Use of Event-Related Potentials in the Study of Typical and Atypical Development

CHARLES A. NELSON, III, PH.D. AND JOSEPH P. McCLEERY, PH.D.

ABSTRACT
A variety of neuroimaging tools are now available for use in studying neurodevelopment. In this article, we focus our attention on one such tool—the event-related potential (ERP). We begin by providing an overview of what ERPs are, their physiological basis, how they are recorded, and some constraints on their use. We then provide an abbreviated glossary of ERP components, that is, what processes are reflected in ERPs. We conclude by summarizing two areas of atypical development that have benefited from this method: children experiencing early psychosocial neglect, and children diagnosed with autism. We conclude by offering recommendations for future research. J. Am. Acad. Child Adolesc. Psychiatry, 2008;47(11):1253–1262. Key Words: ERP, autism, brain development, faces.

In 1997, Nelson and Bloom lamented the paucity of research elucidating the neural bases of behavioral development. For the ensuing 10+ years, the field of developmental cognitive neuroscience has gained considerable traction, with entire single-authored and edited volumes dedicated to this field, along with special issues of journals (e.g., Journal of Cognitive Neuroscience, Neuropsychologia: Developmental Review). Among the many reasons for the progress of this field has been the advances made in neuroimaging. Specifically, the refinement of existing tools (e.g., event-related potentials [ERPs], functional magnetic resonance imaging) and the development of new tools (e.g., functional near infrared spectroscopy) have now made possible the ability to examine the neural correlates of cognitive and emotional development.

In this article, we focus our attention on one particular tool—the recording of the ERP. The ERP reflects the brain’s electrical activity recorded from electrodes placed on the scalp surface and can be used across the entire life span, thereby permitting one to use the same methodological tool and dependent measure across a broad range of ages.

WHAT IS THE ERP?
Event-related potentials represent the synchronous activation of electrical fields associated with the activity of large populations of neurons. This activity volume conducts to the scalp surface and is configured in such a way that their individual electrical fields summate to yield a dipolar field (a field with positive and negative charges between which current flows).

Event-related potentials reflect changes in the brain’s electrical activity in response to a discrete stimulus or event. They are typically collected during the presentation of stimuli that repeat many times. Recording generally begins 100 or more milliseconds before a stimulus is presented and then continues for 500 to 2,000 milliseconds after the stimulus has terminated. Each “trial” or epoch is generally averaged to eliminate background noise that is not related to the stimulus of interest. As a result of averaging, the noise theoretically

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Correspondence to Charles A. Nelson III, Ph.D., Laboratories of Cognitive Neuroscience, 1 Autumn Street, 6th Floor, Marlboro 713, Office A0621, Boston, MA 02215; e-mail: charles.nelson@childrens.harvard.edu.

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goes to zero, and the signal emerges from the background, yielding a series of positive and negative deflections—so-called components—in the ongoing EEG, each of which is presumed to reflect a different neural and perceptual/cognitive operation. Because of the high temporal resolution (on the order of milliseconds), ERPs are well suited to index changes in the mental chronometry of a given neural response.

**HOW DOES ONE COLLECT ERPS?**

Until recently, one typically recorded from 32 or fewer electrodes, mostly because of limitations in how electrodes were fixed to the scalp and in the size of the amplifiers. However, the field has increasingly moved to higher-density arrays of electrodes, made possible by new means of applying electrodes and the miniaturization of the hardware. As a result, it is common for many investigators to record from 64, 128, or even 256 electrodes. The advantages to these larger arrays are multiple. First, the greater spatial sampling permits one to identify components that might have eluded capture with smaller arrays, where the interelectrode distances were greater. Similarly, greater spatial sampling permits one to distinguish one component from another based in part on scalp topography. Third, great advances have been made in source modeling/localization, which depend critically on the use of many electrodes. A final benefit, which has little to do with science per se, is that some dense array systems are quick and easy to put on, such as the EGI electrode net. As a result, this makes possible the ability to test, using many electrodes, infants or other difficult-to-test children.

