12 ERPs in Developmental Populations

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A primary goal of developmental cognitive neuroscience is to elucidate the relation between brain development and cognitive development (see Nelson & Luciana, 2001). The study of this relation in children older than 5–6 years lends itself to many of the same tools used in the adult, such as functional magnetic resonance imaging (fMRI). However, in children younger than this, limitations in motor and linguistic abilities, coupled with abbreviated attention spans, make using such tools impractical. In contrast, event-related potentials (ERPs) provide one of the only methodological techniques in the armamentarium of cognitive neuroscientists that allow researchers to examine the relation between brain and behavior beginning at birth. ERPs are noninvasive and can be utilized across the entire lifespan, thereby permitting one to use the same methodological tool and dependent measure across a broad range of ages (although comparisons across large age spans may be challenging due to qualitative differences in the ERP response). Furthermore, due to the high temporal resolution of ERPs (on the order of milliseconds), researchers can index changes in the mental chronometry of a given system. Finally, ERPs do not require an overt behavioral or verbal response and therefore permit the study of phenomena that cannot be studied with behavioral methods (e.g., responses to the simultaneous presentation of multiple stimuli or stimuli presented so briefly so as to preclude a behavioral response). However, when a behavioral response is obtainable, ERPs can also provide an invaluable complement and an additional level of analysis to that behavioral measure by permitting one to glimpse (albeit imperfectly) the neural circuits underlying the behavior.[1]

Study Formation and Experimental Design

Hypotheses

Despite an increase in the use of ERPs with developmental populations, several obstacles remain that prevent testable hypotheses from appearing more often in the literature. First, the field has only begun to define ERP components of interest across development, and thus much discontinuity remains between age groups and across

components of interest. Second, because relatively little is known about human brain development, it can be challenging to derive hypotheses based on the development of discrete neural circuits. Third, almost nothing is known about how physiologic activity in the developing brain propagates to the scalp surface, and thus, we do not know what the relation is between activity *in* the brain vs. *at* the scalp. With these caveats in mind, in this chapter we attempt to illustrate the kinds of questions that are particularly amenable to an electrophysiological investigation with developmental populations, but we also challenge researchers to perform the appropriate exploratory investigations so they can conduct more theoretically driven experiments with testable hypotheses.

Task Design

ERPs are, by definition, time-locked to the presentation of a stimulus. Therefore, constraints are constantly placed on the types of tasks amenable to ERP experiments, in both adult and developmental populations. However, due to the limited capacity of attention and restricted behavioral repertoire of infant and child populations, further considerations are necessary when designing experiments for these groups. Some developmental ERP tasks can be derived from ERP tasks used with adults and adjusted to take developmental differences into consideration (e.g., decreasing the number of independent variables or the complexity of the stimuli). However, as accommodations such as these are made it must be acknowledged that infants and children are not typically tested under the same conditions as adults (e.g., infants do not benefit from instructions) and therefore direct comparisons across large age differences are often difficult to interpret. Other age-appropriate ERP tasks can arise from modified versions of behavioral tasks known to tap certain cognitive functions of interest (e.g., speech discrimination tasks, habituation tasks, and recognition memory tasks). Finally, tasks used with other imaging techniques (such as those used in fMRI procedures) can be tailored to suit the constraints of developmental ERP research (e.g., the go/no-go tasks and serial reaction time tasks; see Davis et al., 2003).

Most developmental ERP studies conducted to date have used either the standard oddball paradigm or a combination of the oddball paradigm with an infant habituation paradigm. In the former, two or more stimuli are presented repeatedly, but with different frequencies. For example, in one study, 4- to 7-week-old infants were shown pictures of checkerboard patterns and geometric shapes. ERPs were recorded while one stimulus was repeated frequently (80% of the time) and the other stimulus was presented infrequently (20% of the time; Karrer & Monti, 1995). The combined oddball/habituation paradigm involves first familiarizing or habituating an infant to a stimulus (e.g., a face), and then presenting a series of stimuli, consisting of the now familiar stimulus and a novel stimulus (e.g., a new face) repeatedly with equal frequency (i.e., 50% of the time for each) while recording ERPs (e.g., Pascalis et al., 1998).

Important Considerations in Developmental Populations

Beyond paradigm considerations, one must also consider (1) age-related changes in the morphology and timing of ERP components of interest, and (2) changes in behavioral measures, including the availability, quality, and validity of these measures. We will discuss the above factors briefly in this section, but we will return to them throughout the chapter, as they are relevant to the remaining sections.

Developmental changes that are apparent in the morphology of the ERP waveform are often difficult to describe, and increasingly difficult to explain due to their complex and multifaceted nature. For instance, major developmental changes in synaptic density, myelination, and other physical maturational processes (e.g., changes in skull thickness and closing of the fontanel) may combine to influence amplitude and latency increases and decreases across different ages (Nelson & Luciana, 1998). Unexpectedly, ERPs of adults and newborns are similar to each other in amplitude, but very dissimilar compared to ERPs from older infants and young children (see figure 12.1 and plate 6 for illustration). Furthermore, in the first two years of life, reduced synaptic efficiency results in greater slow wave activity rather than peaked activity, the latter being more typical of adult ERPs. Thus, the infant ERP does not show as many well-defined peaked responses (especially in anterior components) when compared to adult responses. The characteristics of the peaked adult waveform typically begin to emerge when children reach 4 years of age and continue to develop well into adolescence (Friedman et al., 1984; Nelson & Luciana, 1998). In fact, because the distribution of activity across the scalp (i.e., topography) changes with age, we can infer that important changes are still taking place in the neural substrate generating the components of interest throughout development. Amplitudes also vary with task demands imposed on the participant. Presumably the easier the task, the less effort expended, and the less cortical activation required, ultimately resulting in smaller amplitudes (Nelson & Luciana, 1998). Finally, the general heuristic for changes that take place from early adulthood to later adulthood is that, overall, latencies of several ERP components appear longer and amplitudes appear smaller (see Kurtzberg et al., 1984; Nelson & Monk, 2001; and Taylor & Baldeweg, 2002 for further discussion).

A major change that also occurs with increasing age is the ability to "ground" the measure in behavior or correlate the brain's electrophysiological response with task performance. Infant ERP paradigms by necessity do not involve issuing instructions, nor do they require an overt behavioral response. However, most adult ERP paradigms include both instructions and a behavior response (even if only to ensure continued attention to the task). Therefore, because of the differences in testing conditions it is possible that, at some level, differences in ERP morphology are due to differences in task requirements.

The "passive" viewing paradigm (i.e., one in which no instructions are given) is useful for two reasons. First, developmental populations can be tested and their data

