplified fear-potentiated startle in a subgroup of negatively reactive 9-month-olds at risk for behavioral inhibition in childhood, which can act as a precursor to anxiety disorders in childhood. This increase in startle amplitude was specific to a laboratory stranger approach paradigm, as no differences in baseline startle were found. This work provides evidence that amplified startle responses may be used as an index of early risk for the subsequent development of anxiety-related conditions.

In short, although the developmental literature in affective modulation of startle is far from sufficient, adult studies such as those of Patrick and his colleagues (Patrick, 1994; Patrick et al., 1993) and infant work by Schmidt and Fox (1999) illustrate the potential benefits of applying the measure to young samples who are at risk for the development of conditions associated with the processing of fear, be it increased or deficient fear-related reactivity. Of particular importance, following such children who have manifested early behavioral and physiological risk across childhood and adolescence will enable researchers to explore the degree to which environmental factors alter the developmental trajectories of children marked by psychologically substantiated risk.

CONCLUSIONS AND FUTURE DIRECTIONS

Unlike many chronic diseases, psychopathology, in the form of either the diagnosable disorder or its developmental precursors, is often evident early in life (Giaconia, Reinherz, Silverman, & Pakiz, 1994; Institute of Medicine, 1989; World Health Organization, 2000). This early appearance is a vital component of attempts to both treat and prevent psychopathology in the population. This is in line with Kohlberg, LaCrosse, and Ricks's (1972, p. 217) view that the ability to predict outcome is the “single most important area of study of clinical theory and practice with children.” Yet, although researchers and clinicians are skilled at describing and categorizing these early phenotypes, their larger work is hampered by the fact that the phenotypes are only moderately predictive of later psychopathology (Kagan, 1994).

In addressing these concerns, Stroufe and Rutter (1984) have made the distinction between developmental coherence and developmental stability. That is, although psychologists have found very few traits or abilities that remain truly stable over time, the course of an individual’s development is both lawful and coherent in nature. They argue that continuity lies not in the presence of a specific behavior across time, but in the lawful relationship between early and later behavior, even if the link is exceedingly complex. This is true in the case of both normative and atypical development (Cicchetti & Stroufe, 1978). This view of development as a dynamic yet lawful progression suggests that researchers must rely on multiple measures, collected over time, to describe and assess the relationships among the components within the person-biology-experience structure. These multiple measures are then used to assess multiple components of the observed outcomes. These include the factors, processes, and mechanisms involved in producing both typical and atypical development (Garvey, 1996).

In looking for the antecedents of later psychopathology, researchers familiar with the adult presentation of a disorder may begin their study of children by trying to find phenotypically similar behaviors in the young. For example, does the 7-year-old bipolar child behave similarly to the 27-year-old bipolar adult (Biederman et al., 2003; Tillman & Geller, 2003)? The same is true for high-risk studies in which risk is linked to one prescribed outcome. Erlenmeyer-Kimling (1996) points out that many Schizophrenia studies predicted that their participants would either be “manifestly schizophrenic or clinically unremarkable.” Instead, the data indicate that children at risk for a specific disorder can display their vulnerability in a wide variety of behaviors. These findings reinforce Stroufe and Rutter’s (1984) suggestion that researchers may do better in deemphasizing phenotypic mirrors throughout development and instead focus on failures in adaptation, which are defined through core developmental issues.

As the preceding discussion makes clear, psychophysiological measures are ideal for this work. Varying in the systems of interest, the time course of measures, and the psychological constructs addressed, psychophysiological measures, particularly when used in combination, can provide an additional window onto the psychological mechanisms underlying both risk and resilience in early development. The flexibility found in psychophysiology allows researchers to address some of the core questions surrounding developmental psychopathology. To illustrate, we can use Keller et al.’s (2000) summary of important questions that the field of developmental psychopathology should address.

First, what are the psychological and physiological causes of the psychophysiological differences? Systematic
use of psychophysiological measures that are anatomically and functionally well-defined, like the startle response, in conjunction with traditional behavioral measures, will help target the root forces underlying observed differences. Second, at what stage of processing do individuals with psychopathology begin to diverge from controls? This question can be answered at the micro level across the span of milliseconds, as seen in the ERP, or at the level of the relatively laconic LHPA system. Third, under what conditions are individuals with psychopathology able to mimic controls in their performance of mental operations? This question is analogous to studies attempting to examine the conditions under which children display adult-like performance on a task. Psychophysiological measures allow researchers to address this question across a number of domains, from cognition to motivation and emotion. Fourth, do the processing differences seen within or across diagnostic groups reflect a deficit or a compensatory tactic? This question is of particular interest when comparisons between psychophysiological and behavioral data show a dissociation in findings. If, for example, two groups of children display identical behavioral outcomes in a task but diverging psychophysiological functioning, one may then begin to explore the possibility that the groups are using different strategies or processes to achieve the presented goal.