**WHAT PROCESSES HAVE BEEN INVESTIGATED USING ERPS?**

Topics that have received the most attention in ERP research include recognition memory, attention, working memory, executive functions, auditory and visual sensory processing, face processing, and language processing. In this section, we review a selection of the processes that have been examined in developmental populations using ERPs and some of the associated ERP components, with an emphasis on those that are most relevant for a developmental approach to studying psychiatric disorders. We also include a glossary of these and other ERP components in this section (Table 1).

**Sensory Processing**

An auditory sensory component relevant to developmental psychopathology research is the mismatch negativity (MMN). The MMN is a negative-going component recorded from centrofrontal electrodes approximately 175 milliseconds after a rarely presented auditory stimulus, reflecting an automatic change-detection response. This early obligatory component is present from birth through adulthood, typically presented and analyzed as a difference wave (i.e., standard stimulus waveform minus oddball stimulus waveform), and is robust to cognitive state to such an extent that it occurs not only when participants are ignoring the stimuli but also when they are engaged in a cognitively demanding task in another modality. The MMN reflects the earliest stage of obligatory auditory attention and is generally believed to be the outcome of a mechanism that compares current auditory input with memory traces from previous auditory inputs and signals (but see also reference). The MMN has already been used to examine low-level auditory sensory abilities in infants, children, and adults with a variety of medical and psychiatric disorders.

**Face Processing**

Human faces provide critical signals for normal social and communicative interaction, and face processing and the neural and perceptual mechanisms that underlie it are directly or indirectly relevant for a wide variety of psychiatric disorders. The face-sensitive adult N170 component is a negative deflection recorded from electrodes over the occipital-temporal cortex that peaks at approximately 170 milliseconds after the presentation of a picture of a face or object. Decades of research indicate that the N170 exhibits larger amplitude and shorter latency responses to faces than to a variety of other stimuli. The N170 also exhibits face inversion effects, characterized by larger amplitude and/or longer latency responses to inverted faces relative to upright faces but not for inverted objects relative to upright objects. In terms of its neural sources, converging evidence suggests that the N170 reflects specialized activity in several regions of the occipital and temporal lobes that are involved in face processing.

The N170 has been studied extensively as a marker for the specialized neural and perceptual mechanisms associated with the early stages of face processing, and recent evidence suggests that the face-sensitive...
<table>
<thead>
<tr>
<th>Process</th>
<th>Component</th>
<th>Ages Observed</th>
<th>Function</th>
<th>Scalp Distribution, Timing, ms</th>
<th>Notes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Auditory</td>
<td>MMN</td>
<td>Birth onward</td>
<td>Obligatory auditory discrimination and/or sensory memory</td>
<td>Frontocentral, 100–250</td>
<td>Plotted as a difference wave (deviant stimulus–response minus standard stimulus–response)</td>
</tr>
<tr>
<td></td>
<td>P50/P1</td>
<td>Early adolescence onward</td>
<td>Reduction of amplitude after repetition, indexes sensory inhibition</td>
<td>Vertex, ~50 in adults</td>
<td>This function may be observable in neonates. This may also be observable in the visual domain.</td>
</tr>
<tr>
<td></td>
<td>repetition suppression</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>N2</td>
<td>Infancy onward</td>
<td>Stimulus complexity, tone processing, speech vs. nonspeech in children and adults</td>
<td>Frontocentral, 150–250 in adults; ~250–350 in children</td>
<td></td>
</tr>
<tr>
<td>Visual</td>
<td>P100</td>
<td>Birth/infancy</td>
<td>Visual pattern reversal, visual thresholds, visual discrimination thresholds</td>
<td>Occipital, ~100 in adults; 250–300 in neonates</td>
<td></td>
</tr>
<tr>
<td>sensory</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>C1</td>
<td>Adulthood</td>
<td>Initial cortical processing in V1 (~56 ms)</td>
<td>Occipital, ~60</td>
<td></td>
</tr>
<tr>
<td></td>
<td>P1</td>
<td>Infancy, adulthood</td>
<td>Under unique circumstances, may index magnocellular visual pathway functioning</td>
<td>Occipital, ~100</td>
<td></td>
</tr>
<tr>
<td></td>
<td>N1</td>
<td>Birth/infancy, adulthood</td>
<td>Under unique circumstances, may index parvocellular visual pathway functioning</td>
<td>Occipital, 65–85</td>
<td></td>
</tr>
<tr>
<td>Face</td>
<td>N290</td>
<td>Infancy and early childhood</td>
<td>Sensory-perceptual processing of faces</td>
<td>Occipital-temporal, ~290</td>
<td>See also N170 and P400</td>
</tr>
<tr>
<td>processing</td>
<td>P400</td>
<td>Infancy and early childhood</td>
<td>Sensory-perceptual and early cognitive processing of faces</td>
<td>Occipital-temporal, ~400</td>
<td>See also N290 and N170</td>
</tr>
<tr>
<td></td>
<td>P1/P100</td>
<td>Birth onward</td>
<td>Face processing during childhood, face inversion during childhood</td>
<td>Occipital-temporal, ~100</td>
<td>Significant developmental changes, sometimes indexing face processing</td>
</tr>
<tr>
<td></td>
<td>N170/N1</td>
<td>Middle childhood onward</td>
<td>Sensory-perceptual processing of faces, perceptual experience</td>
<td>Occipital-temporal, ~170</td>
<td>See also VPP, P100, N290, and P400</td>
</tr>
<tr>
<td></td>
<td>VPP</td>
<td>Adulthood</td>
<td>Sensory-perceptual processing of faces</td>
<td>Centrufrontal, ~170</td>
<td>Highly similar functionally to the N170</td>
</tr>
</tbody>
</table>