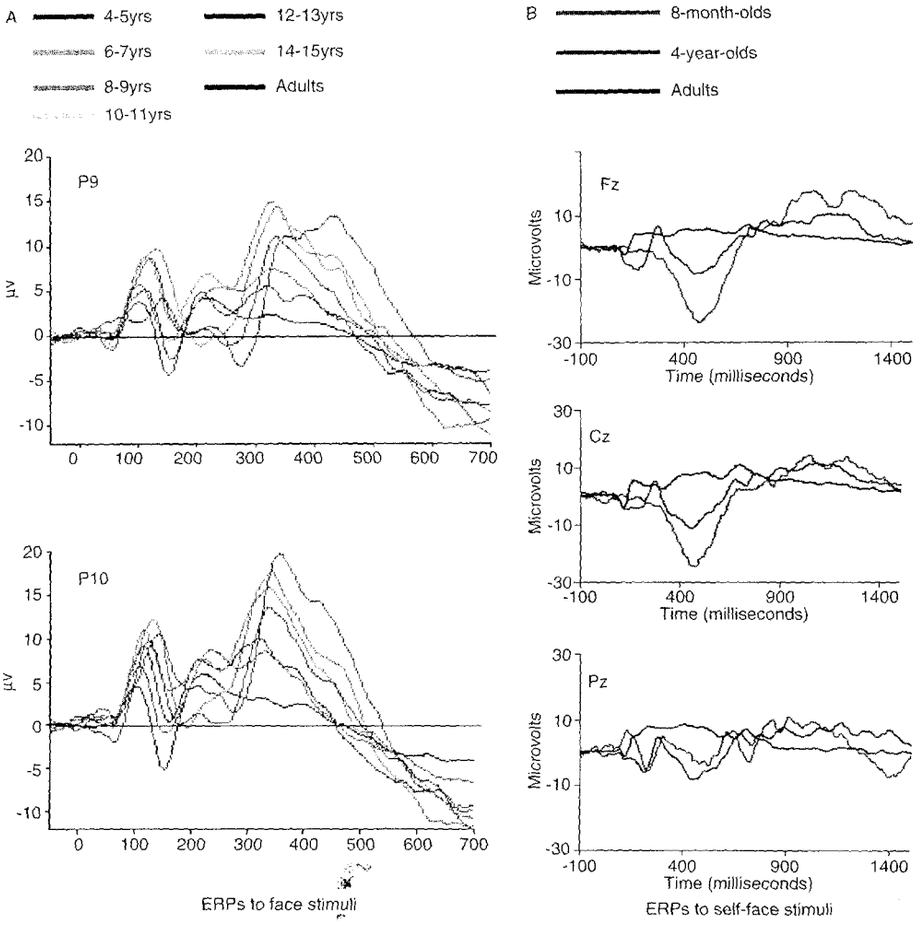

Figure 12.1

(*A*) Grand averaged ERPs from posterior, inferior temporal electrodes P9 (left parietal lobe) and P10 (right parietal lobe) in response to face stimuli for seven age groups. (*B*) Grand averaged ERPs from midline electrodes taken from a pilot study in which 8-month-olds, 4-year-olds, and adults passively viewed images of their own face in the context of a face recognition task. (*A* courtesy of Margot Taylor, Centre National Cervau et Cognition, Toulouse, France, and *B* courtesy of Lisa S. Scott, Institute of Child Development, University of Minnesota.) (See plate 6 for color version.)

compared to adults without modification to the paradigm. Second, passive paradigms may evoke basic perceptual components, without the added activity (or noise) that may be recorded when the subject is engaged in some task and/or a behavioral response is required. The drawback to using a passive task is that it is difficult to determine whether participants maintain attention throughout the task, or whether they are doing the task at all. Depending on the specific hypotheses, it may be important to be able to compare data sets across ages and use other means of monitoring attention (for example, video taping participants to ensure the infant was looking at the stimuli, and/or repeating trials in which it was obvious the participants were not attentive).

Although below the age of 4–5 years traditional button press responses cannot be used, there are some behavioral measures that researchers have used in developmental populations in conjunction with ERPs. The most informative behavioral measures are those that can be directly correlated with the electrophysiological response. For example, after recording ERPs in a visual oddball paradigm using two stimuli with different presentation frequencies, Karrer and Monti (1995) immediately presented the infant with four additional trials, and recorded visual fixations, analogous to a post-test after a traditional behavioral habituation paradigm. Specifically, they presented one of the two stimuli repeatedly until the infant looked away, followed by the presentation of the other stimulus until they looked away, and so on. Similarly, Snyder (2002) employed a design analogous to a habituation/dishabituation procedure that consists of recording ERPs during an initial exposure to a stimulus (the habituation phase), and then recording the duration of infants' visual fixations during a dishabituation phase. Snyder's study is unique in that it reflects a compromise between ERP methodology and stimulus exposure during a conventional infant controlled habituation procedure. During the familiarization phase, trials were continuously presented until the infant either became fussy, or looked away from the screen three times for at least 3 seconds each time. After the familiarization phase, infants were presented with serial presentations of familiar and novel stimuli and allowed one continuous look at each. Infant's visual preferences for test stimuli were computed as the proportion of fixation to the novel stimulus versus the total fixation time. Infants were subsequently divided into three groups: infants who showed a novelty preference at test (looked at the novel stimulus 55% or more of the time), those who showed a familiarity preference (looked at the novel stimulus 45% or less of the time), and those who did not show a preference. This method of combining ERPs with conventional behavioral measures permits researchers to examine directly the relation between preferential looking, which may be indicative of some aspect of attention or memory, and brain activity. A combination of techniques such as this provides information not accessible by either method alone.

Unfortunately, due to the highly constrained testing environment required by ERPs, it is not always feasible to record behavioral measures immediately following ERP collection. Therefore, some researchers have elected to record behavioral measures

separately (e.g., after removing the electrodes when the infant is more attentive or better able to perform a required task). For example, Carver, Bauer, and Nelson (2000) combined behavioral performance on a deferred imitation task (which has been purported to tap explicit memory functions; see Bauer, 1995; Nelson, 1995) with electrophysiological responses. Before ERP recording, 9-month-old infants were behaviorally exposed to a unique sequence of events (e.g., the experimenter places a red cylinder into a wooden block, which is then pushed into the base of the apparatus, causing a green dinosaur puppet to pop up). After a one-week delay, the infant's ERP response to photographs of the now familiar event sequence and a novel event sequence were recorded. Four weeks later, the infants' delayed recall performance on the deferred imitation memory task was assessed. Infants were split into groups based on their behavioral performance: those who recalled the sequence and those who did not. Based on these groupings, Carver and colleagues (2000) examined the electrophysiological responses and found differentiation between the familiar and novel conditions for the infants who recalled after a one-month delay, but no such differentiation for the infants who did not display delayed recall.

In short, it is important that researchers continue to ground ERP measures in behavior. Such a combination will yield converging evidence and lead to more reliable results in predominately exploratory studies typical of the field at this time.

Breadth of Developmental ERP Research

Most developmental ERP studies to date have utilized only a single sensory modality to investigate any given cognitive process of interest. For example, recognition memory has typically been investigated using visual stimuli (Nelson, 1997, 1998), whereas language development has primarily utilized auditory stimuli (Cheour, Leppanen, & Kraus, 2000; Mills, Coffey-Corina, & Neville, 1993, 1997; Molfese, Narter, & Modglin, 2002; Molfese & Molfese, 2000). Few developmental ERP studies have used olfactory, gustatory, or tactile stimuli, although there are important exceptions. For example, Nelson, Henschel, and Collins, 1993, and Nelson et al., 2003, have employed a cross-modal task, in which infants are familiarized to a stimulus in the haptic modality and tested for recognition memory in the visual modality. However, it remains unknown whether the components observed in response to stimuli in one modality generalize to stimuli in another, nor is it apparent whether some pre-adult components are modality independent (such as the adult P300).

Over the past two decades, investigators have increasingly begun to use ERPs to examine early cognitive and linguistic development. Some specific abilities that researchers have studied include: attention (e.g., Richards, 2000, 2003; Taylor, Khan, & Malone, 1999), memory (Carver, Bauer, & Nelson, 2000; Nelson, 1995; Nelson & Monk, 2001), face and object processing (Courchesne, Ganz, & Norcia, 1981; de Haan,

Pascalis, & Johnson, 2002; de Haan & Nelson, 1997; Taylor et al., 1999), language (Holcomb, Coffey, & Neville, 1992; Mills & Neville, 1997; Molfese, Narter, & Modglin, 2002; Molfese & Molfese, 2000), and general cognitive development (for review, see Kurtzberg et al., 1984; Regan, 1989).

Developmental ERP Components

In the previous discussion of experimental design, we identified one of the major challenges presented by developmental ERP research as the limited information available on components of interest at various ages. We also commented on the complex changes that occur with increasing age in ERP morphology, amplitude, latency, and topography due to changes in physiology of the head, skull, and underlying brain tissue. In fact, although there are several well-documented infant ERP responses, studies of the development of these responses into more adultlike components remains limited (Nelson & Luciana, 1998). It is generally thought that by the age of 4 years, some semblance of the adult waveform can be discerned. However, relatively little work has been done in children 1.5–4 years of age, and changes in components during this time remain largely undocumented (Nelson & Luciana, 1998).

Extensive discussion of all ERP components found across development is beyond the scope of this *methodological* chapter. However, in the following section, we identify a few developmental ERP components and provide references for recent comprehensive reviews. However, due to space constraints, we will only elaborate on recognition memory components, which have been studied in infants and children in order to elucidate cognitive processes underlying memory development (i.e., the mid-latency negative component, positive slow wave, and negative slow wave activity) and the N170, a component reflecting face processing that has been studied from a developmental perspective from infancy to adulthood. This review of the face-processing component provides an excellent illustration of issues that arise when comparing ERP data across different age groups.