In addition to Keller et al.'s (2000) questions, psychophysiology can also help address two interrelated issues of central importance in developmental psychopathology: differential diagnosis and comorbidity. To date, Diagnostic and Statistical Manual of Mental Disorders diagnostic categories are almost exclusively reliant on observed behavior coupled with self- or parent report (American Psychiatric Association, 1994). However, as our understanding of the biological substrates of behavior grows, it may be wise to incorporate psychophysiological measures into the diagnostic process. The early work in this process can be illustrated by recent research with ADHD. ADHD is a highly comorbid disorder often co-occurring with Conduct Disorder and Oppositional Defiant Disorder (Bird, Gould, & Staghezza-Jaramillo, 1994), anxiety disorders (August, Realmuto, MacDonald, & Nagent, 1996), depression (Woolston et al., 1989), and learning difficulties (August & Garfinkel, 1990). For example, 40% to 70% of children with ADHD are also diagnosed with either ODD or CD (Banaschewski et al., 2003), and these children tend to exhibit more psychosocial difficulties than their counterparts who also have ADHD but show no co-occurring psychopathology (Kuhne, Schacher, & Tannock, 1997).

Recent work has attempted to aid diagnosis and classification through the use of psychophysiological measures. For example, Mann et al. (Mann, Lubar, Zimmerman, Miller, & Muenchen, 1992) found that EEG measures incorporated into a discriminant function analysis could accurately predict group membership 80% of the time. Chabot and Serfontein (1996) found that a similar analysis using nine EEG variables had a correct classification rate of 95% and 93% for ADHD and non-ADHD children, respectively. Clarke and colleagues (Clarke, Barry, McCarthy, & Selikowitz, 2001b) used EEG-based cluster analyses to create three distinct subtypes within their sample of boys with ADHD. In a related vein, Banaschewski et al. (2003) have used ERP component differences to argue that ADHD comorbid with Conduct Disorder constitutes a "separate psychopathological entity" from ADHD in its pure form.

With the addition of new sources of information, particularly if they bring information from a different level of functioning, we may better define the boundaries and characteristics of our target population (Kagan, 1996). This allows the researcher to reduce the amount of heterogeneity within a group or even create subgroupings (Cicchetti & Rogosch, 1996; Richters, 1997). In this way, research can continue with greater precision, parsing out the multiple pathways to and manifestations of an underlying maladaptation. From a historical perspective, the addition of new technology, coupled with rigorous methodology, has moved the study of pathology in childhood from the nineteenth century's reliance on "degeneracy" as the broad-brush answer to maladaptation (S. H. White, 1996) to the current complex, and perhaps confusing, network of explanatory mechanisms.

Further complicating our understanding of deviant processes underlying pathological states is the dynamic nature of the system itself. Although the use of psychophysiological indices provides a window onto the biology underlying behavior, these measures are not impervious to contextual forces. Indeed, the transactional model set forth by Sameroff and Chandler (1975), which emphasized dynamic relationships between the child and his or her environment across time, is quite meaningfully applied to studies of psychophysiology, as physiological mechanisms reorganize in response to environmental demands (Campos et al., 1989). Our model of neuroplasticity holds that behavioral change is the result of a complex series of transactions between genetic programs that direct the formation and connectivity of brain structures and environmental modifiers of these codes (N. A. Fox, Calkins, & Bell, 1994). An emergent
body of literature supports this notion, as changes in physiology based on environmental circumstances have been documented in humans (N. A. Fox et al., 2001) and nonhuman primates (Bennett et al., 2002). Curtis and Cicchetti (2003, p. 803) have indicated that "the incorporation of a biological perspective into research on resilience still requires adherence to a dynamic, transactional view that respects the importance of context."

Given such evidence, it is clear that the field of physiology will make a significant contribution to the study of psychopathology only by rising to the challenges posed by the transactional model of development. One way to do this is by studying children early—an option nicely accommodated with the use of psychophysiological measures. Groups found to be at risk behaviorally and/or physiologically should then be followed at critical junctures of development and reevaluated not only behaviorally or psychophysically but also in terms of the presence or absence of environmental stressors. Indeed, Sameroff and MacKenzie (2003) caution that the success of such models hinges on the outlining of a careful schedule of assessments that target the developmental periods when the environment and the child are most likely to be altered by each other (and hence most likely to change).

It is because of the bidirectional environment-physiology relationship that developmental psychophysiology holds great promise for the study of developmental psychopathology, as psychophysiological measures allow for the quantification of proximal influences at the most basic biological level. However, our greatest potential for contribution may also be our downfall, as research attempts that fail to monitor the degree of change in physiology in accordance with the presence or absence of relevant ecological influences will lead to short-sighted, overly simplistic conclusions. Research programs that adhere to transactionally oriented designs will likely be the most profitable in advancing current understanding regarding the antecedents and consequences of normative and aberrant development. Indeed, measures of psychophysiology reflect only one dimension of an intricate ensemble of systems, individual and contextual, which together alter the course of development.

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