(Continued on next page)
<table>
<thead>
<tr>
<th>Process/ Component</th>
<th>Ages Observed</th>
<th>Function</th>
<th>Scalp Distribution, Timing, ms</th>
<th>Notes</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Memory/ attention</strong></td>
<td><strong>Nc</strong></td>
<td>Infancy and childhood</td>
<td>Attention, recognition memory</td>
<td>Frontocentral, ~550</td>
</tr>
<tr>
<td></td>
<td><strong>NSW</strong></td>
<td></td>
<td>Recognition memory</td>
<td>Frontocentral, ~1,000–1,500</td>
</tr>
<tr>
<td></td>
<td><strong>PSW</strong></td>
<td></td>
<td>Updating of memory representations</td>
<td>Frontocentral, ~650–1,250</td>
</tr>
<tr>
<td></td>
<td><strong>P3a</strong></td>
<td>Middle childhood onward</td>
<td>Attentional engagement, sensory working memory</td>
<td>Midline with frontal maximum, 250–500</td>
</tr>
<tr>
<td></td>
<td><strong>P3b</strong></td>
<td>Middle to late childhood onward</td>
<td>Context updating relevant to memory storage</td>
<td>Midline with parietal maximum, 350–550</td>
</tr>
<tr>
<td><strong>Language</strong></td>
<td><strong>N200–400</strong></td>
<td>Toddlerhood</td>
<td>Word familiarity, hemispheric specialization for words</td>
<td>Temporal-parietal, 200–400</td>
</tr>
<tr>
<td></td>
<td><strong>N400</strong></td>
<td>Early childhood onward</td>
<td>Semantic context match/mismatch, semantic integration</td>
<td>Centroparietal, ~400</td>
</tr>
<tr>
<td></td>
<td><strong>P600/SPS</strong></td>
<td>Early childhood, adulthood</td>
<td>Syntactic violations, rule-based violations</td>
<td>Centroparietal, ~600</td>
</tr>
<tr>
<td></td>
<td><strong>LAN/ELAN</strong></td>
<td>Middle childhood onward</td>
<td>Syntactic structure violations, rule-based sequence violations</td>
<td>Left frontal, ELAN, ~200, LAN, 300–700</td>
</tr>
<tr>
<td><strong>Executive functioning</strong></td>
<td><strong>ERN/Ne</strong></td>
<td>Late childhood onward</td>
<td>Error monitoring, response evaluation</td>
<td>Centromedial, 50–150</td>
</tr>
<tr>
<td></td>
<td><strong>N2</strong></td>
<td>Late adolescence onward</td>
<td>Response inhibition</td>
<td>Frontocentral, 200–300</td>
</tr>
<tr>
<td></td>
<td><strong>Pe</strong></td>
<td>Adolescence onward</td>
<td>Cognitive/emotional evaluation or response errors</td>
<td>Centroparietal, 200–400</td>
</tr>
<tr>
<td></td>
<td><strong>CNV</strong></td>
<td>Late childhood onward</td>
<td>Stimulus evaluation, motor and cognitive preparation</td>
<td>Frontocentral, 400–800</td>
</tr>
</tbody>
</table>