Researchers have identified several ERP components in infants, children, and adolescents (for review see: Nelson, 1994, 1995, 1996; Nelson & Luciana, 1998; Nelson & Monk, 2001; and Taylor & Baldeweg, 2002). These include components that are hypothesized to reflect sensory processing (e.g., the N1 component; Pang & Taylor, 2000; Polich & Luckritz, 1995; Taylor & Baldweg, 2002), obligatory attention (e.g., the negative component or Nc; Nelson, 1996), memory updating (e.g., positive slow wave activity, or PSW; Nelson, 1996), detection of expectant or discrepant events (e.g., the Pb component; Karrer & Ackles, 1990; and mismatch negativity or MMN; Cheour et al., 1998a; Cheour et al., 1998b; Cheour, Leppanen, & Kraus, 2000; Oades, 1997; Shafer, 2000), detection of novelty (e.g., negative slow wave, or NSW; Nelson, 1996), processing of linguistic stimuli, (e.g., the N400 component; Kutas & Hillyard, 1980; Mills, Coffey-Corina, & Neville, 1993; Neville, Mills, & Bellugi, 1994), and general

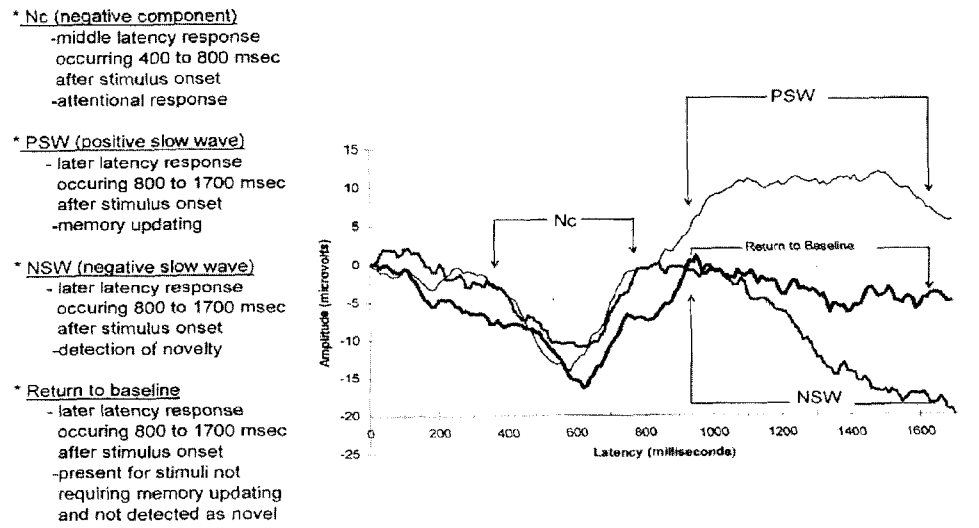

Figure 12.2
Schematic of different components observed in the infant event-related potential during a visual recognition memory task. (Reprinted with permission from M. de Haan and C. A. Nelson, 1997. Recognition of the mother's face by six-month-old infants: A neurobehavioral study. In *Child Development, 68,* 187–210.)

cognitive components commonly found in adults (e.g., the P300, P3a, or P3b; Regan, 1989).

Recognition Memory Components: An Elaboration The negative component, or Nc, has been consistently observed in recognition memory paradigms (see figure 12.2). The Nc has a well-defined negative peak with maximum amplitude over central and frontal scalp leads (corresponding to Cz and Fz in the 10/20 classification system). The latency of this response generally declines from approximately 1000–1200 ms in the newborn to about 500 ms at 1 year (see Nelson, 1996 for a discussion). This negative peak can easily be discerned in both the single and averaged trial data and is presumed to reflect processes of attention (i.e., obligatory attention; Courchesne, 1977, 1978; Courchesne, Ganz, & Norcia, 1981; Karrer & Ackles, 1987, 1988; Karrer & Monti, 1995; Nelson & Collins, 1991, 1992). Whether this response is exogenous or endogenous in nature has not been determined, although it does share some similarities to the endogenous mismatch negativity in studies of auditory selective attention and is related to both the global and local probabilities of stimuli (Karrer & Ackles, 1990; Nelson & Luciana, 1998). Recently, Reynolds and Richards (2003) have used high-density recording, principle components analysis (PCA), and equivalent current dipole analysis to localize

the cortical source of the Nc to several regions of the frontal cortex, including the anterior cingulate.

Following the Nc, there is typically one of three responses: a positive slow wave (PSW), negative slow wave (NSW), or return to baseline (see figure 12.2). Slow wave activity represents a deflection of the brain's electrical response to an event or stimulus, and is thought to reflect general or diffuse activation of neural systems that is characteristic of infant brain responses (de Haan & Nelson, 1997). A PSW is a positive shift late in the waveform that appears maximal at central and frontal scalp locations. It is thought to reflect the partial encoding of a stimulus that requires updating or periodic revision.

The NSW, on the other hand, is a negative shift in the waveform after the resolution of the Nc component that is only observed when novel stimuli are presented against a background of familiar or partially familiar stimuli. Therefore, the NSW is thought to reflect a comparative process, one that detects genuine novelty amidst relatively familiar surroundings (Nelson, 1994) or a disconfirmation of expectancy (Karrer & Ackles, 1990).

Finally, a return to baseline reflects a resolution of the waveform back to baseline indicating that the stimulus does not require memory updating. For example, de Haan and Nelson (1997) found a return to baseline response when 6-month-old infants viewed pictures of their mothers' faces (a fully encoded stimulus), but not when they viewed pictures of an unfamiliar woman's face.

The Face Processing Component: A Developmental Approach A component that has received considerable attention from a developmental perspective is the N170 (see figure 12.1). In adults, studies using ERPs have found a negatively peaked component occurring approximately 170 ms after stimulus onset that differentiates faces and objects (for example, Jeffreys, 1989; Bentin et al., 1996; Carmel & Bentin, 2002) that is typically prominent over occipital and lateral leads (de Haan, Pascalis, & Johnson, 2002).

As an illustration of the complexities of investigating the development of a typical adult component, we will describe two compelling investigations that have attempted to find the developmental analog of this negative component. First, Taylor et al. (2001) investigated the neural changes associated with face and eye processing using ERPs in children 4–15 years old. Participants were presented with upright and inverted faces and eyes, to determine whether children were using featural versus configural information while processing faces. Findings revealed that the N170 undergoes developmental changes, including a decrease in peak latency and an increase in peak amplitude with increases in age. In addition, de Haan and colleagues (de Haan, Pascalis, & Johnson, 2002) studied both adults and 6-month-olds in a human and nonhuman primate face recognition ERP task in order to determine whether adults and infants

show the same cortical specificity during face processing. This study was designed to answer questions regarding the basic nature of the face processing system as well as changes in specificity across development. Adults and infants were shown both nonhuman primate and human faces in upright and inverted orientations. In adults, all stimuli evoked an N170 over temporal and occipital leads. This N170 was larger in amplitude and longer in latency for upright monkey faces compared to upright human faces. Furthermore, inversion effects (i.e., increased amplitude and latency to inverted faces) were apparent in the human but not the monkey conditions. However, results also indicated that no component of the infant ERP showed the same specificity as the adult N170. Six-month-olds did show sensitivity to both inversion and species but it was distributed across two components in occipitotemporal leads. An early negative component (260–336 ms) was greater to human than monkey faces, and a later positive component (P400) was greater for upright compared to inverted faces. These findings suggest that adultlike patterns of face processing are not evident at 6 months of age. The authors suggest that these findings reflect a gradual specialization of cortical face processing systems. The above results illustrate that comparing components across age groups may be more difficult than originally thought, in that two or more developmental components may later combine into one mature adult component.

There are several factors to consider when identifying and interpreting components and tracking their changes across development. One challenge for future research is to create guidelines for choosing and labeling components that are revealed through new tasks and in previously unstudied age groups. When embarking on such an endeavor, one must keep in mind the variability both within and between participants and rely on subsequent replication before making strong conclusions. Furthermore, because of the relative lack of information on developmental components, it may be necessary for future research to extend initial study hypotheses and report additional components found post hoc. If this is the case, we encourage methods sections of developmental studies to clearly and consistently document paradigm parameters as well as component identification and analysis procedures in an attempt to find consistencies in component identification and selection across studies.