**Note:** CNV = Contingent negative variation; ELAN = Early left anterior negativity; ERN = Error-related negativity; LAN = Left anterior negativity; LPC = Late positive component; MMN = Mismatch negativity; N = Negative; Ne = Negative central; Ne = Error negativity; NSW = Negative slow wave; P = Positive; Pe = Error positivity; PSW = Positive slow wave; SPS = Syntactic positivity shift; VPP = Vertex positive potential.

Components are typically labeled according to the polarity of the deflection (i.e., P = positive; N = negative), and the peak latency of the component are in milliseconds (e.g., N170 peaks approximately 170 milliseconds after the presentation of a visual stimulus). Alternatively, components are sometimes labeled based on the topography of the ERP waveform (e.g., the auditory N2 is the second negative deflection observed in response to an auditory stimulus). Finally, the names of other components are derived from their apparent functional significance (e.g., error-related negativity is observed after an errant motor response) or their scalp topography (e.g., left anterior negativity).
responding of the N170 may index a collection of specialized early-stage neural and perceptual mechanisms that are unique to the recognition and identifica-
tion of faces as a salient and important visual stimulus.25-26 Most notably, the results of several studies suggest that the large amplitude of the N170 component in response to faces compared with objects may reflect the extensive long-term experience we have with identifying and discriminating faces from one another.26,27

There are considerable functional differences between the face sensitivities of N170 responses in children and adults.28 However, the N170 is observable in children as young as 4 years, and the electrophysiological processing of faces becomes adultlike during adolescence. Additionally, researchers have identified two infant ERP components, the N290 and the P400, which may represent developmental precursors to the adult N170.29 Like the N170, these components are recorded from electrodes over the occipital-temporal cortex and are sensitive to faces on a number of dimensions. Specifically, the N290 has been observed to elicit larger amplitude responses to human faces relative to monkey faces or matched visual noise stimuli,30-32 P400 latency is shorter for faces than for other objects,33 and the N290 and P400 both exhibit face inversion effects, with larger amplitude responding for upright compared with inverted faces.30,31

We also recently found that the occipital-temporal P400 (in infants) and N170 (in adults) were similar in that they both exhibited larger amplitude responses to fear faces versus happy or neutral faces.34 These findings complement previous research in which we showed that a later ERP component recorded from electrodes over the frontal cortex (negative central [Nc]) also exhibited increased amplitude responses to fearful versus happy faces.35-37 We have also shown that the Nc component indexes familiarity in face processing, in that it is larger for familiar faces as compared with unfamiliar faces in the first year of life.38 Taken together, these data suggest that increased neural resources are allocated to the processing of a variety of face-related processes at the perceptual (N290/P400) and early cognitive stages (Nc) and that several important aspects of face processing at these two stages are already indexed differentially in ERP components in infancy. Furthermore, developmental changes observed in face-sensitive ERP components are believed to reflect the effects of experience in shaping the neural systems that underlie face processing. Therefore, studying the development of face-related ERP components in psychiatric populations is an especially promising area of current and future research.