Data Collection Systems

Currently, there are several commercial systems available for purchase and use. These systems differ on features such as electrode and montage type, quantity, location, and placement. A major distinction among systems available to date is whether they are high- or low-density electrode montages. A low-density montage provides less coverage over the scalp (ranging from 1 to 32 electrodes), whereas high-density montages provide greater coverage across the scalp (ranging from 32 to 256 electrodes). The main advantages of high-density systems are increased opportunity for source localization,

use of the average reference, and increased ability to detect subcortical electrical activity. When deciding whether to use a high- or low-density system in developmental populations there are several things to consider, such as: (1) where the data will be collected (e.g., in a MRI scanner that does not permit the presence of metal), (2) what hypotheses will guide data analysis (e.g., how important is spatial information), and (3) the proposed dependent measures for data analysis (e.g., amplitude differences at one electrode site or source localization procedures).

We have used two different methods for recording low-density ERPs in our developmental ERP lab. These methods differ in the number of electrodes and the method of placing the electrodes on the scalp. For both methods, the location of electrode placement follows the international 10–20 system of electrode placement commonly used in adults (Jasper, 1958). Each electrode is placed a percentage of the distance between the inion and nasion to ensure the ERPs are being recorded from approximately the same neural structures across all individuals regardless of age or head size. In addition, these low-density systems require slight scalp abrasion and the use of conductance cream in order to conduct the signal into the electrode on the scalp. Abrading the scalp may increase the risk of infection, and although it is not likely to occur, certain precautions are necessary (see Ferree et al., 2001; Putnam, Johnson, & Roth, 1992).

The first low-density approach is derived from methods with adults, in which researchers use a form of glue (collodion) to fix single electrodes filled with conductance cream to the scalp, and a solvent (acetone) to remove them. The advantage to this method is that the electrodes remain in the same place throughout the experiment. However, the disadvantage is that safety glasses, rubber gloves, and ventilation are recommended when using these products, as they may be irritating to the nose and throat. The modification we have used involves first slightly abrading the scalp with a cleansing solution such as NuPrep and holding single electrodes filled with conductance cream (EC2 cream) in place with adhesive backed foam pads, which in turn are held in place with Velcro headbands (see figure 12.3A). In studies with newborns, one can use disposable electrodes—which stick directly to the infant's scalp—instead of the single electrodes and foam (figure 12.3B). The advantage is that this procedure is typically no more aversive than putting on a hat. However, the disadvantage is that the foam pads can stick poorly to infants who have a great deal of hair or where the hair is braided, and thus have the potential to move around on the scalp unless one takes extra care. Typically 6–12 electrodes are used with this procedure, and it is most appropriate for infants under 12 months of age.

The second approach utilizes an electrode cap, made out of Spandex-like material that has electrodes sewn into it at standardized coordinates (this method is also commonly used with adults; see figure 12.3C). The advantage to this procedure is that one can position a greater number of electrodes on the scalp in relatively little time in comparison with the Velcro headband procedure and disposable electrodes. The scalp

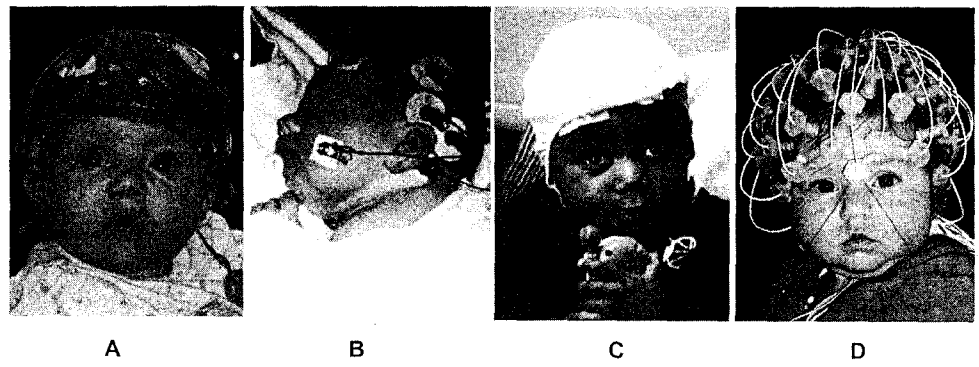

Figure 12.3
(*A*) Infant wearing 16 electrodes held in place with adhesive foam pads and Velcro headbands, (*B*) single disposable electrodes typically used in the newborn and NICU nurseries, (*C*) a 32-channel Electro-Cap, and (*D*) a 64-channel Electro Geodesic Sensor net.

is lightly abraded and conductance jelly inserted under each electrode site after the placement of the cap (this is typically done with a blunt tip syringe and cotton swab). This may be bothersome to some infants as it produces a sensation of a light scratching on the scalp. A chin or chest strap holds the cap in place. Although this strap does not entirely ensure that the cap will not shift on the head during the experiment, it does greatly reduce the risk of electrodes moving out of position. A disadvantage is that some infants' heads are asymmetrical and varied in size, making it difficult to ensure that the electrodes are fixed in the same location. In addition, the chin or chest strap used to hold the electrodes in place may bother some infants. Typically, electrode caps have 16–32 electrodes and can be used with infants as young as 9 months of age up through adulthood.

Recording high-density ERPs in developmental populations has been made possible by the Geodesic Sensor Net (GSN), which allows a very large number of electrodes (ranging from 64 to 256 electrodes) to be applied quickly to the surface of the scalp (Tucker, 1993). The GSN consists of an array of electrodes arranged in an elastic tension structure, which can be relatively quickly and easily slipped on and off the participants' head (see figure 12.3D). The arrangement of electrodes does not follow the international 10–20 system due to the fact that the tension structure conforms to the geometry of each individual's head, but ensures that the electrodes are all equidistant from one another, even on a variety of head shapes (which is a requirement for localization of underlying dipoles). One advantage of the GSN is its high-operating impedance level, which, when combined with amplifiers that allow high-input impedance, removes the need for scalp abrasion and conductance cream. The net is soaked in an electrolyte solution prior to application, which allows the signal to be conducted,

recorded, and amplified by the high-input impedance amplifiers. A second advantage is the use of the average reference, which results in an unbiased estimate of noise across the scalp and thus unconfounds estimates of the amplitude and topography of components with the location of the reference electrode. A third advantage is that high-density montage arrays provide greater coverage of the scalp and thus are able to pick up activity in superficial cortical tissue (which, due to its proximity to the scalp, tends to produce smaller, more discrete patterns of activity). Finally, it takes a relatively short amount of time to apply the net in comparison to other procedures (Johnson et al., 2001).

There are a few disadvantages of high-density recordings worth mentioning as well. First, due to the fact that the electrodes are not fixed rigidly to the scalp, movement artifacts are common, and in some cases infants (6–12 months of age and older) may attempt to grab the net, frequently causing displacement and possible damage to the net (Johnson et al., 2001). A second disadvantage is that high-density systems are considerably more expensive than low-density systems, due to the increased cost of equipment and the need for several different net sizes to accommodate small differences in head size among participants. Nets are available in many different sizes, useful with newborns (64 or 128 electrodes), children up to 6 years of age (64 or 128 electrodes), and children age 6 years to adults (64, 128, or 256 electrodes). (For a complete review of recording high-density ERPs and strategies for analyzing high-density data with infants using the GNS, see Johnson et al., 2001.)

Thus far, comparisons of data collected from high- and low-density systems appear similar in quality (Carver et al., 1999; Johnson et al., 2001). The overall advantage of high-density montages is that they may allow for the use of the average reference, source separation and source localization, and due to greater spatial coverage of the scalp, high-density montages may be able to better pick up superficial cortical and subcortical activity. In contrast, low-density systems are more widespread in their use and are less expensive.

Participants

Ages

When selecting participants for a study, one should provide rationale for the selected age group. Common sources of rationale relate to (1) known changes occurring at the neurological or physiological level during some period in development, or (2) changes in behavior that are hypothesized to be related to changes in neurological substrates during a specific time in development. It is important, however, to keep in mind that the relation between ERPs and behavior is associative and not causal (Hood, 2001). Furthermore, as Hood (2001) argues, one should use caution when interpreting ERP data, because ERPs do not reflect the cause of the behavior, nor do they provide an

adequate explanation of the behavior. Areas may become activated simply as a consequence of connections with other more relevant areas. Nonetheless, once an age of interest has been selected for a given study, a specific age range must be set due to changes in ERPs that occur with increases in age. The previous discussion of the complex changes in ERPs should help with conceptualizing the fact that averaging over a wide age range may obscure developmental changes resulting from response variability (Taylor & Baldeweg, 2002). In fact, some recommend that in developmental studies, averages of group ERPs not be combined over more than 1- to 2-month intervals in infant studies, 1–2 years in childhood, and 2–3 years in adolescence (Taylor & Baldweg, 2002; Picton et al., 2000). Our laboratory (based on knowledge of both brain and child development) typically recommends that averages for infants not be combined over more than 10 days in infants, 1 month in childhood, and 1 year in adolescence. Final decisions regarding age ranges of participant groups must be based on the specifics of each study, including considerations of task demands, task difficulty, and components of interest.

Screening

As in any research study, participants should be screened for several factors that might influence the dependent variable, although specific exclusion criteria may vary depending on the hypotheses, population, and age group of interest. For most populations, one should describe and/or document the following due to presumed or unknown influences these factors may have on the ERP response: age, gender (Hirayasu et al., 2000; Lavioe et al., 1998; Oliver-Rodriguez, Guan, & Johnston, 1999), sensory problems, medications, neurological and psychiatric disorders, and handedness (possibly including handedness of first degree relatives; see Oldfield, 1971, for an example of a handedness assessment). In addition, the following are relevant for developmental populations: pre- or postnatal difficulties, including prematurity (Lavioe et al., 1998; Stolarova et al., 2003), iron deficiency (deRegnier et al., 2000), head size (circumference, inion to nasion, and ear to ear measurements; Polich, Ladish, & Burns, 1990), memory span or intelligence assessment (Polich, Ladish, & Burns, 1990; Stauder, Van Der Molen, & Molenaar, 1998), time of day (especially in relation to feeding, see Geisler & Polich, 1990), and the main source of nutrition in early months of life (i.e., breast milk or formula). Finally, in late childhood and early adolescence it may also be important to document cognitive abilities (e.g., memory span), and pubertal status as studies have found that these factors may influence the ERP response (see Kaiser & Gruzelier, 1999; Polich, Ladish, & Burns, 1990).

Sample Size

A further consideration in developmental ERP studies is the number of participants required to obtain enough power to detect significant results. First, due to large vari-

ability in the ERP response (both between and within participants at younger ages), one must take care to ensure adequate power. Second, although collecting ERPs is considered a noninvasive procedure, preparation and participation in ERP studies does require a considerable amount of patience and cooperation on the part of the participant. In developmental populations this requirement is not easily realized. The behavioral and emotional state of young infants and children is extremely variable; many participants are unable to tolerate the preparation procedure or ERP recording and therefore do not produce utilizable data due to extreme fussiness or excessive movement artifacts. It is currently thought that it is this excessive movement (of the eyes and/or head) that accounts for much of the increased variability in developmental groups, although other sources of variability are suspected. Typical infant studies in our lab have enrollment numbers of 40 participants, with an expected 50–75% retention rate that is highly age dependent (e.g., 65% at 9 months, 50% at 12 months). However, we make every attempt to increase the amount of useable data from every session, such as using toys to distract the infant during electrode placement, having multiple testing partners who are experienced with children, and testing at a time of day that is best for the infant (see the section on data collection for more specific suggestions broken down by age group). However, due to high and variable rejection rates of developmental data, one must be mindful of differences that may arise due to the differential ability of infants and young children to successfully complete one condition versus another. Therefore, we strongly recommend that manuscript methods sections include complete descriptions of rejection criteria, including the number of participants indicated by the specific reasons for their exclusion.

Data Collection and Management

Recording

Due to developmental changes in skull thickness (including closure of fontanels in infancy) and variation in cell density, synaptic efficiency, and other physiological parameters, developmental groups require differences in the setup of the data acquisition system. Specifically, amplifier gain settings (i.e., resolution settings) must be altered in order to adequately resolve the ERP signal; sampling rates (i.e., the analog to digital conversion rate) may need to be adjusted in order to register signals of differing frequencies (with the minimum rate being twice the highest frequency of the signal to be measured); and filtering and scoring parameters need to be specified. For instance, in an experiment with 9-month-olds using a low-density Grass-Astromed amplifier, we commonly use a gain of 20,000 μV, a sampling rate of 200 Hz, a notch filter at 60 Hz, and headroom of ±250 μV. However, for the same study in adults, we would use a gain of 50,000 μV, a sampling rate of 200 Hz, a notch filter at 60 Hz, and headroom of ±100 μV. In short, headroom is a function of the range of values accepted by the A/D board

Table 12.1
Recommendations for event-related potential recording parameters in developmental populations

Age	Amplification Factor[a] (Gain)	Sampling Rate	Headroom	Scoring Parameters (A/D units)
0–2 months and 6 years and above	50,000	200 Hz	±100 μV	±100 μV
3 months to 6 years	20,000	200 Hz	±250 μV	±100 to ±225 μV[b]

[a]High-density systems, such as the EGI system, have high input impedance amplifiers and gain settings may vary.

[b]For example, using the following equations: Minimum A/D units: 0 + (headroom/2) – *X* μV/precision) and Maximum A/D units: 4096 – (headroom/2) – *X* μV/precision). If headroom is ±250 μV, the gain is 20,000, and data that exceeds ±100 μV needs to be rejected, the calculation (using a 16-bit data acquisition board) is

Min A/D units: 0 + (250 – 100) μV/(500/4096)) = ~1229,

Max A/D units: 4096 – (250 – 100) μV/(500/4096)) = ~2867.

and the gain. For adults, data are typically collected with a ±100 μV headroom; this usually does not need to be reduced (or "scored down") any further off line because normal adult brain activity falls within these bounds. However, for infants, due to the large variability and increased amount of movement artifacts, researchers use a wider headroom range for data collection. This range is then reduced off line, in order to remove large artifact signals. Although there is still debate about the range of amplitude of typical infant and child brain activity, current consensus is somewhere between ±100 to 150 μV. Table 12.1 provides guidelines from our laboratory. However, these values may differ for various recording systems. Furthermore, these settings may be changed depending on how the data are to be used. For example, if directly comparing 6- and 9-month-olds, it would be appropriate to have the same recording specifications for both ages.

Testing Session Specifics

There are several factors in developmental ERP testing sessions that differ from adult ERP testing sessions. For groups of all ages, researchers should consider the session length (including preparation) and the number of trials attempted and expected to be completed. In our laboratory, we have found the following recommendations useful regardless of the age of the participant group; in the sections following, we make additional recommendations that apply to specific age groups. First, experience with infants and children is desirable due to the fact that the procedure is often a very novel

experience to infants and children and it is important to make the participants and their caregivers comfortable. Second, a welcoming preparation room with many toys and "distracter" items will also help both the child and the caregiver feel comfortable in the unfamiliar surroundings during the introduction to the procedure and preparation. In the actual testing room we recommend placing a screen around the area where the infant or child is sitting and removing any distracting items from the room, in order to keep their attention focused on the computer screen. This will help minimize movement artifacts. Finally, we recommend, for all age groups, that the experimenter(s) have some means, either during data collection or during data analysis, to ensure that data are accepted only when the infants are motionless and attending to the stimuli. For example, experimenters could monitor infants' looking during the task and have access to both a repeat button and a pause button. This will reduce artifacts due to either movement or eye blinks and will allow the experimenter to take short breaks from testing if the infant becomes fussy.

Newborns Data collection with newborn infants involves "passive" viewing or listening paradigms. During auditory tasks newborns are typically in an active state of sleep or awake, and artifacts are uncommon due to the newborn's limited range of movement. In fact, most newborn infants are able to complete 50–200 trials, as the experiment can usually be paused to accommodate changes in the newborn's state (e.g., if the newborn becomes fussy). One important consideration when studying newborns is the portability of the ERP collection system. Often it is desirable to record ERPs within a day of birth, which requires that these studies take place in a hospital setting, preferably in a different hospital room so that disturbance to baby and mother is minimal.