Memory and Attention

Mnemonic and attentional ERPs are relevant for the study of psychiatric disorders in at least two respects. First, abnormalities of memory and/or attentional processes are part and parcel of many psychiatric disorders. Therefore, the use of ERPs can shed light on the nature and timing of the neural abnormalities that underlie them as well as their developmental course. Second, ERPs that reflect memory or attention have proven to be invaluable tools for exploring new ground in a variety of cognitive domains in both typical and atypical development (e.g., language, face processing).

The Nc component observed in infants and children is one of the most studied developmental ERP components. This negative deflection is recorded from electrodes over the frontal cortex, exclusively to visual stimuli, and is involved in both memory and attention. The Nc is present at birth, and initial studies showed that it is consistently larger in amplitude and/or longer in latency in response to infrequently presented stimuli (e.g., 25%) as compared with frequently presented stimuli (e.g., 75%) from 3 months of age onward.39-41 As noted earlier, the Nc has also been observed to be of larger amplitude in response to fearful versus happy facial expressions.39 Based on these and other data, it has been suggested that the Nc may specifically index the allocation of attentional resources to interesting or salient stimuli.39,42,43

In addition to the role it may play in indexing attentional mechanisms, there is evidence that the Nc component also indexes mnemonic mechanisms, either directly or indirectly. For example, several studies have shown that the Nc distinguishes mother's face from a stranger's face across several ages, even when the two stimuli are presented with equal probability.33,38,44,45 (but see also reference 46). Furthermore, in studies of memory for actions performed with objects in 9- and 10-month-old infants, the latency of the Nc was found to be longer for pictures of the familiar action sequences versus unfamiliar action sequences. Critically, the magnitude of the latency difference between the familiar and unfamiliar stimuli predicted behavioral performance in the memory test 1 month later, suggesting that the Nc

J. AM. ACAD. CHILD ADOLESC. PSYCHIATRY. 47:11, NOVEMBER 2008 www.jaacap.com 1257
was modulated by mnemonic mechanisms. The role of mnemonic mechanisms in modulating the Nc component has also received support from research using a cross-modal recognition memory paradigm in typically developing infants and those with putatively impaired memory systems.

The specific roles of attention versus memory in modulating the Nc component under various circumstances remain a topic of debate. However, the results of a recent source modeling study may provide a basis for resolving this debate in the future. Specifically, these data suggest the possibility that there may actually be two major generators that underlie the Nc component, which differentially index mnemonic and attentional mechanisms. One of the sources identified in this study was a prefrontal source that was active earlier and influenced by stimulus familiarity, and the other was a frontal pole source that was active later and not influenced by stimulus familiarity. These findings suggest the distinct possibility that the scalp-recorded Nc may reflect two somewhat distinct processes, which may be more clearly distinguishable from one another with future research.

Two slow-wave components, one positive (positive slow wave [PSW]) and one negative (negative slow wave [NSW]), have been observed to follow the Nc component. These components seem to be more distinctly involved in mnemonic versus attentional processing. Specifically, the PSW is believed to reflect the updating of memory representations for partially en-

![Baseline Assessment: Occipital Components](https://example.com/baseline.png)

**Fig. 1** Event-related potentials recorded from institutionalized and never-institutionalized infants at baseline (before placement in foster care; average age = 22 months) to happy, fear, anger, and sad faces. Because there were no group differences in responding to the four emotions, the data were collapsed across emotion to highlight the amplitude differences between the groups.

![Baseline Assessment: Occipital Components](https://example.com/baseline2.png)

**Fig. 2** Event-related potentials recorded from institutionalized and never-institutionalized infants at baseline (before placement in foster care; average age = 22 months) to pictures of the child's caregiver and the face of a stranger. As noted in the text, the groups showed a differential response to these faces; for purposes of this figure, however, we have collapsed across stimulus to reveal the differences in ERP amplitudes across the two groups.

coded stimuli, and evidence suggests that it may reflect activity in temporal lobe regions involved in memory. The NSW has been interpreted to reflect the detection of novelty, and evidence suggests that it may be generated by regions of the frontal cortex. Together, these three components (Nc, PSW, and NSW) provide a strong context for the study of memory development in infants and children.