Infants Data collection in infants also typically involves passive viewing or listening paradigms. For the most part, infants are easily distracted during preparation by playing with a second experimenter, or engaging with toys. Depending on the age and locomotor abilities of the child, we recommend using a highchair or self-contained walker to keep the infant from crawling around the room during preparation. During ERP recording, it is preferable if infants remain in a highchair or car seat in front of the computer screen presenting stimuli, with the caregiver seated a little behind and to the side. It is important to minimize the amount the infant turns to look at his/her caregiver. In some cases, infants may be more comfortable sitting on their caregiver's lap during stimulus presentation and ERP recording, but this typically increases movement artifact. If the infant sits on the caregiver's lap, we recommend instructing the caregiver to let the infant move around only as much as necessary, but request that the caregiver not bounce the infant on his/her knee, as such movement creates artifacts in

the data. Furthermore, in looking paradigms (such as habituation paradigms) we suggest that the parent be blindfolded to reduce possible biases.

Often during ERP recording, infants become inattentive, restless, or fussy. Therefore, in visual experiments an experimenter usually sits next to the infant and directs infants' attention to the stimuli by tapping or pointing at the screen. (Note: To decrease potential biases in the data due to artifacts that result from consistent movements to only one side, the side on which the experimenter sits should be counterbalanced or randomized.) Additionally, the experimenter who is directing the infants' attention to the stimuli should be naive to stimuli or conditions of interest in order to reduce possible biases.

In auditory ERP studies, it is also important to achieve eye fixation and reduce movement in order to minimize artifacts. In such cases, providing an interesting screen saver or object (e.g., bubbles) for the infant to watch can be quite useful.

One can either present visual stimuli at a constant rate, with the option to repeat a trial or pause the experiment if the infant is not attending to the stimuli, or the experimenter can control stimulus presentation and only present stimuli when the infant is attending. One experimenter may need to control the stimulus presentation and determine when the infant is attending to the stimulus, while the other experimenter directs the infant's attention. If necessary, the infant may have a pacifier, bottle, dry cereal, cookie, or teether, although there is some concern that sucking on such objects may result in movement artifacts and thus should be well documented and examined to determine any influence such items have on the data (cf. Picton et al., 2000; Johnson et al., 2001).

Younger Children (Ages 2–6 Years) Many of the same concerns that we addressed with infants regarding stimulus presentation and artifacts remain when testing young children. In addition, our laboratory has found it helps to use a theme that makes the experience more interesting and/or familiar (such as referring to the electrode cap as a "toy hat," "astronaut hat," or letting the child put a different cap on a stuffed animal or doll). In addition, if using single adhesive electrodes to record eye movements or for reference electrodes, the experimenter may give stickers to the children to allow some comparison with familiar items. Children may also perform more attentively if the experimenter sits next to them during ERP recording providing words of encouragement at random intervals (e.g., "Great job!" or "Just a few more pictures!").

Older Children (Ages 6–12 Years) Similar concerns addressed with infants and young children regarding stimulus presentation, artifacts, and testing environment remain when testing older children. Additionally, at older ages, a behavioral response (e.g., button press or verbal response) may be desirable. We recommend using a button press with only one or two buttons with older children, as we have found that requiring

more than this increases movement artifacts as the children tend to look at their fingers when making responses. In addition, there needs to be enough time between trials for responses due to children's slower reaction times. Finally, one should obtain informed assent from children ages 8 years and above, in addition to obtaining informed consent from their caregiver. When explaining the procedure and obtaining informed assent, one should use caution in order to ensure that both the details of the procedure and the reason for doing the experiment are clear to the child. Furthermore, it should be clear to the child that they can ask questions or withdraw from the experiment at any time if they do not wish to participate.

Adolescents Although testing adolescents is very similar to testing adults and many of the issues discussed for younger age groups do not apply, one recommendation is that the pubertal status of adolescents be determined due to unknown effects that hormonal changes during this period may have on the central nervous system and, therefore, the ERP response. For example, Kaiser and Gruzelier (1999) reported P3 latency differences in late versus early maturing females at posterior midline electrode sites. It is important to note, however, that this investigation was based on adults' retrospective reports regarding pubertal maturation; therefore, it is not possible to determine what factors other than pubertal timing may have contributed to the pattern of findings.

In sum, there are several ways to create a more comfortable atmosphere for developmental ERP participants and their caregivers both during preparation and ERP recording. We encourage researchers to try several of the suggestions mentioned above and create new strategies that are appropriate for different types of studies. However, we conclude this section by acknowledging that there is a trade off between entering in exogenous factors that may influence data (e.g., pacifiers, short breaks, etc.) and keeping participants comfortable and happy in order to acquire useable data.

Reference Montages

The appropriate type of recording reference depends primarily on the inter-electrode distance. Typically, low-density montages (32 electrodes or fewer) use a common bipolar reference. The difference in amplitude between the scalp electrode of interest and a reference electrode that is equidistant from all other electrodes (commonly the vertex or Cz in the 10–20 system) is recorded during data collection, and then the data are re-referenced off line to a mathematically linked reference recorded separately from two single sources (e.g., the ear lobes or mastoids). With high-density montages such as the EGI system (64, 128, 256 electrodes), researchers typically use an average reference, calculated by subtracting the mean of all electrodes from each channel. An important note here is that it is not the density that determines the type of reference per se, but instead the inter-electrode distance. Experimenters can use an average reference when

the inter-electrode distance is less than 2–3 cm. Junghöfer and colleagues (1997) suggest that the optimal number of electrodes on an adult head is approximately 256, and on the infant head about 128 (although 64, and possibly 32, electrodes can yield a sampling density of less than 3 cm in infants depending on the age of the infant and size of the infant's head; Junghöfer et al., 1997, cited in Johnson et al., 2001).

In our experience, the best way to record a linked reference is by affixing electrodes to an adhesive foam pad and placing them behind the infant's or child's ears on the mastoid bone. However, this is problematic if the infant has a great deal of hair; the adhesive pad may stick to the hair and not remain in place. Ear clips are also available that clip to the infant's ear lobes, but our lab has found that these do not consistently remain on the infant's ears and have to be replaced frequently during the recording session. In contrast, an average reference is recorded from one of the electrodes on the scalp (usually the vertex) and therefore does not present any unique problems except ensuring that this essential electrode has a low impedance connection with the scalp.

Data Reduction

Artifact Rejection Artifacts refer to unwanted noise in the ERP signal that can result from many sources. The largest source of artifact in infant ERPs is movement artifact unrelated to EMG (i.e., high-amplitude or off-scale activity as opposed to high-frequency activity of electromyogram, or EMG). However, artifacts can also be caused by EMG (e.g., head or body movements) and eye movements (e.g., blinking). In the previous section, we made several suggestions as to how to reduce artifacts and ensure that the infant attends to the stimuli. Far more challenging are artifacts resulting from eye movements, which may disproportionately contaminate anterior recording electrodes. These artifacts may result in the misattribution of the component source to the frontal region of the brain, when it rightly belongs in the eyes and should be excluded from data analysis (Nelson, 1994). Fortunately, infant ERPs tend to be much larger than adult ERPs (most likely due to physiological differences such as thinner skulls and less dense cell packing in brain tissue). As a result, developmental researchers have found that it takes considerably more eye activity to contaminate the ERP signal in infants compared to adults (see Nelson, 1994 for further discussion). However, to ensure against contamination due to electro-oculogram (EOG) activity, we recommend recording eye movements, using computer algorithms and visual inspection of the data to identify and delete corrupted trials (see Nelson, 1994, for details).

Specifically, our lab uses a bipolar recording for the EOG recording (i.e., referencing the upper eye to the lower eye), which provides us with a measure of the eye activity itself. Typically, the recording configuration consists of two electrodes placed on the supra and inferior orbital ridges of the eye. This configuration allows for detecting blinks and, with somewhat less precision, horizontal eye movements (e.g., saccades).

In an ideal situation, recording both vertical and horizontal eye movements is preferable, but from a practical perspective, if participants are not able to tolerate multiple electrodes near the eye, vertical eye movements are considered more essential and should be recorded. If the study involves presenting stimuli in the periphery, it is necessary to record both vertical and horizontal eye movements. Although it is becoming increasingly common with adult participants to use mathematical routines for identifying and subtracting artifacts due to eye movements to preserve the trial for averaging and analysis, this technique should only be used when it is ensured that the infant's eyes were not moving during stimulus presentation. Moreover, given differences in head size and shape between infants and adults, different propagation factors may dictate the utilization of different algorithms for subtracting EOG artifacts. In practice, our lab has adopted the following procedures for dealing with EOG activity. If the EOG activity exceeds 250 μV, we reject the entire trial. If EOG activity is below 250 μV *and* the infant's eyes were fixated during the stimulus presentation, we apply a blink correction algorithm (Gratton, Coles, & Donchin, 1983). After editing the data for EOG artifacts, we visually inspect each individual participant's data; if it appears that eye movements were occurring consistently and appear to distort the ERP signal, especially at the anterior electrode sites, we reject those trials from the average and subsequent analyses.

With older children, blink activity remains a problem, and although they may be able to follow instructions, we do not recommend giving instructions regarding eye movements (i.e., blinking). However, if instructions become necessary, we recommend that participants be instructed *when* to blink, as opposed to when *not* to blink, and that these instructions be given in a similar manner across all conditions to all participants as they may alter the ERP response by adding an additional component to the task (Ochoa & Polich, 2000).

When editing data for artifacts, one can detect many benign sources of activity (e.g., head movements, eye movements, blinks, and so on). In addition, sources of abnormal activity, such as seizure activity, may also become apparent during data collection or data analysis. A final recommendation is that researchers be generally familiar with the appearance of seizure activity and establish procedures for reporting it if and when it is suspected (either during or after data collection). Although this is very rare, due to the young age of some participants, many seizure disorders may not yet be detected (situations such as this are similar to incidental findings of structural abnormalities in the brains of normal or typical participants in fMRI studies and should be handled in a similar manner). Notifying the parents of such a possible concern should be done with great care and accompanied with a referral to a competent physician.

Averaging Another issue pertinent to developmental ERP data concerns the large variability in waveforms (both between and within subjects). Indeed, Nelson and

colleagues report more between-subject variability in infants than in adults and children tested under the same conditions (Nelson, 1994). Although part of this variability is the result of increases in artifacts (as discussed above), there is a great deal of variability between subjects as a function of the total number of trials contributed by each infant during the ERP session (Snyder, Webb, & Nelson, 2002). Infants vary widely in the number of trials they complete in an ERP session, with some completing as few as 20 trials and others completing over 100 trials. Importantly, between-subject differences that arise from differences in the number of completed trials have been associated with both amplitude and latency differences in certain components (e.g., the Nc component in 6-month-olds; see Snyder, Webb, & Nelson, 2002).

In addition to the differences that lead to increased between-subject variability, there is often a great deal of within-subject variability in developmental ERP data. In fact, some have reported variability in the infant's brain response to the same stimulus over time. Differences in topography (of both the Nc and slow wave activity) have been detected in the same subject's data depending on whether the first half or the second half of their data from one testing session was included in their final data set. These differences may depend on the infant's familiarity with the stimulus (Snyder, Webb, & Nelson, 2002), yet they also may arise from state changes in the infant during data collection (e.g., changes in sleepiness, fussiness, or comfort level).

Such individual differences are important and can be analyzed separately to answer a different line of questions. However, these differences can result in an extraordinary amount of variability in group data sets. In fact, it is not uncommon to fail to find statistical differences between two experimental conditions that visually appear to be vastly different from one another. These findings may, of course, reflect the actual equivalence of two experimental conditions. However, null findings can also be due to insufficient power to detect differences due to large between and within subject variability. Although methods for analyzing such variability exist (e.g., analyzing variances instead of means) these methods are not common in the literature due to the fact they are mathematically complex and not easily implemented or interpretable (Nelson, 1994; Taylor & Baldeweg, 2002). Therefore, our solution to date has been to collect as many artifact free trials as possible from a large number of infants and to be conservative in reporting our findings (Nelson, 1994). Although it varies from study to study, our current heuristic is to require that an infant contribute *at least* 10–20 artifact-free trials to their individual average and at least 10–15 infants contribute data for each experimental condition. Without these or more stringent criteria, the signal-to-noise ratio is often compromised and significant results remain elusive despite genuine differences between experimental conditions (i.e., a type II error). Therefore, we recommend that investigators report estimates of effect size and conduct power analyses to determine the number of participants required to obtain significant effects and caution the interpretation of null findings with small sample sizes.

Statistical Analysis

In the following sections we comment on the utilization of different techniques used to statistically analyze developmental data, including ANOVA and MANOVA, hierarchical linear modeling (HLM), independent components analysis (ICA), and principle components analysis (PCA). For a full discussion, we refer the reader to other chapters in this book on these selected topics, as our discussion will highlight concepts that are especially relevant when working with developmental data.

In adult ERP studies, the typical dependent or response variables include average or peak amplitude, area below or above the curve, and latency to peak measurements. The independent or predictor variables include condition or task factors. Researchers typically use average amplitude measurements and area measures with components that do not exhibit a distinctly peaked component. For example, some investigators have used average amplitude to analyze the N400 component (e.g., Eimer, 2000; Bentin & Deouell, 2000). For data occurring in longer latency windows, such as slow wave activity, researchers typically use area measurements. Area measurements tend to be less sensitive to noise but may also underestimate differences among participants, conditions, and electrodes (van Boxtel, 1998). For clearly defined components, such as the N170 or the P300, researchers often use peak amplitude and corresponding latency measures with similar criteria as those used in adult data (Carmel & Bentin, 2002; Donchin et al., 1983).

Statistical Tests

Currently, statistical analyses that use the appropriate dependent variable mentioned above are similar if not the same as those analyses conducted with adult ERP data. Picton and colleagues (2000), as well as van Boxtel (1998), provide guidelines for statistical analyses with ERP data that we summarize briefly. The experimenter should use statistical analyses that are appropriate to both the nature of the data and the goal of the study. Typically, one uses repeated measures ANOVA models to test hypotheses with ERP data (see chapter 4 of this volume). As with any ANOVA, repeated measures ANOVAs test the equality of means. This type of analysis is used when all members of a random sample are measured under a number of different conditions. As the sample is exposed to each condition, the measurement of the dependent variable is repeated (i.e., amplitude or latency at different leads). Using ANOVA techniques is not appropriate in this case because it fails to model the correlation between the repeated measures (the psychophysiological data often violate the ANOVA assumption of independence). To compensate for violations, one can reduce the degrees of freedom by calculating epsilon, as described by Greenhouse and Geisser (1959) or Huynh and Feldt (1970).

One can also use MANOVA analyses to analyze ERP data. As long as the sample size exceeds the number of repeated measures by "a few," MANOVA analyses will range

from being slightly less powerful than the adjusted method (described above) to infinitely more powerful (Davidson, 1972). Davidson (1972) suggests that the MANOVA approach is the best in cases when one expects small but reliable effects. He also suggests that when using MANOVA, one should choose a sample size that exceeds the number of repeated measurements by 20 or more. Thus, the only case when one should use adjusted ANOVA tests is when the sample size becomes as small as the number of repeated measurements in the design. These typical statistical methods used with ERP data in adults (ANOVA, MANOVA, etc.) that can also be utilized for the statistical analysis of developmental ERP data have several assumptions. For instance, (1) there cannot be any missing data (cases are deleted listwise), (2) all subjects must be measured at the same equally spaced time points (e.g., using the same leads across all subjects), (3) the response variable must be normally distributed, and (4) there is homogeneity of variance (either across time or across measurements). Violations in the above assumptions that, unfortunately, are often common in developmental ERP data, result in deletion of cases and an unbalanced design. However, recent statistical advances such as the use of hierarchical linear modeling (HLM) to analyze longitudinal and repeated measure data sets may be especially relevant for developmental ERP data due to the fact that it is not constrained by these assumptions. For example, HLM can accommodate unbalanced designs or data sets by estimating missing data. This accommodation may allow researchers to include more data that ultimately results in an increase in the retention rate. HLM can be used to include data from participants who may have unusable or artifact contaminated data at specific electrode locations (e.g., subjects with data that was selectively contaminated at anterior electrode sites by eye artifacts). Furthermore, infants will often only finish one of two experimental conditions (e.g., due to fussiness). The use of HLM may allow one to keep data from the first condition for subsequent data analysis, as opposed to deleting all of this participant's data.