**HOW HAVE ERPS BEEN USED TO STUDY ATYPICAL DEVELOPMENT?**

Event-related potentials have been used extensively to study atypical development or infants/children at risk for falling off a typical developmental trajectory. Below, we sample broadly from just two such areas: children experiencing early and varying degrees of psychosocial deprivation, and autism.

**Neural Correlates of Emotion Processing in Children Experiencing Early Psychosocial Neglect**

Zeanah et al. have charted the development of three groups of children in Romania: those abandoned at birth, placed, and then raised in institutions; those abandoned at birth, placed in institutions, and then placed in high-quality foster care; and those reared since birth with biological families (for details, see reference). Two ERP manipulations were performed. In one, infants/children were presented with alternating images of their caregiver's face and the face of a stranger; in
another, they were presented with images of happy, fearful, angry, and sad faces. Across both manipulations, at baseline (before randomization to foster care; mean age 22 months), infants in the institutionalized group showed remarkably reduced ERP amplitudes compared with the never-institutionalized group (Figs. 1 and 2). Similarly, at 42 months of age, children now living in foster care showed ERP amplitudes that were at the midpoint between the institutionalized and never-institutionalized children (Figs. 3 and 4).

Over and above reduced ERP amplitudes, two additional observations are worth noting. First, regarding emotion recognition, the institutionalized group performed similarly to the never-institutionalized group; that is, the NC was largest to fearful faces than other faces. Thus, it seems that institutionalization has no effect on discriminating facial expressions of emotion. Second, there were rather dramatic group differences between institutionalized versus never-institutionalized children, with the former showing larger ERP responses to stranger’s faces and the latter showing larger responses to caregiver’s faces. Therefore, institutionalization does seem to have an impact on the neural systems involved in facial recognition (for discussion, see References 60-62).

Overall, these findings illustrate how ERPs have been used to study the neural correlates of different dimensions of face processing among children experiencing early psychosocial deprivation. Similar investigations have been conducted on children experiencing maltreatment, although space limitations prevent us from discussing this work.63-66

**Autism**

Researchers using ERPs have revealed abnormalities in the early stages of face processing in autism. For example, McPartland and coworkers68 found that adolescents and adults with autism exhibited slower than normal peak N170 responses to faces but normal latency responses to objects relative to typically developing controls. Individuals with autism in this study also failed to show a “face-inversion effect” in the N170 component.68 The latter finding suggests a reduced reliance on holistic processing mechanisms for face processing. Further evidence for impaired holistic processing of faces in autism comes from a study showing no difference in EEG power in the gamma band (~40 Hz) in response to upright versus inverted faces in adults with autism, which was due to reduced gamma power during upright face processing relative to controls.69 This finding suggests reduced neural/perceptual binding in response to the upright faces in the individuals with autism.70,71 More recent ERP data collected from children with autism spectrum disorders (ASDs; ~11 years old) showed that these children exhibited...
reduced source power in frontal regions during the time window of the N170 component during the processing of faces that were filtered to include only low spatial frequency information but no differences in the processing of faces filtered to include only high spatial frequency information. These results also suggest a reduced degree, or reduced depth, of holistic processing in individuals with autism.

In an effort to determine whether the broader autism phenotype is associated with abnormalities in early-stage face processing, Dawson and coworkers studied ERPs to upright and inverted faces and objects in parents of children with autism and control participants. They found that N170 responses were faster to faces than to objects in the control group but not in the parents of children with autism. They also found that control participants exhibited right-stronger-than-left responses to the faces, but the parents of children with autism did not. These data reflect early-stage face processing abnormalities that are consistent with those observed in individuals diagnosed with autism and, therefore, indicate that abnormalities in the neural circuitry involved in the early stages of face processing may be a functional trait marker for genetic risk for autism.

Several other studies conducted by Dawson and coworkers have shed light on the nature of face-processing impairments in young children with autism. In one study, Dawson and coworkers examined the neural correlates of familiar and unfamiliar face and object processing in 3- to 4-year-old children with ASDs, children with developmental delays (DDs), and typically developing (TD) children. As expected, the ERPs of TD children differentiated between familiar and unfamiliar faces in two ERP components: the P400 recorded from the electrodes over the occipital-temporal cortex, and the Nc recorded from the frontal and midline electrodes. Unlike these TD children, 3- to 4-year-old ASD children did not show differentiation of familiar and unfamiliar faces in either of these ERP components. Like the TD children, however, they did show differential responses to familiar and unfamiliar objects in both the P400 and Nc components. Control children with DD in this study did not show differential P400 or Nc responses to familiar and unfamiliar faces or to familiar and unfamiliar objects. However, they showed differentiation of both in a positive component that followed the Nc, the PSW, which neither the ASD nor the TD children did. These results suggest that autism is associated with face-specific recognition memory impairment early in life.

In a follow-up study, Dawson et al. examined facial emotion processing in young children with autism. In this study, they found that TD children exhibited larger amplitude responses in the N290 and NSW components to a face posed in a fearful expression compared with a face posed in a neutral expression, whereas the children with ASD did not. Furthermore, the latency of the N290 component in response to the fear face was associated with better performance on naturalistic experimental assessments of diagnostic social behaviors (i.e., social orienting, joint attention, attention to distress). These data provide evidence for abnormal processing of facial expressions of emotion at both the perceptual and early cognitive stages of processing and further suggest that these abnormalities are meaningfully related to impaired social functioning in these children.

In 2006, Webb et al. examined early-stage face versus object processing in 3- to 4-year-old children with autism. To do so, they reanalyzed the ERP data collected in the study of familiar and unfamiliar face and object processing (described previously), collapsing the data across familiarity. Statistical analysis of the face-sensitive N290 component revealed abnormal patterns of face and object processing in the ASD children relative to children in the two control groups. Specifically, comparisons of N290 latencies revealed a significant interaction whereby TD children processed faces faster than objects, but ASD children processed objects faster than faces. Unlike the TD or ASD children, DD children showed similar latency N290 responses to faces and objects. However, the relation between stimulus type and subject group was different between the ASD children (object latencies shorter than faces) and DD children (equal latency responses to faces and objects). The ASD children also exhibited a reduced amplitude response to the object stimulus relative to both groups of control children. Because effects of familiarity on the N290 were not examined, it is possible that the observed effects were driven by an interaction among familiarity, stimulus type, and the subject groups. However, these data provide preliminary evidence to suggest that early-stage face versus object processing is abnormal in young children with autism and further suggest that these abnormalities may be characterized by differences in both object and face processing in these children relative to controls.
DISCUSSION

Our goal in writing this article was to introduce the reader to the use of recording ERPs in the context of studying both typical development and developmental psychopathology. There is a growing literature using this method with a variety of risk and impaired populations, including children with attention-deficit/hyperactivity disorder, children with histories of maltreatment, children experiencing prenatal drug exposure, children with dyslexia and other learning (and memory) problems, and children on the autism spectrum (and those at risk for developing autism). The advantages ERPs hold over other neuroimaging tools include their ease in application, the fact that they can be used across the entire life span, their superb temporal resolution and their (relative) inexpensiveness. Their disadvantages include (relatively) poor spatial resolution.

What does the future hold? First, serious efforts are currently being implemented to improve the spatial resolution of ERPs by using higher density arrays of electrodes and in more sophisticated methods of source modeling. Second, a number of laboratories are currently coregistering ERPs with other imaging modalities (e.g., functional magnetic resonance imaging). We contend that continued refinement of this method, combined with the development of other imaging tools (e.g., near infrared spectroscopy), has the potential to revolutionize our understanding of disorders. When combined with genetic/genomic information, we are optimistic that we are on the threshold of making dramatic breakthroughs in our understanding of mental health problems in children.

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