Source Separation and Localization Techniques

An increase in the number of electrodes and a concomitant decrease in inter-electrode distances results in increased spatial resolution in high-density recording methods (see chapter 8 of this volume). Conventional methods of analyzing ERP data do not take advantage of this added spatial information; thus, several investigators have used source separation and localization techniques to statistically identify source generators in the brain (for further illustration, see Johnson et al., 2001; Reynolds & Richards, 2003; and Richards, 2000).

A well-known challenge in ERP research is localizing activity that is volume conducted to the scalp surface. This problem, known as the inverse problem, refers to the relative difficulty we have calculating the distribution of electrical current in the brain from surface measurements (see chapter 7 of this volume). Electrical recordings

taken from the scalp reflect a mixture of the activity of a number of underlying neural sources (dipoles) in the brain. Source separation consists of identifying sources that account for the largest portion of variance in the data. One method of source separation is independent component analysis (ICA), which decomposes spatiotemporal data into separate, or independent, components. One can think of ICA as an extension of a more commonly applied method, principal component analysis (PCA), which uses factor analysis to identify the components that account for the largest amount of variance in the data, then the next largest and so on. Compared to ICA, which is not restricted to normally distributed components, PCA yields statistically independent components if they are normally distributed (Johnson et al., 2001). ICA assumes that electrical activity recorded at scalp electrode sites represents a linear combination of the concurrent electrical activity evoked by networks of neurons within the brain. It is assumed that these networks are spatially fixed and operate independently in time. However, the "sources" of ICA components may be one or more distributed brain networks rather than modularly active brain regions. Source localization procedures assume that brain networks (or dipoles) are physically isolated from one another, whereas ICA procedures only assume that brain networks act independently. Therefore, ICA may be useful as a preprocessing step prior to attempting source localization (Makeig et al., 1996). However, this does not solve the problem of source localization. Johnson and colleagues (2001) suggest that ICA may be useful in reducing intertrial variability in analyses of infant ERP data. They state that ICA may be able to extract components from more noisy data (common in infant data) that are similar to those extracted from a data set that has been previously corrected for artifacts. In sum, for developmental ERP data, ICA could provide a method for examining both intersubject and intertrial variability.

Source localization is a different process than source separation. Source localization attempts to identify the location, orientation, and magnitude of dipoles in the brain that may be responsible for specific ERP components (Nunez, 1990). The software package Brain Electrical Source Analysis (BESA) identifies candidate dipoles in the brain by analyzing the distribution of electrical activity recorded at the scalp (Scherg & Berg, 1996). This activity is applied to simplified models of the head in order to determine neural sources. Johnson and colleagues (2001) voice several concerns regarding the use of source localization methods in infants. First, skull thickness, density, and fontanel closure are different in adults relative to infants. Thus, localization techniques used with adults may not be applicable to all developmental populations. Second, the spherical head model used in source localization may be less appropriate for developmental populations, as factors such as skull thickness and head circumference may be more variable in infant compared to adult populations. To date, there are currently no software packages (such as BESA) that attempt to compensate for these differences. Developmentally appropriate head models may increase the feasibility of source

localization in developmental populations. Although high-density ERP techniques appear to provide researchers will the ability to estimate sources of neural activity, source localization should only be combined with strong theoretical foundations concerning anatomical localization (e.g., Richards, 2003). In fact, Hood argues that although relatively specific areas may "light up" under some conditions, such localization is of limited value on its own as explanation, and provocatively claims that "in most cases it [source localization] simply confirms the experimenters expectation that there is event-related activity occurring in the brain" (Hood, 2001, p. 215).

Converging Measures

A general consensus in psychology is that the most reliable test of a theory is convergent evidence. It is not surprising, then, that many have begun to argue that ERPs should be used in conjunction with other imaging techniques, such as fMRI, and behavioral measures, such as reaction time. The combination of these techniques and measures provides complementary information that may strengthen data interpretations (see chapter 15 of this volume).

Specifically, due to the excellent spatial resolution of fMRI and superior temporal resolution of ERPs, the combination of these two techniques is well suited to provide spatiotemporal information superior to either method alone (de Haan & Thomas, 2002). For example, research on face processing, face detection, and recognition of facial expressions of emotion has combined ERP and fMRI research, and similar collaborative innovations are encouraged in other areas (for further discussion see de Haan & Thomas, 2002).

ERPs and Special Populations

Recently several researchers have begun to use ERPs as a tool to investigate deficits and impairments across a wide range of developmental disorders, including autism spectrum disorder (Dawson et al., 2002a, 2002b), attention deficit hyperactivity disorder (Jonkman et al., 2000), language disorders (Molfese, Molfese, & Modglin, 2001), individuals who have experienced maltreatment (Pollak et al., 2001), individuals who are at high risk for alcoholism (Hill et al., 1999), or individuals who, due to pre- or perinatal complications, are at risk for neurobehavioral sequelae (deRegnier, Georgieff, & Nelson, 1997; deRegnier et al., 2000; Nelson et al., 2000; for review of examples of atypical development, see Nelson & Luciana, 1998). For example, Dawson et al. (2002a) used high-density ERPs to examine whether children with autism spectrum disorder (ASD) have impairments in face recognition abilities that originate at the cortical level. Relative to a typically developing group of children and a group of children with developmental delays, children with ASD failed to show differences in ERPs to fa-

miliar (i.e., their mother's face) versus unfamiliar faces, but did show differentiation to familiar versus unfamiliar toys. These results imply that children with autism may have deficits in face processing cortical circuitry but concurrent sparing of object processing circuitry.

Indeed, combined with typical behavioral assessment and diagnostic tools, ERPs may prove useful in understanding developmental disorders, as well as for prevention and intervention programs (Otto et al., 1984). Elucidation of the cause, nature, and treatment of childhood disorders may require an integration of approaches and empirical techniques informed by multilevel analyses from brain to behavior. Although the application of ERP techniques to special populations for clinical purposes is encouraging, researchers must exert caution when looking at individual and group data. Results are often based on averaged responses from groups of individuals, and until single-trial analyses are possible in individual participants, such research is limited to general statements regarding groups of individuals who have experienced a set of common circumstances or exhibit similar symptoms.

Future Directions

There are several areas of developmental ERP research in need of improvement. First, more headway in grounding developmental ERP research in behavior is needed. Researchers need to use new behavioral measures in conjunction with ERP measures, and need to design new paradigms that facilitate a convergence of behavioral and electrophysiological data. Second, future research should aim to explore the development of ERP components. We can combine such knowledge with our increasing knowledge of the development of the brain in order to refine data collection parameters. This will allow ERP recordings to accurately capture the dynamic development of the brain. Third, we should apply statistical methods that can accommodate missing data to developmental data sets. This strategy will help ensure that valuable information is not lost due to insufficient statistical techniques. In addition, experimenters should alter algorithms used to identify artifacts in adult ERP data analysis to accommodate the wide variability in infant data. This will ensure that similar techniques will be useful across age groups. Finally, if researchers continue to use source localization techniques, they need to develop parameters suitable for infant and child data and establish them in available software.

In conclusion, the challenges of developmental research include issues ranging from designing studies that are sufficiently interesting in order to recruit and sustain infants' attention, to successfully placing the desired number of electrodes on infants' heads, to the careful reduction of variability in data and rejection of artifact contaminated data. However, the ultimate challenge in conducting developmental ERP research is to take what we know from other areas of research, which utilize different methodologies,

and combine this information with electrophysiological data in innovative ways to produce converging evidence in support of theoretical claims. The use of consistent and appropriate methods will, we hope, contribute to this goal. Furthermore, we hope that methods for developmental ERP research will continue to be refined. We underscore the importance of a collaborative approach that will prove to be the most powerful tool in examining complex developmental changes in the brain from infancy forward.

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Note

1. The field of developmental electrophysiology is continually evolving; subsequently, developmental electrophysiological research remains a broad area. Currently, the term *developmental* is used not only to refer to authentic change overtime (e.g., changes in components, changes in brain structures, or changes in children's behavior) but also is used to refer to research that, ultimately, will contribute to knowledge regarding such change. Therefore, in this chapter, we will use "developmental" to refer to both circumstances (e.g., studying the development of actual entities, such as components, and the utilization of ERP components in developmental [i.e., child] populations to better understand development more generally).

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